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Demand for plasma-derived medicinal products in Italy. 2024

F. Candura, M.S. Massari, S. Profili, L. De Fulvio, V. Zambito, C. Chelucci, C. Brutti, V. De Angelis, L. Teofili

EPIDEMIOLOGIA E SANITÀ PUBBLICA

ISTITUTO SUPERIORE DI SANITÀ

Demand for plasma-derived medicinal products in Italy. 2024

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2026, vii, 153 p. Rapporti ISTISAN 26/18 EN

With the aim of fulfilling the task assigned it pursuant to national regulations regarding coordinating and providing technical support to the planning of self-sufficiency in blood components and plasma-derived medicinal products at regional and national level, the Italian National Blood Centre has conducted an analysis in collaboration with the Department of Planning, Medical Devices, Pharmaceuticals, and Policies Supporting the National Health Service of the Italian Health Ministry. The analysis of the demand for plasma-derived medicinal products and recombinant therapies included the assessment of self-sufficiency levels achieved and the costs sustained by the Italian National Health Service for the provision of these products. The content of this document, an update of the data for the year 2024 published in the *Rapporto ISTISAN* 25/7, was obtained by conducting a comparative analysis of the available data sources. The document is also an invaluable tool for planning self-sufficiency at national level.

Key words: Plasma-derived medicinal products; Demand; Self-sufficiency; Expenditure

Istituto Superiore di Sanità
Analisi della domanda di medicinali plasmaderivati in Italia. 2024
Fabio Candura, Maria Simona Massari, Samantha Profili, Lucia De Fulvio, Valentina Zambito, Cristiana Chelucci, Chiara Brutti, Vincenzo De Angelis, Luciana Teofili
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Al fine di adempiere ai compiti ad esso assegnati dalla normativa vigente in materia di coordinamento e supporto tecnico alla programmazione dell'autosufficienza regionale e nazionale di emocomponenti e medicinali plasmaderivati, il Centro Nazionale Sangue ha effettuato, in collaborazione con il Dipartimento della programmazione, dei dispositivi medici, del farmaco e delle politiche in favore del Servizio Sanitario Nazionale del Ministero della Salute, l'analisi della domanda dei prodotti medicinali plasmaderivati e delle alternative terapeutiche di natura ricombinante, le valutazioni dei livelli di autosufficienza regionale e nazionale e la stima della spesa farmaceutica a carico del Servizio Sanitario Nazionale. Il confronto delle diverse fonti dati disponibili ha consentito l'elaborazione del presente documento che riporta l'aggiornamento relativo all'anno 2024 dei dati sull'argomento pubblicati nel *Rapporto ISTISAN* 25/7 e che si configura come uno strumento fondamentale per la programmazione dell'autosufficienza nazionale.

Parole chiave: Medicinali plasmaderivati; Domanda; Autosufficienza; Spesa

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ACRONYMS AND ABBREVIATIONS

3F-PCC	3-Factor Prothrombin Complex Concentrate
4F-PCC	4-Factor Prothrombin Complex Concentrate
AIC	Autorizzazione di Immissione in Commercio (Marketing Authorisation)
AIFA	Agenzia Italiana del FArmaco (Italian Medicines Agency)
AP	Autonomous Province
aPCC	Activated Prothrombin Complex Concentrate
AT	AntiThrombin
ATC	Anatomical Therapeutic Chemical classification system
BE	Blood Establishment
BCU	Blood Collection Unit
BHK	Baby Hamster Kidney fibroblasts
BZ	Bolzano
CHO	Chinese Hamster Ovary cells
CMV	CytoMegaloVirus
DL	Decreto Legge (Decree Law)
DL.vo	Decreto Legislativo (Legislative Decree)
DM	Decreto Ministeriale (Ministerial Decree of the Ministry of Health)
ELC	Essential Levels of Care
E.-Romagna	Emilia-Romagna
pdFVII	Plasma-derived Factor VII
pdFVIII	Plasma-derived Factor VIII
pdFIX	Plasma-derived Factor IX
FVG or Friuli V. Giulia	Friuli Venezia Giulia
FU	FEIBA Unit
IG	ImmunoGlobulin
ISTAT	Istituto Italiano di STATistica (Italian National Statistics Institute)
IU	International Unit
IVIG	IntraVenous ImmunoGlobulin
LHC	Local Health Centre
LPS	Lombardy-Piedmont-Sardinia Agreement
Min. of Def.	Ministry of Defence
MoH	Ministry of Health
NAIP	Nuovo Accordo Interregionale per la Plasmaderivazione (New Interregional Agreement for plasma-derived medicinal products)
NHS	National Health Service
NSIS	Nuovo Sistema Informativo Sanitario (New Health Information System)
PDMP	Plasma-Derived Medicinal Product
rFVIIa	Recombinant activated Factor VII
rFVIII	Recombinant Factor VIII
rFIX	Recombinant Factor IX
RTI	Raggruppamento Temporaneo d'Impresa (Temporary Business Grouping)
S/D	Solvent / Detergent (plasma)
SC/IM	SubCutaneous/IntraMuscular
ST	Transfusion Service
UdR	Collection Units run by Donor Associations
VAT	Value Added Tax
vWF	von Willebrand Factor
WHO	World Health Organisation

FOREWORD

The Italian National Blood Centre (Centro Nazionale Sangue, CNS) is a technical branch of the Italian Ministry of Health (MoH) that operates under the National Institute of Health (Istituto Superiore di Sanità) in Rome. In compliance with current legislation, the CNS supervises and coordinates technical and scientific support for all aspects of the production of plasma and plasma-derived medicinal products (PDMPs).

The CNS primarly provides guidelines regarding the strategic objectives of the transfusion system, which include achieving and maintaining regional and national self-sufficiency in labile blood components and PDMPs.

This Report covers the 2024 calendar year and includes the PDMP demand outlines featured in the new regional calls for tender for industrial toll fractionation services. Managing these contract services is a well-established activity that contributes to planning plasma and PDMP production, while also monitoring consumption and pharmaceutical expenditure.

The primary aim of this annual Report, continuing the series published from 2007 to 2023, is to provide the strategic instruments and indications necessary to achieve and maintain regional and national self-sufficiency. These goals align with the national planning objectives drafted in the National Plasma and Plasma-Derived Medicinal Products Programme 2016-2020 (established by the Ministerial Decree of December 2, 2016) and the National Self-Sufficiency in Blood and Blood Products Programme 2024 (issued by the Ministerial Decree of June 20, 2024).

Prof. Luciana Teofili
Director General
Italian National Blood Centre

INTRODUCTION

Plasma-Derived Medicinal Products (PDMPs) are pharmaceutical specialties produced through the industrial processing of plasma, that is the liquid component of the blood collected from voluntary donors through apheresis, or recovered from the whole blood by centrifugation. PDMPs play a key, sometimes irreplaceable, role in the treatment of many acute and chronic clinical conditions (1).

Due to their biological nature, the quality and safety of PDMPs derive from quality checks carried out on the raw material – "plasma" – and on its origin, as well as on the industrial manufacturing processes, including removal and viral inactivation procedures (2).

National self-sufficiency of PDMPs is one of the objectives of the Transfusion System, achieved through the collection of plasma from voluntary, anonymous, unpaid donations, mostly coming from periodic donors, and the plasma sent to pharmaceutical companies authorized to sign agreements with the Regions and Autonomous Provinces (hereinafter Regions) for the purpose of producing PDMPs by toll fractionation system.

Regions, individually or in consortia, supply with the plasma collected by the Blood Establishments (BEs), the companies holder of the agreements for its industrial transformation aimed at the production of PDMPs. The contract with these companies, acting as service providers, is considered a "third party processing" method, which the Regions implement by means of tender procedures in compliance with the current legislation (3, 4).

In June 2017, the New Interregional Agreement for Plasma-Derived Medicinal Products (Nuovo Accordo Interregionale per la plasmaderivazione, NAIP), led by the Veneto Region, started to send plasma for fractionation to CSL Behring, under a contract providing for the production of the following PDMPs: albumin, normal human immunoglobulins for intravenous use (IntraVenous ImmunoGlobulin, IVIG), Subcutaneous (SC) / IntraMuscular (IM) immunoglobulins (IG), plasma-derived Factor VIII concentrates (pdFVIII), pdFVIII and von Willebrand Factor (vWF) concentrates in combination (pdFVIII / vWF), and fibrinogen. These products were distributed for the first time to the Regions adhering to the NAIP in 2018 and since then, they too have been the subject of this Report.

In the second half of 2020, the Regions part of the Plasma Network agreement (PLANET), led by the Tuscany Region, and to the Plasma/Plasma-Derived Interregional Grouping (*Raggruppamento Interregionale Plasma e Plasmaderivati*, RIPP), led by Emilia-Romagna Region, have begun to send plasma to companies awarded in the latest tenders, Takeda Italia SpA on one hand and, on the other, Kedrion SpA and Grifols Italia SpA grouped in a temporary business association (RTI). The launch of new agreements has significantly impacted the quantity and type of PDMPs by toll-fractionation available for the national System, starting from 2021 as per records available.

In actual fact the agreement with the company Takeda envisages an expansion of the basket of ancillary products returned by toll fractionation, such as FVII, 4-factor prothrombin complex (4F-PCCs), activated prothrombin complex concentrates (aPCCs) and Protein C, as well as the supply of mandatory products, and the production of 3-factor prothrombin complex (3F-PCCs), plasma-derived Factor IX concentrates (pdFIX) and FVIII/vWF. With regard to the RIPP agreement, on the other hand, the agreement with Grifols and Kedrion also provides for the return of Anti-Thrombin (AT), FVIII/vWF, SCIG, pdFIX, 3F-PCCs, alpha 1-antitrypsin.

While waiting for the awards of the tender within the fourth interregional agreement for toll fractionation, involving Lombardy, Piedmont and Sardinia, the following PDMPs albumin, IVIG, SCIG, AT, pdFVIII, pdFIX, 3F-PCCs and solvent/detergent virus-inactivated plasma,produced by toll fractionation by Kedrion SpA (hereafter Kedrion) under the contract prior to the enlargement to other possible commercial partners, also contributed to the 2024 national self-sufficiency.

Inasmuch as the clinical interest and its impact on the pharmaceutical expenditure, the Report also describes the demand for other PDMPs and for the recombinant medicinal products used for the treatment of congenital and acquired bleeding disorders, distributed through commercial channels, with a particular concern to long-acting and innovative haemostatic products.

Hence, for each of the PDMPs whose supply is provisioned for in the contracts between the different Regions and the relevant contracted fractionator, the level of regional and national self-sufficiencies is estimated on a case-by-case basis.

Finally, it is outlined the pharmaceutical expenditure incurred by the NHS for drugs procurement on the market, in both cases when it is a portion of the NHS demand not covered by toll fractionation agreements, and otherwise.

The Report, after stating the data sources and the methodology used, analyses the demand for each active ingredient, the level of self-sufficiency in the PDMPs produced by toll fractionation, and the pharmaceutical expenditure. It is divided in four analytical sections:

– *Part A*
  PDMPs currently provisioned for in toll fractionation agreements.

– *Part B*
  Other PDMPs.

– *Part C*
  National and Regional PDMPs self-sufficiency in regard with the PDMPs provisioned for in toll fractionation agreements.

– *Part D*
  Pharmaceutical expenditure for plasma-derived and alternative recombinant medicinal products.

SOURCES AND METHODOLOGY

Data sources

Drug traceability flow

Since January 2005, the medicinal products traceability database (5) is being daily updated with data gathered from the delivery notes of medicinal products acquired regardless their being part of different reimbursement categories or dispensation regime. Every actor involved in the production and distribution - production sites, warehouses and wholesalers, pharmacies, hospitals etc. - is assigned a unique identifying code and each single package is tracked by a marketing authorisation code (Autorizzazione all'Immissione in Commercio - AIC code) at every step throughtout the entire supply chain process (Figure 1).

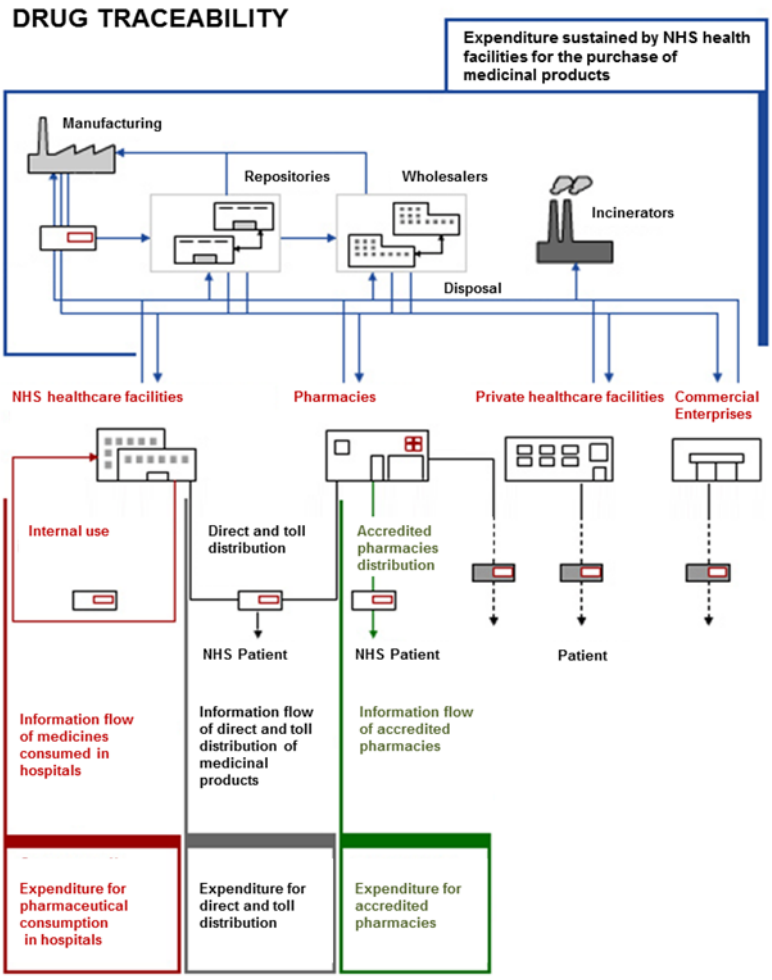

Figure 1. The drug traceability system in Italy (adapted by the CNS on data from www.salute.gov.it)

Pursuant to Italian law, if the final receiver is a public entity (e.g. hospital pharmacies, public healthcare facilities, etc.), the payment due is detected together with the quantity of the product, in order to monitor the pharmaceutical expenditure, in compliance with the law. Thus, the drug traceability system keeps track of the handling from one logistics site to another of all medicinal products identified by the AIC code and quantified by the number of packages, (cfr. all details below the dotted horizontal line in Figure 1) without considering the final users.

Therefore, the drug traceability system is suitable to quantify the total demand for PDMPs because it takes into account the quantities distributed to both public and private health facilities, and to pharmacies regardless of the dispensation regime, and whether or not charged to the Italian NHS.

Information flow of accredited pharmacies

The "Health Card" project (326/2003 Law) (6), established the information flow that records all data regarding the prescription drugs with the aim of monitoring the pharmaceutical services funded by the NHS and provided by public pharmacies.

This dispensation regime concerns the medicinal products as included in the Essential Levels of Care (ELC).

This information flow on nominal basis appears to be the most suitable for calculating the demand for PDMPs supplied through the public pharmacies network and managed by the Italian Medicines Agency (Agenzia Italiana del Farmaco - AIFA) (Figure 2).

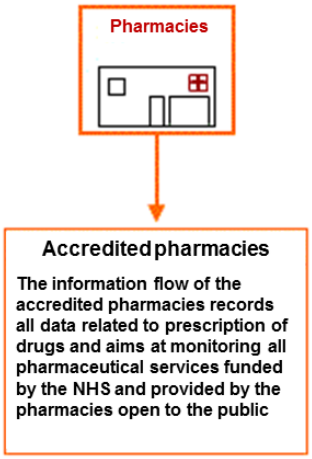

Figure 2. Scope of the information flow of accredited pharmacies (adapted by the CNS on data from www.salute.gov.it)

Information flow of the direct supply of medicinal products

The institutional information flow of the direct supply of medicinal products keeps record of the home use of medicinal products distributed by public healthcare facilities; direct supply can also occur through specific agreements with public pharmacies (toll distribution).

This information flow, established by the DM of 31 July 2007 (7), is to detect:
- medicinal products given to patients for home consumption;
- medicinal products provided directly by healthcare facilities after hospital discharge or medical examination;
- medicinal products provided to chronic patients within disease-specific therapeutic plans and to patients for home care;
- medicinal products distributed to prison facilities;
- medicinal products provided by public and private pharmacies on behalf of local health centres (LHCs) (toll distribution).

The medicinal products considered in this information flow are all drugs with an AIC (MA), regardless of their class of reimbursement (A-C-H), including magistral formulations, officinal formulas and foreign pharmaceuticals not authorised to be sold in Italy and yet used pursuant to the DM of 11 February 1997 (8). In the latter cases, the pharmaceutical features is identified through the Anatomical Therapeutic Chemical (ATC) classification system, (see dedicated paragraph).

This information flow consists of the following details, which are monthly submitted by the Regions to the MoH: accounting for the following: facility, prescription barcode (which through the prescription pad database can be traced to the prescriber), patient, medicinal product code, date of delivery, quantity delivered and related expenditure. Until 2009, only the costs, and not the related quantities, were recorded.

The institutional information flow of the direct supply of medicinal products, shown in Figure 3, records their delivery on a nominal basis.

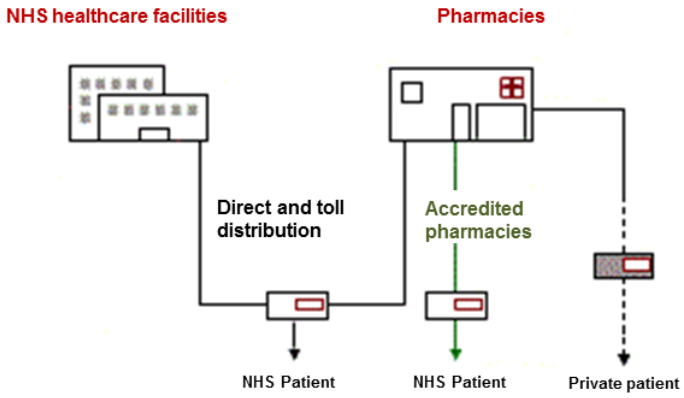

Figure 3. Medicinal products information flow (adapted by theCNS on data from www.salute.gov.it)

This information flow is the most suitable for quantifying the NHS demand for PDMPs, supplied through the direct distribution channel. The information recorded in this flow helps assessing the appropriateness of the prescriptions with regard to the facility in charge of the patients' care, as well as the suitability of the total number of medicinal products consumed by patients, while comparing the drug acquisition costs incurred by the single health facility, allows an indirect evaluation of the purchase tenders.

Information flow of medicines consumed in hospitals

The information flow regarding the monitoring of the consumption of medicinal products in hospitals takes into consideration the medicinal products used by public healthcare facilities in their typical functions (i.e. hospitalization, specialist day-surgery activities and diagnostic ones).

These include all medicinal products with an AIC code, regardless of their reimbursement class (A, C, H), masterly formulations, medicinal formulas and foreign medicines not authorised to be sold in Italy and yet used in accordance with the DM of 11 February 1997 (8). In the latter cases, pharmaceutical performance is identified by the ATC code.

The information flow provides for the following details, which are monthly submitted to the MoH: providing facility, receiving operating unit, recipient activity regimen, drug code, disbursement date, quantity delivered and related expenditure (the average weighted cost per unit sustained by the health facility for the medicinal products purchase).

The transfer of toll-manufactured PDMPs is not associated with a purchase cost; however, an estimate of the aforementioned costs can be reckoned through the exchange fees as defined in the 17th of June 2021 State-Regions Agreement (9).

Therefore, the information flow monitoring the consumption of medicinal products in hospitals, detects the internal movements of drugs purchased or made available for use by healthcare facilities directly managed by the Italian NHS, with the exception of those delivered through the direct distribution. The hospital information flow records the movements of single packages to the operating units, as shown in Figure 4. This flow is the most suitable for quantifying the consumption of those PDMPs whose costs are covered by the NHS and which are used during hospitalisation or outpatient regimens.

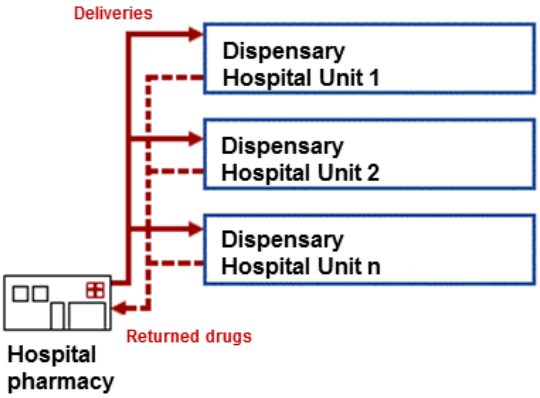

Figure 4. Information flow of medicines consumed in hospitals (adapted by the CNS on data from www.salute.gov.it)

Data on plasma-derived medicinal products produced from Italian plasma

CNS receives the data regarding the PDMPs distributed by Kedrion, CSL Behring, Grifols and Takeda on behalf of the Regions from the aforesaid companies, as part of their toll-manufacturing contracts. These figures add to the database for the analysis of PDMP production from national plasma.

Data on plasma-derived medicinal products subject to import procedures

Data related to the PDMPs imported by Italy due to a national shortage, registered abroad and subject to import procedures pursuant to the DM of 11 February 1997 (8), and the DM of 11 May 2001 (10), are provided by the AIFA Product Quality Office.

Data processing and the ATC drug classification system

For the purpose of this Report, different data sources have been accessed to detect the number of packages – by the reference year and their unique AIC codes – to identify the quantities of active ingredients in distributed PDMPs. Each AIC code was traced back to its relevant active ingredient and to its corresponding ATC code.

The ATC system is a drug classification system managed by the Nordic Council on Medicine and the Collaborating Centre for Drug Statistics Methodology of the World Health Organisation (WHO) in Oslo, Norway (www.whocc.no).

Under the ATC system, drugs are classified in different groups according to the target organ, their mechanism of action, as well as their chemical and therapeutic properties. The main groups of the ATC system are further divided into 5 hierarchical levels, shown in Table 1.

Table 1. ATC classification system

Level	Description	Note
I	anatomical main group	consists of one letter
II	therapeutic main group	consists of two digits
III	therapeutic subgroup	consists of one letter
IV	chemical/therapeutic subgroup	consists of one letter
V	chemical subgroup	consists of two digits

For example, the classification of FVIII and von Willebrand Factor (vWF) in combination is B02BD06 and is based on the composition as shown in Table 2.

Table 2. ATC classification system of FVIII and von Willebrand Factor (vWF) in combination

Level	Description
B	Blood and Blood haemopoietic organs
B02	Antihaemorrhagics
B02B	Vitamin K and other haemostatics
B02BD	Blood coagulation factors
B02BD06	Von Willebrand Factor and coagulation Factor VIII in combination

The ATC classification system is based on the principle of assigning a unique code to every pharmaceutical product (AIC code). Medicinal products are thus classified according to their main therapeutic use. A medicinal product, however, can be used for two or more therapeutic indications of equal importance with different classification possibilities. When a drug is available

in two or more dosages or pharmaceutical forms for different therapeutic uses, the classification is determined on the basis of the actual therapeutic use. Finally, preparations that cannot be uniquely classified in a particular group are coded in the fourth level with the letter X.

Therefore, through the ATC classification, it is possible to perform a progressively more detailed identification of all drugs and substances for therapeutic use. Moreover indirectly, through the analysis of the active ingredients or of the prescribed therapeutic groups, it is possible to formulate hypotheses on the incidence or prevalence of specified pathologies in the general population (11).

When a medicinal product is placed on the market, AIFA assigns it a specific AIC code. Based on the active ingredient and the therapeutic indications, it is possible to associate an ATC code and the quantity of the active ingredient contained (expressed in specific units of measurement: mg, IU, g, etc.) to a specific medicinal product.

In order to make aggregate data comparable at regional level, the absolute quantities of each active ingredient of PDMPs are standardised for the resident population as of the 1st of January of each year in question taken from the Italian National Statistics Institute (Istituto Italiano di STATistica - ISTAT) figures (12) (Table 3).

Table 3. Resident population by Region and Autonomous Province, 2023-2024 (adapted by the CNS on data from ISTAT, 10/02/2025)

Region	2023	2024
Abruzzo	1,272,627	1,269,571
Aosta Valley	123,130	122,877
AP Bolzano	534,147	537,533
AP Trento	542,996	545,169
Apulia	3,907,683	3,890,661
Basilicata	537,577	533,233
Calabria	1,846,610	1,838,568
Campania	5,609,536	5,593,906
Emilia-Romagna	4,437,578	4,451,938
Friuli V. Giulia	1,194,248	1,194,616
Latium	5,720,536	5,714,745
Liguria	1,507,636	1,509,140
Lombardy	9,976,509	10,012,054
Marche	1,484,298	1,482,746
Molise	290,636	289,224
Piedmont	4,251,351	4,251,623
Sardinia	1,578,146	1,570,453
Sicily	4,814,016	4,797,359
Tuscany	3,661,981	3,660,530
Umbria	856,407	853,068
Veneto	4,849,553	4,852,216
Italy	58.997.201	58.971.230

Active ingredients and measurement units

For the purpose of quantifying the demand for PDMPs, Table 4 shows measurement units used for each active ingredient. As regards local haemostatics and combinations (ATC B02BC and B02BC30), the diverse commercial products are composed of a mixture of different active ingredients, whose relevant data are expressed in millilitres, with the exception of formulations where the number of sponges utilised are provided yearly.

Table 4. Active ingredients, ATC codes and measurement units

Active ingredient	ATC Code	Measurement unit
3-factor prothrombin complex concentrates	B02BD	IU
4-factor prothrombin complex concentrates	B02BD01	IU
Activated prothrombin complex concentrates	B02BD03	FU
Activated recombinant Factor VII	B02BD08	mg
Albumin	B05AA01	g
Alpha-1 antitrypsin	B02AB02	mg
Anti-D (Rh) immunoglobulin	J06BB01	IU
Antithrombin	B01AB02	IU
Coagulation Factor X	B02BD13	IU
Coagulation Factor XI	B02BD	IU
Cytomegalovirus immunoglobulins	J06BB09	U
Emicizumab	B02BX06	mg
Hepatitis B immunoglobulins	J06BB04	IU
Human fibrinogen	B02BB01	g
Local haemostatics and combinations	B02BC B02BC30	mL/sponges
Normal human Immunoglobulins for extravascular administration	J06BA01	g
Normal human Immunoglobulins for intravascular administration	J06BA02	g
Other plasma proteins fractions	B05AA02	mL
Plasma-derived and recombinant coagulation Factor VIII	B02BD02	IU
Plasma-derived C1-inhibitor	B06AC01	IU
Plasma-derived coagulation Factor IX	B02BD04	IU
Plasma-derived coagulation Factor VII	B02BD05	IU
Plasma-derived coagulation Factor XIII	B02BD07	IU
Protein C	B01AD12	IU
Rabies immunoglobulins	J06BB05	IU
Recombinant coagulation Factor IX	B02BD04	IU
Recombinant coagulation Factor XIII	B02BD11	IU
Tetanus immunoglobulins	J06BB02	IU
Varicella/zoster immunoglobulins	J06BB03	IU
Von Willebrand Factor	B02BD10	IU
Von Willebrand Factor and coagulation Factor VIII in combination	B02BD06	IU

Self-sufficiency and pharmaceutical expenditure

For every PDMPs considered in the agreements between the different Regions and their affiliated companies (Kedrion, CSL Behring, Grifols and Takeda), the degree of self-sufficiency achieved has been assessed by comparing the actual supply with the NHS demand, except for polyvalent immunoglobulins. In consideration of the different models of health care organization recorded in the Italian Regions, the actual supply was related to the total demand. In this Report, by productive capacity (or potential supply) is meant the theoretical quantity of PDMPs obtainable from the plasma sent by each Region for fractionation from July 2023 to June 2024. By contrast, by effective supply (or toll fractionation) is meant the quantity of PDMPs *de facto* distributed by companies to each Region during the 2024 calendar year. Data related to the productive capacity and effective supply are provided by the companies themselves. Both productive capacity and effective supply are strictly influenced by the quantity and quality of plasma sent by the Regions, the industrial yields and the planning.

By total demand is meant the regional PDMP consumption through all distribution channels (public and private healthcare facilities, pharmacies, etc.). While by NHS demand is meant the share of the total demand funded by the NHS.

Potential self-sufficiency is the percent ratio between the productive capacity and the NHS demand (unlike polyvalent immunoglobulins, whose potential supply is compared with total demand). While effective self-sufficiency is the percent ratio between the effective supply and the NHS demand (except for polyvalent immunoglobulins as explained above).

In the dedicated chapter, pharmaceutical expenditure is defined as the expenditure for the supply of PDMPs covered by the NHS in public health facilities and accredited pharmacies. As far as the first channel is concerned, the aggregate purchase cost of PDMPs incurred by public facilities has been detected and quantified by means of the traceability information flow. The quantities and the monetary value of PDMPs delivered to public pharmacies were calculated by using the price relevant on 31/12/2024, and applying any possible discounts provided for by Law 662/1996 (13), amended by Law 122/2010 (14).

As far as albumin, IVIG and FVIII/vWF, are concerned, as identified by the Italian law as the main drivers of the toll fractionation, the average cost per unit purchased on the market, and the average cost per unit purchased in public health facilities and pharmacies are specified in summary tables, to which the related percentages of the demand and expenditure paid through the same distribution channels are added.

In regard with toll-fractionated medicinal products, it is not possible to provide an estimate of the relevant expenditure. Only the total amount paid by the Regions for plasma processing services, not including the costs sustained for the production of plasma as “raw material”, can be accounted for.

PART A
Plasma-derived medicinal products from toll fractionation

ALBUMIN (ATC B05AA01)

Albumin is a plasma protein produced from liver cells and accounts for about 60% of all plasma proteins. Its concentration in the blood (referred to as albuminaemia) can range between 3.5 and 5.0 g / dL. Lower albuminaemia values are mainly due to a reduced production of albumin by the liver. The ability to synthesise proteins by the hepatocyte is compromised in severe liver diseases (15,16).

Table 5 shows the brand names of medicinal products containing albumin currently on the market in Italy and the amount of active ingredient they contain expressed in grams.

Table 5. Products containing albumin currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	g	Manufacturer	NHS class
049507041	ALBUMINA GRIFOLS*1FL 10mL 200 g/L	2	INSTITUTO GRIFOLS S.A	A
034611032	ALBUMINA GRIFOLS*1FL 100mL 5%	5	GRIFOLS ITALIA SpA	C
036504025	ALBUREX* INFUS 1FL 100mL 5%	5	CSL BEHRING GmbH	C
039187012	ALBUNORM*1FL 100mL 5% 50g/L	5	OCTAPHARMA Italy SpA	C
049507015	ALBUMINA GRIFOLS*1FL 100mL 50 g/L	5	INSTITUTO GRIFOLS S.A	C
049507078	ALBUMINA GRIFOLS*1SAC100mL50g/L	5	INSTITUTO GRIFOLS S.A	C(nn)
010317028	ALBUMINA UM.IMMUNO*50mL 20%+S.	10	BAXTER SpA	A
011544020	ALBUMINA BEHRING*IV 50mL20%	10	CSL BEHRING SpA	A
021111024	UMANALBUMIN*INF FL 50mL 200g/L	10	KEDRION SpA	A
022515163	ALBITAL*1FL 50mL SOLUZ 20%+SET	10	KEDRION SpA	A
028989046	PLASBUMIN*EV 1FL 50mL 200g/L	10	GRIFOLS ITALIA SpA	A
029251030	ALBUTEIN*IV FL 50mL 200g/L	10	GRIFOLS ITALIA SpA	A
034611018	ALBUMINA GRIFOLS*1FL 50mL 20%	10	GRIFOLS ITALIA SpA	A
036176016	ALBUMINA LFB*FL 50mL 200mg/mL	10	LBF	A
036504052	ALBUREX*INFUS 1FL 50mL 20%	10	CSL BEHRING GmbH	A
037566054	ALBUMINA BAXTER*FL 50mL 200g/L	10	BAXALTA Italy Srl	A
049507104	ALBUMINA GRIFOLS*1SAC50mL200g/L	10	INSTITUTO GRIFOLS S.A	C(nn)
038109056	FLEXBUMIN*SAC INF 50mL 200g/L	10	BAXALTA Italy Srl	A
038747034	OCTALBIN*IV 50mL 200mg/mL	10	OCTAPHARMA Italy SpA	A
039073022	ALBIOMIN*FL 50mL 200g/L 20%	10	BIOTEST ITALIA Srl	A
039187063	ALBUNORM*1FL 50mL 20% 200g/L	10	OCTAPHARMA Italy SpA	A
042029013	KALBI*FL 50mL 200g/L	10	KEDRION SpA	A
043358011	ALBUMEON*FL 50mL 200g/L 20%	10	CSL BEHRING SpA	A
044549018	PROBUMIN*FL 50 mL 200 g/L	10	GRIFOLS ITALIA SpA	C (nn)
049507054	ALBUMINA GRIFOLS*1FL 50mL 200 g/L	10	INSTITUTO GRIFOLS S.A	A
010317042	ALBUMINA UM.IMMUNO*50mL 25%+S.	12.5	BAXTER SpA	A
021111051	UMANALBUMIN*FL 250mL 5%	12.5	KEDRION SpA	C
021111087	UMANALBUMIN*INF FL 50mL 250g/L	12.5	KEDRION SpA	A
022515136	ALBITAL*1FL 50mL 25g/100mL+SET	12.5	KEDRION SpA	A
028989097	PLASBUMIN*EV 1FL 50mL 250g/L	12.5	GRIFOLS ITALIA SpA	A
029251016	ALBUTEIN*IV FL 250mL 50g/L	12.5	GRIFOLS ITALIA SpA	C
029251042	ALBUTEIN*IV FL 50mL 25%	12.5	GRIFOLS ITALIA SpA	A
034611044	ALBUMINA GRIFOLS*1FL 250mL 5%	12.5	GRIFOLS ITALIA SpA	C
034611069	ALBUMINA GRIFOLS*50mL 25g/100mL	12.5	GRIFOLS ITALIA SpA	A
036504037	ALBUREX* INFUS 1 FL 250mL 5%	12.5	CSL BEHRING GmbH	C
036504076	ALBUREX*INFUS 1FL 50mL 25%	12.5	CSL BEHRING GmbH	A
037566015	ALBUMINA BAXTER*1FL 250mL 50g	12.5	BAXALTA Italy Srl	C
037566092	ALBUMINA BAXTER*FL 50mL 250g/L	12.5	BAXALTA Italy Srl	A
038109070	FLEXBUMIN*SAC INF 50mL 250g/L	12.5	BAXALTA Italy Srl	A
039073010	ALBIOMIN*INF 250mL 50g/L 5%	12.5	BIOTEST ITALIA Srl	C

AIC code	Brand name	g	Manufacturer	NHS class
039187036	ALBUNORM*1FL 250mL 5% 50g/L	12.5	OCTAPHARMA Italy SpA	C
039187101	ALBUNORM*1FL 50mL 25% 250g/L	12.5	OCTAPHARMA Italy SpA	A
042029025	KALBI*FL 50mL 250g/L+SET	12.5	KEDRION SpA	A
049507027	ALBUMINA GRIFOLS*1FL 250mL 50 g/L	12,5	INSTITUTO GRIFOLS S.A	C
049507080	ALBUMINA GRIFOLS*1SAC250mL50g/L	12,5	INSTITUTO GRIFOLS S.A	C(nn)
021111101	UMANALBUMIN*EV FL 100mL 200g/L	20	KEDRION SpA	A
028989059	PLASBUMIN*EV 1FL 100mL 200g/L	20	GRIFOLS ITALIA SpA	A
034611020	ALBUMINA GRIFOLS*1FL 100mL 20%	20	GRIFOLS ITALIA SpA	A
036176028	ALBUMINA LFB* FL 100mL 200 mg/mL	20	LFB	C
036504064	ALBUREX*INFUS 1FL 100mL 20%	20	CSL BEHRING GmbH	A
037566078	ALBUMINA BAXTER*1FL 100mL 200g	20	BAXALTA Italy Srl	A
038109068	FLEXBUMIN*SAC INF 100mL 200g/L	20	BAXALTA Italy Srl	A
038747046	OCTALBIN*IV 100mL 200mg/mL	20	OCTAPHARMA Italy SpA	A
039073034	ALBIOMIN*INF 100mL 200g/L 20%	20	BIOTEST ITALIA Srl	A
039187087	ALBUNORM*1FL 100mL 20% 200g/L	20	OCTAPHARMA Italy SpA	A
043358023	ALBUMEON*FL 100mL 200g/L 20%	20	CSL BEHRING SpA	A
044549020	PROBUMIN*FL 100mL 200 g/L	20	GRIFOLS ITALIA SpA	C (nn)
049507066	ALBUMINA GRIFOLS*1FL100mL 200g/L	20	INSTITUTO GRIFOLS S.A	A
049507116	ALBUMINAGRIFOLS*1SAC100mL200gL	20	INSTITUTO GRIFOLS S.A	C(nn)
029251028	ALBUTEIN*IV FL 500mL 50g/L	25	GRIFOLS ITALIA SpA	C
034611057	ALBUMINA GRIFOLS*1FL 500mL 5%	25	GRIFOLS ITALIA SpA	C
034611071	ALBUMINA GRIFOLS25g/100mL	25	GRIFOLS ITALIA SpA	H
036504049	ALBUREX* INFUS 1FL 500mL 5%	25	CSL BEHRING GmbH	C
036504088	ALBUREX* INFUS 1FL 100mL 25%	25	CSL BEHRING GmbH	H
037566039	ALBUMINA BAXTER*1FL 500mL 50 g/L	25	BAXALTA Italy Srl	C
037566116	ALBUMINA BAXTER*1FL100mL 250g/L	25	BAXALTA Italy Srl	H
038109082	FLEXBUMIN*1SACCA 100mL 250g/L	25	BAXALTA Italy Srl	H
039187051	ALBUNORM" 1 FL 500mL 5%, 50 g/L	25	OCTAPHARMA Italy SpA	C
039187113	ALBUNORM* 1 FL 100mL 25%, 250 g/L	25	OCTAPHARMA Italy SpA	H
049507039	ALBUMINA GRIFOLS*1FL 500mL 50 g/L	25	INSTITUTO GRIFOLS S.A	C
049507092	ALBUMINA GRIFOLS*1SAC500mL50g/L	25	INSTITUTO GRIFOLS S.A	C(nn)
039187024	ALBUNORM*10FL 100mL 5% 50g/L	50	OCTAPHARMA Italy SpA	C
036176030	ALBUMINA 200 mg/mL INF 6*50mL	60	LFB	C
039187075	ALBUNORM* 10FL 50mL20%, 200 g/L	100	OCTAPHARMA Italy SpA	H
036176042	ALBUMINA 200 mg/mL INF 6*100mL	120	LFB	C
039187048	ALBUNORM* 10FL 250mL 5%, 50 g/L	125	OCTAPHARMA Italy SpA	C
039187099	ALBUNORM*10FL 100mL 20%, 200 g/L	200	OCTAPHARMA Italy SpA	H
038109017	FLEXBUMIN*24SACCHE 50mL 200g/L	240	BAXALTA Italy Srl	H
038109031	FLEXBUMIN*12SACCHE 100mL200g/L	240	BAXALTA Italy Srl	H
037566041	ALBUMINA BAXTER*10FL 500mL 50 g/L	250	BAXALTA Italy Srl	C
037566027	ALBUMINA BAXTER* 24FL 250mL 50 g/L	300	BAXALTA Italy Srl	C
038109029	FLEXBUMIN*12SACCHE 100mL 250 g/L	300	BAXALTA Italy Srl	H
038109043	FLEXBUMIN*24SACCHE50mL 250g/L	300	BAXALTA Italy Srl	H
037566066	ALBUMINA BAXTER*70FL 50mL 200 g/L	700	BAXALTA Italy Srl	H
037566104	ALBUMINA BAXTER*70FL 50mL 250 g/L	875	BAXALTA Italy Srl	H
037566080	ALBUMINA BAXTER*56FL 100mL 200 g/L	1120	BAXALTA Italy Srl	H
037566128	ALBUMINA BAXTER*56FL 100mL 250 g/L	1400	BAXALTA Italy Srl	H

Quantification and characterisation of the demand

Table 6 shows the total demand (expressed in grams) and the total standardised demand (expressed in grams per 1,000 population) of albumin1 for the two-year period 2023-2024 with the variations in percentage, both at national and regional levels. In 2024, the national demand for this principle was about 33,237 kilograms (Table 6), equal to about 564 grams per 1,000 population, with a decrease of 3.8% from the previous year.

The three Regions with the highest standardised demand were Sardinia, Emilia-Romagna and Campania, with values equal to 1,014, 758 and 728 grams per 1,000 population, respectively. The Regions with the lowest demand were the AP of Bolzano, Piedmont and Molise, where it is between 314 and 403 grams per 1,000 population (Figure 5). In this two-year period, the total standardised demand for albumin showed a moderate decrease compared to the previous years (-3.8% compared to 2023) (17). The Regions where there was a lesser use most evidently are Lombardy (-19%), Liguria (-17%) and Marche (-12%).While Latium (+23%) and Friuli V. Giulia (+15%) are the Regions where demand shows the greatest growth.

Table 6. Total demand (public and private) and total standardised demand for albumin, expressed in grams and grams per 1,000 population, and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	g	g per 1,000 pop	g	g per 1,000 pop	
Abruzzo	873,298	686.2	920,715	725.2	5.7
Aosta Valley	73,760	599.0	76,780	624.9	4.3
AP Bolzano	184,640	345.7	168,915	314.2	-9.1
AP Trento	265,170	488.3	290,840	533.5	9.2
Apulia	1,891,590	484.1	1,957,875	503.2	4.0
Basilicata	346,753	645.0	356,698	668.9	3.7
Calabria	961,380	520.6	912,988	496.6	-4.6
Campania	4,316,193	769.4	4,074,410	728.4	-5.3
E.-Romagna	3,599,790	811.2	3,373,635	757.8	-6.6
Friuli V. Giulia	491,350	411.4	563,050	471.3	14.6
Latium	2,763,275	483.0	3,399,305	594.8	23.1
Liguria	941,915	624.8	778,553	515.9	-17.4
Lombardy	6,395,853	641.1	5,198,585	519.2	-19.0
Marche	900,445	606.6	791,570	533.9	-12.0
Molise	108,795	374.3	107,250	370.8	-0.9
Piedmont	1,739,503	409.2	1,712,795	402.9	-1.5
Sardinia	1,481,753	938.9	1,592,850	1014.3	8.0
Sicily	2,982,878	619.6	2,701,860	563.2	-9.1
Tuscany	1,547,768	422.7	1,629,718	445.2	5.3
Umbria	564,450	659.1	522,370	612.3	-7.1
Veneto	2,122,453	437.7	2,106,590	434.2	-0.8
Italy	34,553,008	585.7	33,237,350	563.6	-3.8

[1] The data analysed did not consider the use of *Umanserum*™. This product is classified as human plasma protein (ATC B05AA02, see related chapter) within the ATC system, despite its 90% albumin composition.

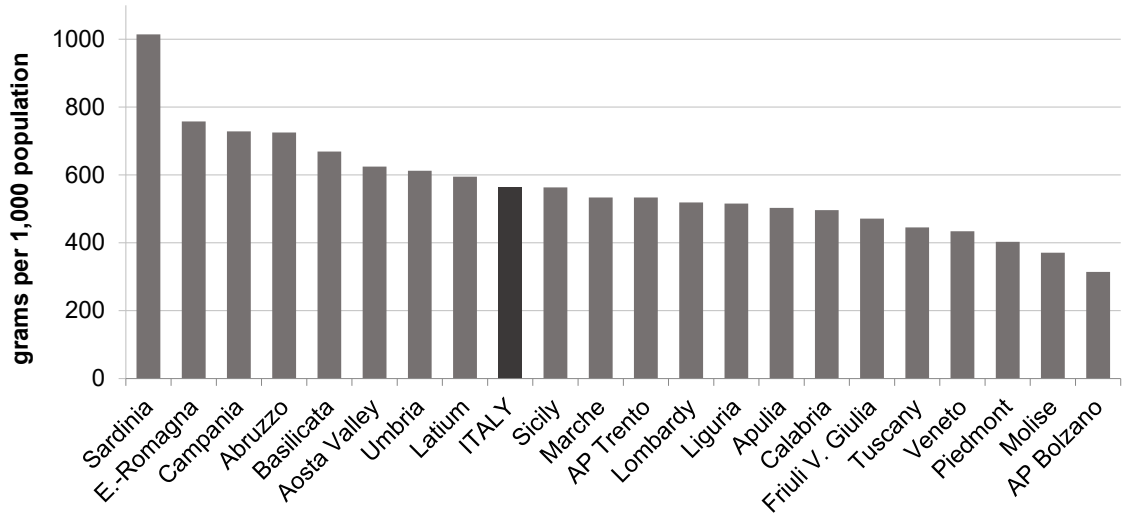

Figure 5. Total and regional demand (public and private) for albumin, expressed in grams per 1,000 population, 2024 (adapted by the CNS on data from the Traceability information flow)

Figure 6 highlights the eleven Regions with a higher demand compared to national demand, with a value higher than 30% for two of them.

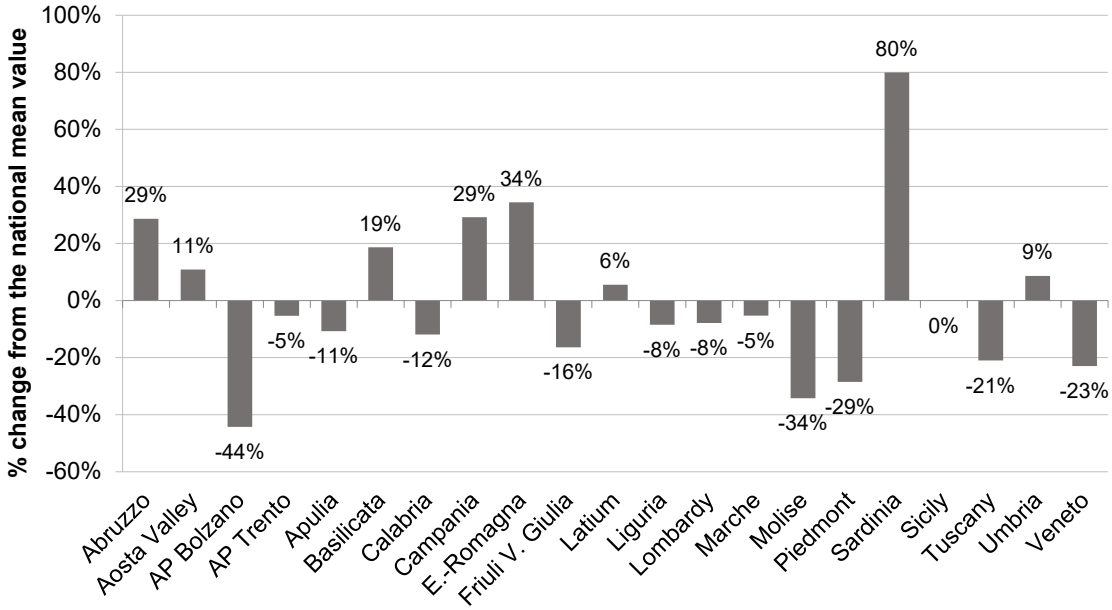

Figure 6. Percentage change from the national mean value of standardised regional demand for human albumin in 2024 (adapted by the CNS on data from the Traceability information flow)

Figure 7 shows the standardised regional demand for albumin recorded in 2024 per distribution channel (public pharmacies compared to other facilities), as shown by the drug Traceability

system (18). In 2024, about 9% of the national demand - approximately 3,137 kilograms - was distributed through public pharmacies.

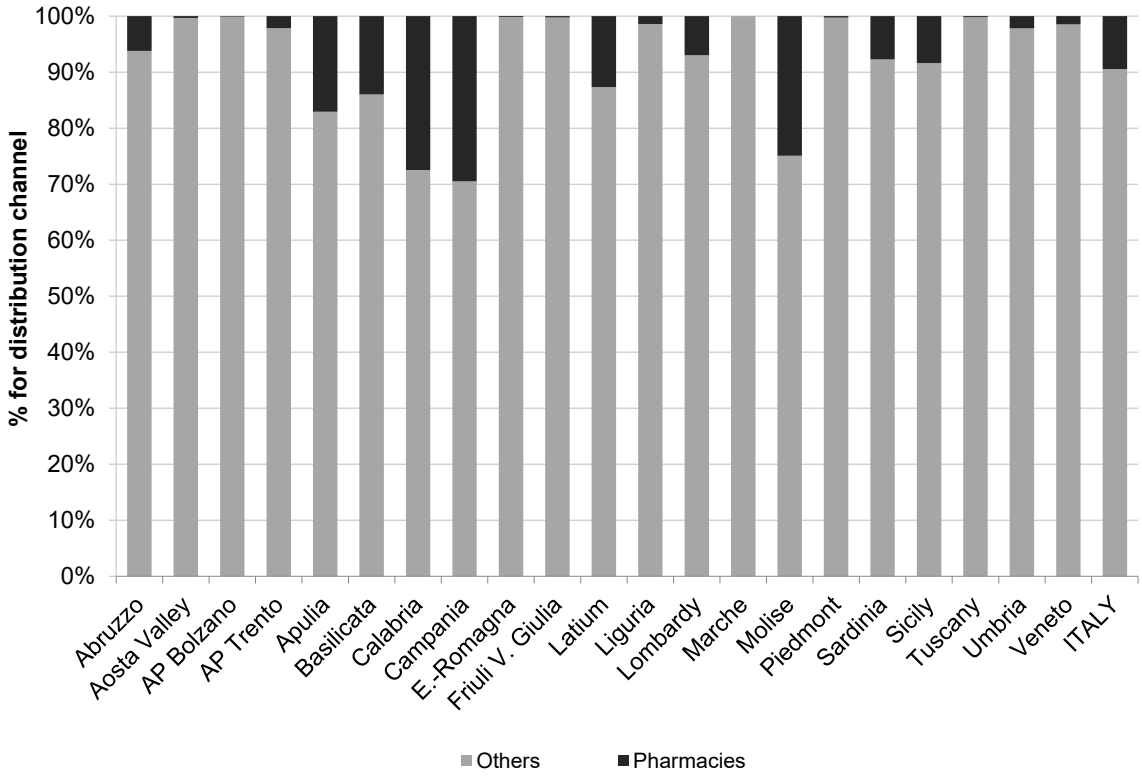

Figure 7. Standardised regional demand for albumin recorded per distribution channel, 2024 (adapted by the CNS on data from the Traceability information flow)

The distribution channel of pharmacies was mostly used in Campania, Calabria and Molise, where they accounted for 29%, 27% and 25% respectively of the regional demand; still used to a lesser extent in Latium, Basilicata and Apulia (with percentages of between 13% and 17% of the total regional demand, while in the other Regions they were rarely used (<10%).

NORMAL HUMAN IMMUNOGLOBULINS FOR SUBCUTANEOUS USE (ATC J06BA01) AND FOR INTRAVENOUS USE (ATC J06BA02)

Immunoglobulins (IGs) are used in substitutive immunodeficiency therapy and in the treatment of autoimmune diseases or systemic inflammatory processes. However, in clinical practice they are used much more extensively even though their use is not always fully justified by the available evidence in the scientific literature. Since 2007, both soluble IG preparations for subcutaneous/intramuscular infusion (SC/IM) and those for intravenous use (IntraVenous, IV) (19) have been available in Italy. IGs, like all other PDMPs, are prepared from human plasma pools, which guarantees the recipient a higher antibody coverage thanks to a significant idiotypical diversity. The preparations contain structurally and functionally intact IGs, with normal half-life and subclass proportions: 95% of monomeric IGG, small amounts of dimers, and variable amounts of IGA and IGM.

Table 7 shows the names of the medicinal products containing IG that are currently marketed in Italy and the amount of the active ingredient they contain expressed in grams.

Table 7. Products containing normal human immunoglobulins for subcutaneous/ intramuscular and intravenous use currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	g	Manufacturer	NHS class
Normal human immunoglobulin for subcutaneous/intramuscular use				
036800011	SUBCUVIA*SC IM FL 5mL 160mg/mL	0.8	BAXALTA Italy Srl	H
036800047	SUBCUVIA*SC IM FL10mL 160mg/mL	1.6	BAXALTA Italy Srl	H
036800023	SUBCUVIA*SC IM 20FL5mL 160mg/mL	16	BAXALTA Italy Srl	H
036800035	SUBCUVIA*SC IM 20FL10mL 160mg/mL	32	BAXALTA Italy Srl	H
Normal human immunoglobulin for subcutaneous use				
045996016	CUTAQUIG*SC 1 FL 6 mL 165 mg/mL	0.9	OCTAPHARMA Italy SpA	C
040652075	OCTANORM*1FL 6mL 165mg/mL	0.99	OCTAPHARMA Italy SpA	H
041157013	HIZENTRA*SC 1FL 5mL 200mg/mL	1	CSL BEHRING SpA	H
041157153	HIZENTRA*SC 1SIR 5mL 200mg/mL	1	CSL BEHRING SpA	H
044244010	CUVITRU*SC 1FL 5mL 200mg/mL	1	BAXALTA Italy Srl	H
049488012	XENBIFY*1FL 5mL 200 mg/mL	1	INSTITUTO GRIFOLS S.A	H
043396011	NAXIGLO*SC FL 10mL 160mg/mL	1.6	KEDRION SpA	H
043398015	KEYCUTE*SC FL 10mL 160mg/mL	1.6	KEDRION SpA	H
040652012	OCTANORM*1FL10mL 165mg/mL	1.65	OCTAPHARMA Italy SpA	H
045996028	CUTAQUIG*SC 1 FL 10 mL 165 mg/mL	1.65	OCTAPHARMA Italy SpA	C
040652101	OCTANORM*FL 12mL 165mg/mL	1.98	OCTAPHARMA Italy SpA	H
045996030	CUTAQUIG*SC 1 FL 12 mL 165 mg/mL	1.98	OCTAPHARMA Italy SpA	C
041157049	HIZENTRA*SC 1FL 10mL 200mg/mL	2	CSL BEHRING SpA	H
041157177	HIZENTRA*SC 1SIR 10mL 200mg/mL	2	CSL BEHRING SpA	H
044244022	CUVITRU*SC 1FL 10mL 200mg/mL	2	BAXALTA Italy Srl	H
049488024	XENBIFY*1FL 10mL 200 mg/mL	2	INSTITUTO GRIFOLS S.A	H
042804017	HYQVIA*SC 1FL 25mL+1FL 1,25mL	2.5	BAXALTA Italy Srl	H
041157076	HIZENTRA*1FL 15mL 200 mg/mL	3	CSL BEHRING SpA	H
040652048	OCTANORM*1FL 20mL 165mg/mL	3.3	OCTAPHARMA Italy SpA	H
045996042	CUTAQUIG*SC 1 FL 20 mL 165 mg/mL	3.3	OCTAPHARMA Italy SpA	C
040652137	OCTANORM*FL 24mL 165mg/mL	3.96	OCTAPHARMA Italy SpA	H
045996055	CUTAQUIG*SC 1 FL 24 mL 165 mg/mL	3.96	OCTAPHARMA Italy SpA	C

AIC code	Brand name	g	Manufacturer	NHS class
041157102	HIZENTRA*SC 1FL 20mL 200mg/mL	4	CSL BEHRING SpA	H
041157191	HIZENTRA*SC 1FL 20mL 200mg/mL	4	CSL BEHRING SpA	H
043396023	NAXIGLO*SC FL 25mL 160mg/mL	4	KEDRION SpA	H
043398027	KEYCUTE*SC FL 25mL 160mg/mL	4	KEDRION SpA	H
044244034	CUVITRU*SC 1FL 20mL 200mg/mL	4	BAXALTA Italy Srl	H
049488036	XENBIFY*1FL 20mL 200 mg/mL	4	INSTITUTO GRIFOLS S.A	H
042804029	HYQVIA*SC 1FL 50mL+1FL 2,5mL	5	BAXALTA Italy Srl	H
040652164	OCTANORM*FL 48mL 165mg/mL	7.92	OCTAPHARMA Italy SpA	H
045996067	CUTAQUIG*SC 1 FL 48 mL 165 mg/mL	7.92	OCTAPHARMA Italy SpA	C
044244046	CUVITRU*SC 1FL 40mL 200mg/mL	8	BAXALTA Italy Srl	H
040652087	OCTANORM*10FL 6mL 165 mg/mL	9.9	OCTAPHARMA Italy SpA	H
045996079	CUTAQUIG*SC 10 FL 6 mL 165 mg/mL	9.9	OCTAPHARMA Italy SpA	C
041157025	HIZENTRA*10FL 5mL 200mg/mL	10	CSL BEHRING SpA	H
041157138	HIZENTRA*SC 1FL 50mL 200mg/mL	10	CSL BEHRING SpA	H
041157165	HIZENTRA*SC 10SIR 5mL 200mg/mL	10	CSL BEHRING SpA	H
042804031	HYQVIA*SC 1FL 100mL+1FL 5mL	10	BAXALTA Italy Srl	H
044244059	CUVITRU*SC 1 FL 50mL 200 mg/mL	10	BAXALTA INN. GMBH	C(nn)
044244061	CUVITRU*SC 10FL 5mL 200 mg/mL	10	BAXALTA INN. GMBH	C(nn)
049488048	XENBIFY*1FL 50mL 200 MG/ML	10	INSTITUTO GRIFOLS S.A	H
049488051	XENBIFY*10FL 5mL 200 mg/mL	10	INSTITUTO GRIFOLS S.A	C(nn)
040652024	OCTANORM*10FL 10mL 165mg/mL	16.5	OCTAPHARMA Italy SpA	H
045996081	CUTAQUIG*SC 10 FL 10 mL 165 mg/mL	16.5	OCTAPHARMA Italy SpA	C
040652099	OCTANORM*20FL 6mL 165mg/mL	19.8	OCTAPHARMA Italy SpA	H
040652113	OCTANORM*10FL 12mL 165mg/mL	19.8	OCTAPHARMA Italy SpA	H
045996093	CUTAQUIG*SC 10 FL 12 mL 165 mg/mL	19.8	OCTAPHARMA Italy SpA	C
045996131	CUTAQUIG*SC 20 FL 6 mL 165 mg/mL	19.8	OCTAPHARMA Italy SpA	C
041157037	HIZENTRA*20FL 5mL 200mg/mL	20	CSL BEHRING SpA	H
041157052	HIZENTRA*10FL 10mL 200mg/mL	20	CSL BEHRING SpA	H
041157189	HIZENTRA*SC 10SIR 10mL 200mg/mL	20	CSL BEHRING SpA	H
042804043	HYQVIA*SC 1FL 200mL+1FL 10mL	20	BAXALTA Italy Srl	H
044244073	CUVITRU*SC 20FL 5mL 200 mg/mL	20	BAXALTA INN. GMBH	C(nn)
044244085	CUVITRU*SC 10FL 10mL 200 mg/mL	20	BAXALTA INN. GMBH	C(nn)
049488063	XENBIFY*10FL 10mL 200 mg/mL	20	INSTITUTO GRIFOLS S.A	C(nn)
041157088	HIZENTRA*10FL 15mL 200mg/mL	30	CSL BEHRING SpA	H
042804056	HYQVIA*SC 1FL 300mL+1FL 15mL	30	BAXALTA Italy Srl	H
040652036	OCTANORM*20FL 10mL 165mg/mL	33	OCTAPHARMA Italy SpA	H
040652051	OCTANORM*10FL 20mL 165mg/mL	33	OCTAPHARMA Italy SpA	H
045996105	CUTAQUIG*SC 10 FL 20 mL 165 mg/mL	33	OCTAPHARMA Italy SpA	C
045996143	CUTAQUIG*SC 20 FL 10 mL 165 mg/mL	33	OCTAPHARMA Italy SpA	C
040652125	OCTANORM*20FL 12mL 165 mg/mL	39.6	OCTAPHARMA Italy SpA	H
040652149	OCTANORM*10FL 24mL 165 mg/mL	39.6	OCTAPHARMA Italy SpA	H
045996117	CUTAQUIG*SC 10 FL 24 mL 165 mg/mL	39.6	OCTAPHARMA Italy SpA	C
045996156	CUTAQUIG*SC 20 FL 12 mL 165 mg/mL	39.6	OCTAPHARMA Italy SpA	C
041157064	HIZENTRA*20FL 10mL 200mg/mL	40	CSL BEHRING SpA	H
041157114	HIZENTRA*10FL 20mL 200mg/mL	40	CSL BEHRING SpA	H
041157203	HIZENTRA*10FL 20mL 200mg/mL	40	CSL BEHRING SpA	H
044244109	CUVITRU*SC 10FL 20mL 200 mg/mL	40	BAXALTA INN. GMBH	C(nn)
044244123	CUVITRU*SC 5FL 40mL 200 mg/mL	40	BAXALTA INN. GMBH	C(nn)
044244147	CUVITRU*SC 20FL 10mL 200 mg/mL	40	BAXALTA GMBH	C(nn)
049488087	XENBIFY*20FL 10mL 200 mg/mL	40	INSTITUTO GRIFOLS S.A	C(nn)
041157090	HIZENTRA*20FL 15mL 200mg/mL	60	CSL BEHRING SpA	H
044244097	CUVITRU*SC 30FL 10mL 200 mg/mL	60	BAXALTA INN. GMBH	C(nn)
040652063	OCTANORM*20FL 20mL 165mg/mL	66	OCTAPHARMA Italy SpA	H
045996168	CUTAQUIG*SC 20 FL 20 mL 165 mg/mL	66	OCTAPHARMA Italy SpA	C
040652152	OCTANORM* 20FL 24mL 165mg/mL	79.2	OCTAPHARMA Italy SpA	H
040652176	OCTANORM*10FL 48mL 165mg/mL	79.2	OCTAPHARMA Italy SpA	H
045996129	CUTAQUIG*SC 10 FL 48 mL 165 mg/mL	79.2	OCTAPHARMA Italy SpA	C

AIC code	Brand name	g	Manufacturer	NHS class
045996170	CUTAQUIG*SC 20 FL 24 mL 165 mg/mL	79.2	OCTAPHARMA Italy SpA	C
041157126	HIZENTRA*20FL 20mL 200mg/mL	80	CSL BEHRING SpA	H
044244150	CUVITRU*SC 20FL 20ML 200 mg/mL	80	BAXALTA GMBH	C(nn)
044244162	CUVITRU*SC 10FL 40ML 200 mg/mL	80	BAXALTA GMBH	C(nn)
049488099	XENBIFY*20FL 20mL 200 mg/mL	80	INSTITUTO GRIFOLS S.A	C(nn)
041157140	HIZENTRA*10FL 50mL 200mg/mL	100	CSL BEHRING SpA	C(nn)
049488075	XENBIFY*10FL 50mL 200 MG/ML	100	INSTITUTO GRIFOLS S.A	C(nn)
044244111	CUVITRU*SC 30FL 20mL 200 mg/mL	120	BAXALTA INN. GMBH	C(nn)
040652188	OCTANORM* 20FL 48mL 165mg/mL	158.4	OCTAPHARMA Italy SpA	H
045996182	CUTAQUIG*SC 20 FL 48 mL 165 mg/mL	158.4	OCTAPHARMA Italy SpA	C
044244135	CUVITRU*SC 20FL 40mL 200 mg/mL	160	BAXALTA INN. GMBH	C(nn)
Normal human immunoglobulin for intravenous use				
029021019*	PENTAGLOBIN*EV FL 50mg/mL 10mL	0.5	BIOTEST ITALIA Srl	C
029249075	PLITAGAMMA *INF 1 FL 10mL 50mg/mL	0.5	INSTITUTO GRIFOLS SA	H
040267015	FLEBOGAMMA*INF 1FL 10mL 50 mg/mL	0.5	GRIFOLS ITALIA SpA	H
025266141	IGVENA*EV 1FL 20mL 50g/L	1	KEDRION SpA	H
035143054	OCTAGAM*IV 1FL 20mL 50mg/mL	1	OCTAPHARMA Italy SpA	H
037107012	KIOVIG*EV FL 10mL 100mg/mL	1	BAXTER SpA	H
037240052	INTRATECT*INF FL 50g/L 20mL	1	BIOTEST ITALIA Srl	H
037240090	INTRATECT*INF FL 100g/L 10mL	1	BIOTEST ITALIA Srl	H
037254012	VENITAL*EV FL 20mL 50g/L	1	KEDRION SpA	H
044187019	GLOBIGA*INF 1FL 1g 100mg/mL	1	OCTAPHARMA Italy SpA	C
045410014	GAMUNEX *INF 1FL 10 mL 100mg/mL	1	Grifols Deutschland GmbH	H
037240126	INTRATECT*INF FL100g/L 200mL	2	BIOTEST ITALIA Srl	H
039457015	GAMTEN*INF 1FL 20mL 100mg/mL	2	OCTAPHARMA Italy SpA	H
043736014	IQYMUNE*FL INF 20mL 100mg/mL	2	LFB	H
025266154	IGVENA*EV 1FL 50mL 50g/L+SET	2.5	KEDRION SpA	H
029021033*	PENTAGLOBIN*EV 1FL 50mg/mL50mL	2.5	BIOTEST ITALIA Srl	C
029249048	PLITAGAMMA*50mL(2,5g)5%+SET	2.5	GRIFOLS ITALIA SpA	H
035143015	OCTAGAM*IV FL 50mL 5%	2.5	OCTAPHARMA Italy SpA	H
037107024	KIOVIG*EV FL 25mL 100mg/mL	2.5	BAXTER SpA	H
037240064	INTRATECT*INF FL 50g/L 50mL	2.5	BIOTEST ITALIA Srl	H
037240138	INTRATECT*INF FL100 g/L 25mL	2.5	BIOTEST ITALIA Srl	H
037254024	VENITAL*EV FL 50mL 50g/L+SET	2.5	KEDRION SpA	H
039712043	PRIVIGEN*EV 1FL 25mL 100mg/mL	2.5	CSL BEHRING SpA	H
040267027	FLEBOGAMMA DIF*FL 50mL 50mg/mL	2.5	GRIFOLS ITALIA SpA	H
044187021	GLOBIGA*INF 1FL 2,5g 100mg/mL	2.5	OCTAPHARMA Italy SpA	C
033240033	GAMMAGARD*EV 1FL 50mg/mL 96mL	4.8	BAXTER SpA	H
025266166	IGVENA*EV 1FL 100mL 50g/L+SET	5	KEDRION SpA	H
029021045*	PENTAGLOBIN*EV 1FL 50mg/mL100mL	5	BIOTEST ITALIA Srl	C
029249051	PLITAGAMMA*100mL(5g)5%+SET	5	GRIFOLS ITALIA SpA	H
035143027	OCTAGAM*IV FL 100mL 5%	5	OCTAPHARMA Italy SpA	H
037107036	KIOVIG*EV FL 50mL 100mg/mL	5	BAXTER SpA	H
037240076	INTRATECT*INF FL 50g/L 100mL	5	BIOTEST ITALIA Srl	H
037240102	INTRATECT*INF FL 100g/L 50mL	5	BIOTEST ITALIA Srl	H
037253034	KEYVEN*EV FL 100mL 50g/L+SET	5	KEDRION SpA	H
037254036	VENITAL*EV FL 100mL 50g/L+SET	5	KEDRION SpA	H
039457027	GAMTEN*INF 1FL 50mL 100mg/mL	5	OCTAPHARMA Italy SpA	H
039712017	PRIVIGEN*EV 1FL 50mL 100mg/mL	5	CSL BEHRING SpA	H
040267039	FLEBOGAMMA DIF*FL 100mL 5g	5	GRIFOLS ITALIA SpA	H
040267066	FLEBOGAMMA DIF*EV 50mL 5g	5	GRIFOLS ITALIA SpA	H
043736026	IQYMUNE*FL INF 50mL 100mg/mL	5	LFB	H
044187033	GLOBIGA*INF 1FL 5g 100mg/mL	5	OCTAPHARMA Italy SpA	C
045410026	GAMUNEX *INF 1FL 50 mL 100mg/mL	5	Grifols Deutschland GmbH	H
045410038	GAMUNEX *INF1FL 50mL 100mg/mL C.o	5	Grifols Deutschland GmbH	H
051243018	YIMMUGO*100 MG/ML EV FL 50 ML	5	BIOTEST PHARMA GmbH	C(nn)
039457054	GAMTEN*INFUS 1FL 60mL 100mg/mL	6	OCTAPHARMA Italy SpA	C(nn)

AIC code	Brand name	g	Manufacturer	NHS class
044187045	GLOBIGA*INF 1FL 6g 100mg/mL	6	OCTAPHARMA Italy SpA	C
033240045	GAMMAGARD*EV 1FL 50mg/mL 192mL	9.6	BAXTER SpA	H
025266178	IGVENA*EV 1FL 200mL 50g/L+SET	10	KEDRION SpA	H
029249063	PLITAGAMMA*200mL(10g)5%+SET	10	GRIFOLS ITALIA SpA	H
035143039	OCTAGAM*IV FL 200mL 5%	10	OCTAPHARMA Italy SpA	H
037107048	KIOVIG*EV FL 100mL 100mg/mL	10	BAXTER SpA	H
037240088	INTRATECT*INF FL 50g/L 200mL	10	BIOTEST ITALIA Srl	H
037240114	INTRATECT*INF FL100g/L 100mL	10	BIOTEST ITALIA Srl	H
037253046	KEYVEN*EV FL 200mL 50g/L+SET	10	KEDRION SpA	H
037254048	VENITAL*EV FL 200mL 50g/L+SET	10	KEDRION SpA	H
039457039	GAMTEN*INF 1FL100mL 100mg/mL	10	OCTAPHARMA Italy SpA	H
039712029	PRIVIGEN*EV 1FL 100mL 100mg/mL	10	CSL BEHRING SpA	H
040267041	FLEBOGAMMA DIF*FL 200mL 10g	10	GRIFOLS ITALIA SpA	H
040267078	FLEBOGAMMA DIF*EV 100mL 10g	10	GRIFOLS ITALIA SpA	H
043736038	IQYMUNE*FL INF100mL 100mg/mL	10	LFB	H
044187058	GLOBIGA*INF 1FL 10g 100mg/mL	10	OCTAPHARMA Italy SpA	C
045410040	GAMUNEX *INF 1FL 100 mL 100mg/mL	10	Grifols Deutschland GmbH	H
045410053	GAMUNEX *INF 1FL100mL 100mg/mL C.o	10	Grifols Deutschland GmbH	H
051243020	YIMMUGO*100 MG/MLEV FL 100 ML	10	BIOTEST PHARMA GmbH	C(nn)
025266192	IGVENA*EV 2FL 200ML 50G/L+SET	20	KEDRION SpA	C(nn)
029249087	PLITAGAMMA*INF 1 FL 400mL 50mg/mL	20	INSTITUTO GRIFOLS SA	H
035143066	OCTAGAM*IV 2FL 200mL 50mg/mL	20	OCTAPHARMA Italy SpA	H
037107051	KIOVIG*EV FL 200mL 100mg/mL	20	BAXTER SpA	H
039457041	GAMTEN*INF 1 FL 200mL 100mg/mL	20	OCTAPHARMA Italy SpA	H
039712031	PRIVIGEN*EV 1FL 200mL 100mg/mL	20	CSL BEHRING SpA	H
040267054	FLEBOGAMMA DIF*FL 400mL 20g	20	GRIFOLS ITALIA SpA	H
040267080	FLEBOGAMMA DIF*EV 200mL 20g	20	GRIFOLS ITALIA SpA	H
043736040	IQYMUNE*FL INF 200mL 100mg/mL	20	LFB	H
044187072	GLOBIGA*INF 1FL 20g 100mg/mL	20	OCTAPHARMA Italy SpA	C
045410065	GAMUNEX *INF 1FL 200 mL 100mg/mL	20	Grifols Deutschland GmbH	H
045410077	GAMUNEX *INF1FL200mL 100mg/mL C.o	20	Grifols Deutschland GmbH	H
051243032	YIMMUGO*100 MG/ML EV FL 200 ML	20	BIOTEST PHARMA GmbH	C(nn)
035143041	OCTAGAM*IV FL 500mL 5%	25	OCTAPHARMA Italy SpA	H
025266204	IGVENA*EV 3FL 200ML 50G/L+SET	30	KEDRION SpA	C(nn)
035143078	OCTAGAM*IV 3 FL 200mL 50mg/mL	30	OCTAPHARMA Italy SpA	H
037107063	KIOVIG*EV FL 300mL 100mg/mL	30	BAXTER SpA	H
037240140	INTRATECT* INF 3FL 200mL 50g/L	30	BIOTEST ITALIA Srl	C
037240153	INTRATECT*INF 3FL 100mL 100g/L	30	BIOTEST ITALIA Srl	C
039457066	GAMTEN*INF 3FL 100mL 100mg/mL	30	OCTAPHARMA Italy SpA	C(nn)
039712056	PRIVIGEN*EV 3FL 100mL 100mg/mL	30	CSL BEHRING GMBH	C
044187060	GLOBIGA*INF 3FL 10g 100mg/mL	30	OCTAPHARMA Italy SpA	C(nn)
044187096	GLOBIGA*INF 1FL 30g 100mg/mL	30	OCTAPHARMA Italy SpA	C
039457080	GAMTEN*INF 1FL 300mL 100mg/mL	30	OCTAPHARMA Italy SpA	C(nn)
051243044	YIMMUGO*100 MG/ML EF 3FL 100 ML	30	BIOTEST PHARMA GmbH	C(nn)
039712070	PRIVIGEN*EV 1FL 400mL 100mg/mL	40	CSL BEHRING GMBH	C(nn)
045410089	GAMUNEX *INF 1FL 400 mL 100mg/mL	40	Grifols Deutschland GmbH	H
045410091	GAMUNEX *INF1FL400 mL 100mg/mL C.o	40	Grifols Deutschland GmbH	H
037240165	INTRATECT* INF 3FL 200mL 100 g/L	60	BIOTEST ITALIA Srl	C
039457078	GAMTEN*INF 3FL 200mL 100mg/mL	60	OCTAPHARMA Italy SpA	C(nn)
039712068	PRIVIGEN*EV 3FL 200mL 100mg/mL	60	CSL BEHRING GMBH	C
044187084	GLOBIGA*INF 3FL 20g 100mg/mL	60	OCTAPHARMA Italy SpA	C(nn)
051243057	YIMMUGO*100 MG/ML EV 3 FL 200 ML	60	BIOTEST PHARMA GmbH	C(nn)

* Normal human immunoglobulins for intravenous use with high titers of IgM indicated as support therapy along with antibiotics for serious bacterial infections and as replacement therapy in immunodepressed patients.

Quantification and characterisation of the demand

Table 8 shows the total demand (expressed in grams) and the total standardised demand (in grams per 1,000 population) for IGs for the period 2023-2024 and the relative variations in percentage at national and regional levels. The same information is reported for both SC/IM (Table 9) and IV (Table 10) preparations.

In 2024, the total national demand for IGs was 6,749,088 grams, equal to 114.4 grams per 1,000 population (Table 8). The three Regions with the highest standardised demand per 1,000 population were Aosta Valley with around 174 grams, and Marche and Tuscany with around 159 grams and 155 grams respectively. The demand was lower in Molise, Calabria, Campania, Basilicata and Sicily where it ranged between 65 and 84 grams per 1,000 population. The demand for these PDMPs shows a slight increase in the two-year period 2023-2024 (+4.3%), featuring notable differences from one Region to another. The greatest increase is recorded in Abruzzo (+28%) and in Sardinia (+19%). The most marked decrease is instead observed in Basilicata (-21%).

Table 8. Total demand (public and private) and total standardised demand for normal human immunoglobulins for intravenous and subcutaneous/ intramuscular use, expressed in grams and grams per 1,000 population, and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	g	g per 1,000 pop	g	g per 1,000 pop	
Abruzzo	124,736	98.0	159,583	125.7	28.2
Aosta Valley	18,951	153.9	21,400	174.2	13.2
AP Bolzano	54,312	101.7	62,272	115.8	13.9
AP Trento	55,751	102.7	60,478	110.9	8.0
Apulia	420,250	107.5	460,627	118.4	10.1
Basilicata	56,955	105.9	44,544	83.5	-21.2
Calabria	114,445	62.0	128,292	69.8	12.6
Campania	420,967	75.0	467,135	83.5	11.3
E.-Romagna	714,645	161.0	681,431	153.1	-5.0
Friuli V. Giulia	160,326	134.2	139,028	116.4	-13.3
Latium	559,537	97.8	585,630	102.5	4.8
Liguria	213,963	141.9	202,614	134.3	-5.4
Lombardy	1,038,612	104.1	1,129,692	112.8	8.4
Marche	228,817	154.2	236,492	159.5	3.5
Molise	21,511	74.0	18,873	65.3	-11.8
Piedmont	528,166	124.2	536,932	126.3	1.7
Sardinia	128,954	81.7	153,180	97.5	19.4
Sicily	390,307	81.1	401,450	83.7	3.2
Tuscany	531,837	145.2	566,867	154.9	6.6
Umbria	125,773	146.9	129,851	152.2	3.6
Veneto	563,151	116.1	562,717	116.0	-0.1
Italy	6,471,964	109.7	6,749,088	114.4	4.3

Figure 8 shows which Regions tended to use more SC/IM formulations and which preferred IV ones. More SC/IM formulations were used in Umbria (41.3%), Latium (36.7%), Tuscany (35.7%) and Calabria (35.5%) while fewer were used in Sardinia, in the AP Bolzano, Aosta Valley

and Friuli V. Giulia (≤8%). At national level, the demand for SC/IM IGs stood at 24% of the total demand for IGs.

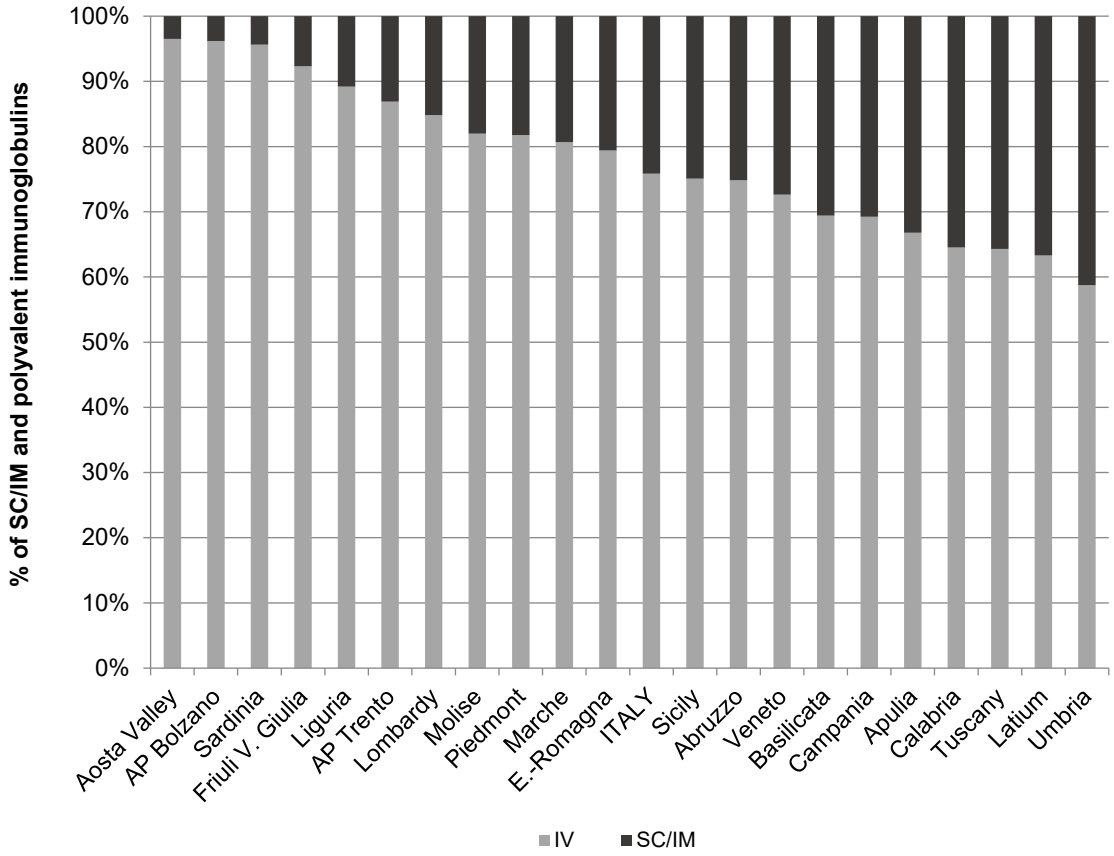

Figure 8. Total standardised demand (public and private) per administration of immunoglobulins (percentage on total), by Region, 2024 (adapted by the CNS on data from the Traceability information flow)

Normal human immunoglobulins for subcutaneous use

In 2024, the total demand for SC/IM IGs reached about 1,630,126 grams (27.6 grams per 1,000 population), with an increase of 13% compared to 2023 (Table 9).

The regional demands proved diversified with the highest value recorded of 63 grams per 1,000 population in Umbria followed by Tuscany and Apulia with 55 and 39 grams per 1,000 population respectively.

However, the lowest values were recorded in Sardinia, AP of Bolzano and in Aosta Valley, where they fluctuated between 4.3 and 6.1 grams per 1,000 population (Figure 9).

In Umbria, Tuscany, Latium, Veneto, Abruzzo, Emilia-Romagna, Apulia and Marche a higher total demand compared to national demand was recorded (range: 12-127%) (Figure 10).

Table 9. Total demand (public and private) and total standardised demand for normal human immunoglobulins for subcutaneous/ intramuscular use, expressed in grams and grams per 1,000 population, and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	g	g per 1,000 pop	g	g per 1,000 pop	
Abruzzo	30,760	24.2	40,155	31.6	30.9
Aosta Valley	1,278	10.4	749	6.1	-41.3
AP Bolzano	2,926	5.5	2,365	4.4	-19.7
AP Trento	9,161	16.9	7,928	14.5	-13.8
Apulia	121,439	31.1	152,983	39.3	26.5
Basilicata	13,237	24.6	13,622	25.5	3.8
Calabria	41,259	22.3	45,511	24.8	10.8
Campania	109,022	19.4	143,700	25.7	32.2
E.-Romagna	123,385	27.8	140,385	31.5	13.4
Friuli V. Giulia	10,821	9.1	10,695	9.0	-1.2
Latium	200,270	35.0	214,974	37.6	7.5
Liguria	23,923	15.9	21,889	14.5	-8.6
Lombardy	149,874	15.0	171,401	17.1	14.0
Marche	37,238	25.1	45,707	30.8	22.9
Molise	2,886	9.9	3,403	11.8	18.5
Piedmont	90,656	21.3	97,949	23.0	8.0
Sardinia	5,199	3.3	6,683	4.3	29.2
Sicily	93,345	19.4	100,003	20.8	7.5
Tuscany	183,036	50.0	202,326	55.3	10.6
Umbria	48,025	56.1	53,586	62.8	12.0
Veneto	148,053	30.5	154,112	31.8	4.0
Italy	1,445,792	24.5	1,630,126	27.6	12.8

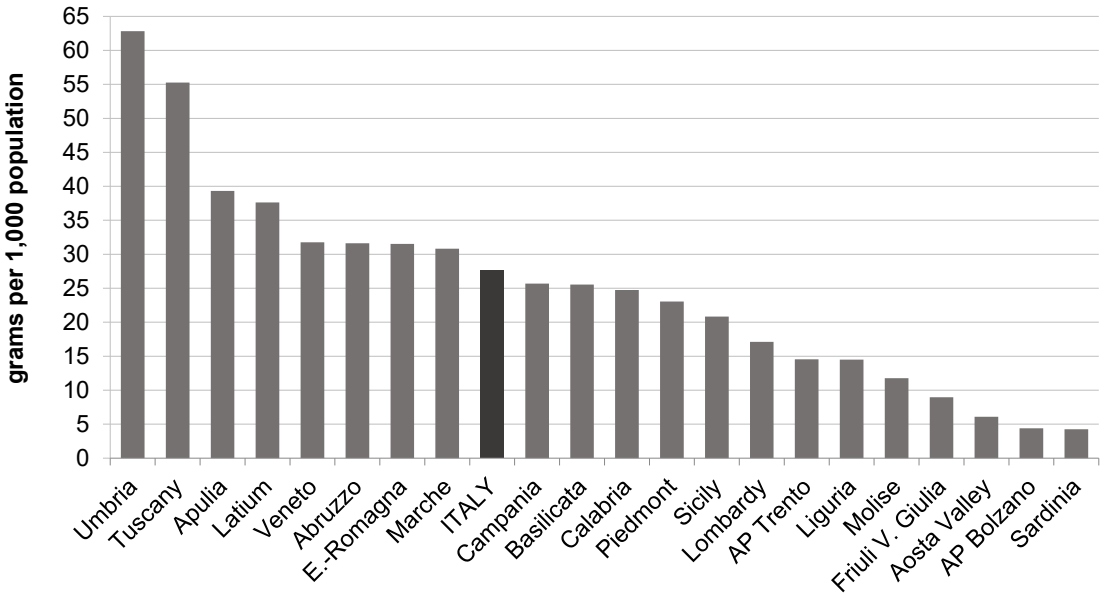

Figure 9.Total and regional demand (public and private) for normal human immunoglobulins for subcutaneous/ intramuscular use, expressed in grams per 1,000 population, 2024 (adapted by the CNS on data from the Traceability information flow)

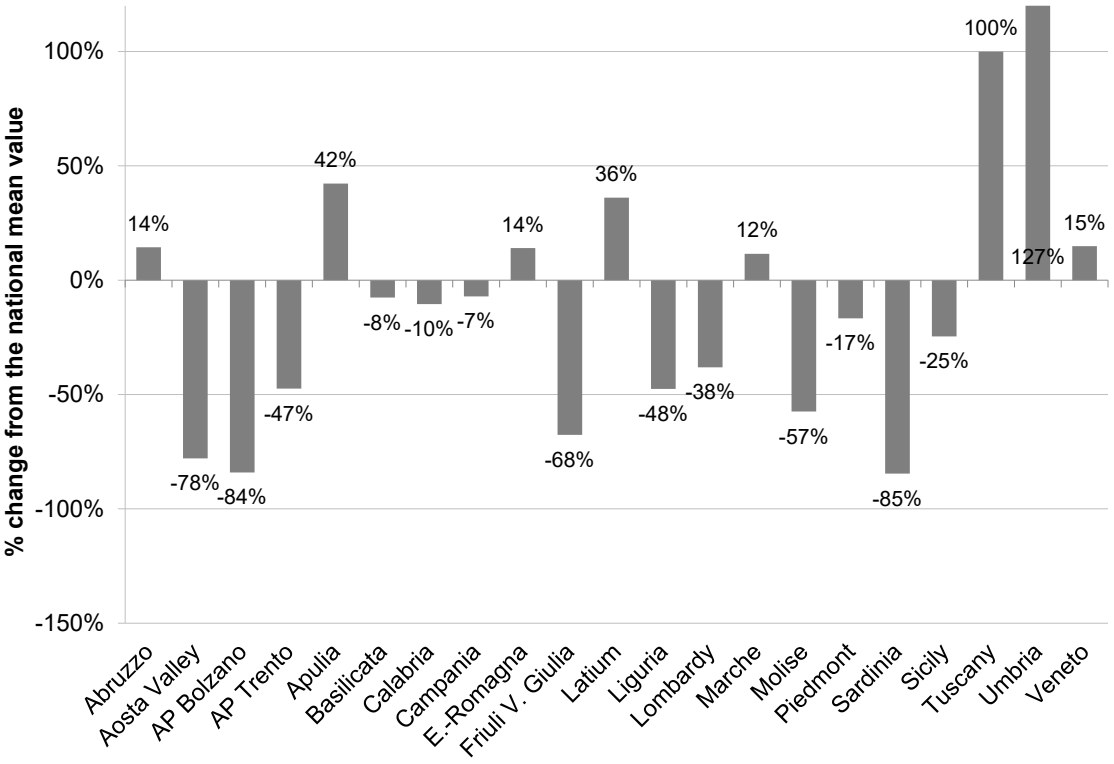

Figure 10. Percentage change from the national mean value of standardised regional demand for normal human immunoglobulins for subcutaneous/ intramuscular use in 2024 (adapted by the CNS on data from the Traceability information flow)

Normal human immunoglobulins for intravenous use

Finally, Table 10 reports on the total and standardised demands for IG for intravenous use in 2023-2024.

Even, in this case, a general increase (about +1.9%) was observed, while it was not confirmed in Basilicata, Emilia-Romagna, Friuli V. Giulia, Liguria, Marche, Molise, Umbria and Veneto.

Figure 11 shows the standardised regional demand for IVIGs in 2024 as recorded by the drug Traceability system. The highest demand for IVIGs was recorded in Aosta Valley, Marche and Emilia-Romagna, with volumes ranging between 168.1 and 121.5 grams per 1,000 population (+94%, +48% and +40% respectively, compared to the national mean value - Figure 12). The Regions where the standardized demand was lower were Calabria and Molise with recorded volumes between 45 and 54 grams per 1,000 population.

Table 10. Total demand (public and private) and total standardised demand for normal human immunoglobulins for intravenous use, expressed in grams and grams per 1,000 population, and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	g	g per 1,000 pop	g	g per 1,000 pop	
Abruzzo	93,976	73.8	119,428	94.1	27.4
Aosta Valley	17,673	143.5	20,651	168.1	17.1
AP Bolzano	51,386	96.2	59,907	111.4	15.8
AP Trento	46,590	85.8	52,550	96.4	12.3
Apulia	298,811	76.5	307,644	79.1	3.4
Basilicata	43,718	81.3	30,922	58.0	-28.7
Calabria	73,186	39.6	82,780	45.0	13.6
Campania	311,946	55.6	323,435	57.8	4.0
E.-Romagna	591,260	133.2	541,047	121.5	-8.8
Friuli V. Giulia	149,505	125.2	128,333	107.4	-14.2
Latium	359,267	62.8	370,656	64.9	3.3
Liguria	190,040	126.1	180,725	119.8	-5.0
Lombardy	888,738	89.1	958,291	95.7	7.4
Marche	191,580	129.1	190,785	128.7	-0.3
Molise	18,625	64.1	15,470	53.5	-16.5
Piedmont	437,510	102.9	438,983	103.3	0.3
Sardinia	123,755	78.4	146,498	93.3	19.0
Sicily	296,963	61.7	301,448	62.8	1.9
Tuscany	348,801	95.2	364,541	99.6	4.6
Umbria	77,748	90.8	76,265	89.4	-1.5
Veneto	415,098	85.6	408,605	84.2	-1.6
Italy	5,026,172	85.2	5,118,962	86.8	1.9

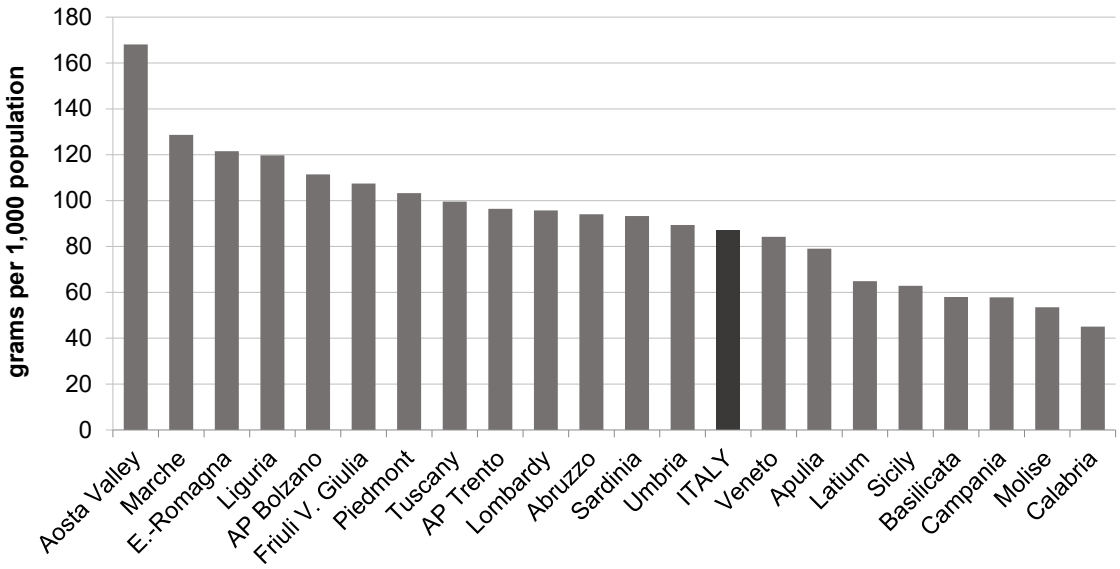

Figure 11. Total and regional demand (public and private) for normal human immunoglobulins for intravenous use, expressed in grams per 1,000 population, 2024 (adapted by the CNS on data from the Traceability information flow)

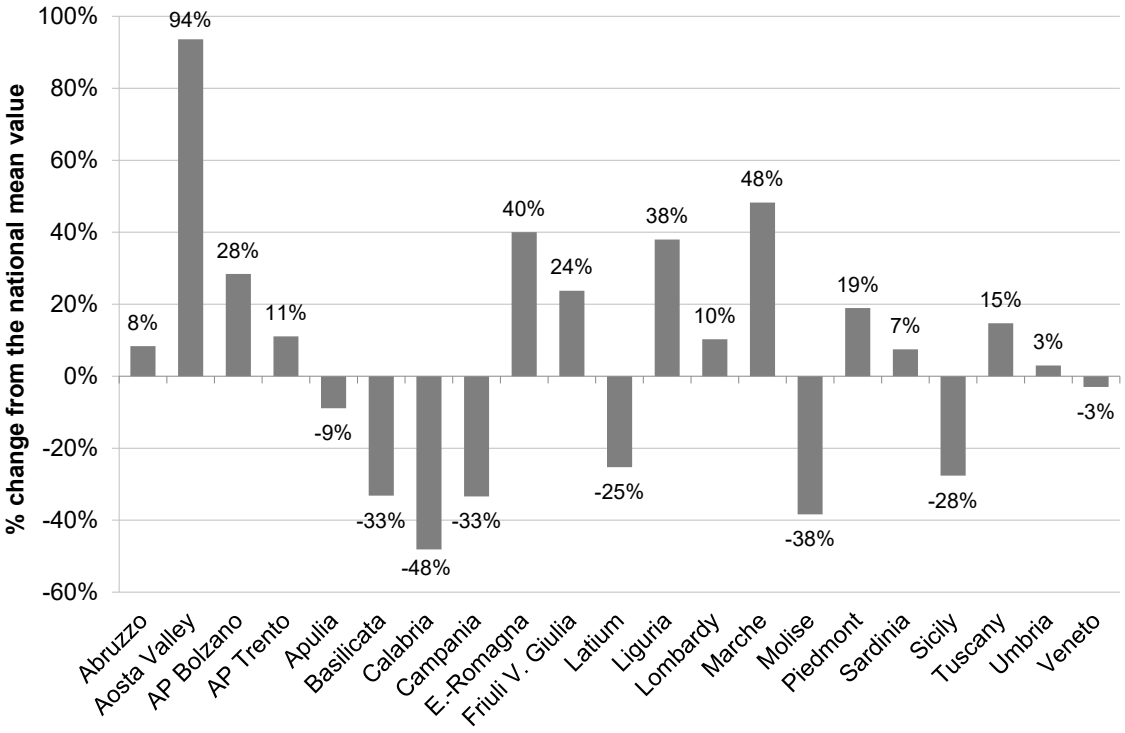

Figure 12. Percentage change from the national mean value of standardised regional demand for normal human immunoglobulins for intravenous use in 2024 (adapted by the CNS on data from the Traceability information flow)

ANTITHROMBIN (ATC B01AB02)

Antithrombin (AT) is a hepatic synthesised glycoprotein present in plasma at a concentration of about 150 µg / mL (19). It is a protease inhibitor, belonging to the serpentine family or serine protease inhibitors. It is the most powerful natural coagulation inhibitor that plays a key role in haemostatic balance. It inhibits the action of all activated coagulation factors, except for FV and FVIII. It has a particular affinity for thrombin and is also called heparin cofactor, as the anticoagulant action of heparin is mediated by AT. It also has anti-inflammatory and anti-aggregating properties mediated by the release of prostacyclines by endothelial cells (20, 21).

Table 11 shows the names of AT drugs currently available on the Italian market and the relative quantity of the active ingredients they contain measured in International Units (IUs).

Table 11. Products containing antithrombin currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
025766039	KYBERNIN P*IV FL 500IU+10mL+SET	500	CSL BEHRING SpA	H
027113012	ANTITROMBINA III IMMUNO*FL10mL	500	BAXALTA Italy Srl	H
029378015	AT III KED*500IU+FL 10mL+SET	500	KEDRION SpA	H
031118019	ATENATIV*IV FL 500IU+FL 10mL	500	OCTAPHARMA Italy SpA	H
034330035	ANBINEX*FL 500IU+SIR 10mL+SET	500	GRIFOLS ITALIA SpA	H
041800018	ATKED*FL 500IU+FL 20mL+SET	500	KEDRION SpA	H
044565012	ATTERTIUM FL 500IU+SIR 10mL	500	GRIFOLS ITALIA SpA	C(nn)
025766027	KYBERNIN P*IV FL 1000IU+F 20mL	1000	CSL BEHRING SpA	H
027113024	ANTITROMBINA III IMMUNO*FL20mL	1000	BAXALTA Italy Srl	H
029378027	AT III KED*1000IU+FL 20mL+SET	1000	KEDRION SpA	H
031118021	ATENATIV*IV FL 1000IU+FL 20mL	1000	OCTAPHARMA Italy SpA	H
034330047	ANBINEX*FL 1000IU+SIR 20mL+SET	1000	GRIFOLS ITALIA SpA	H
041800020	ATKED*FL 1000IU+FL 20mL+SET	1000	KEDRION SpA	H
044565024	ATTERTIUM FL 1000IU+SIR 20mL	1000	GRIFOLS ITALIA SpA	C(nn)
029378039	AT III KED*2000IU+FL 20mL+SET	2000	KEDRION SpA	H
041800032	ATKED*FL 2000IU+FL 20mL+SET	2000	KEDRION SpA	H

Quantification and characterisation of the demand

Table 12 shows the total demand (expressed in IUs) and the total standardised demand (expressed in IUs *per capita*) for AT in the two-year period 2023-2024 with the relative percentage changes at national and regional levels.

In 2024, total AT demand was 88,839,500 IUs, equal to 1.5 IUs *per capita*, showing a strong decrease from the consumption recorded in the previous year (-25% compared to 2023). The decrease affected all Regions and APs. The Region where there was the most evident usage restraint was the AP of Trento (-99.8%).

Figure 13 shows the regional and national standardised demand for AT in 2024. The Regions with the highest *per capita* demand were Calabria, Sicily, Molise and Friuli V. Giulia, with a demand of 3.3 IUs for the first one and 2.9, 2.4 and 2.0 IUs respectively for the other three Regions. The lowest demand, less than 1 IUs *per capita*, was recorded in the AP of Trento, Aosta Valley, Basilicata, AP of Bolzano, Veneto and Umbria (range 0.002-0.9 IUs).

Table 12. Total demand (public and private) and total standardised demand for antithrombin, expressed in International Units and International Units *per capita*, and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	3,304,500	2.6	1,443,500	1.1	-56.2
Aosta Valley	414,000	3.4	105,000	0.9	-74.6
AP Bolzano	200,000	0.4	200,000	0.4	-0.6
APTrento	502,000	0.9	1,000	0.0	-99.8
Apulia	6,818,500	1.7	6,610,000	1.7	-2.6
Basilicata	1,470,000	2.7	409,000	0.8	-72.0
Calabria	7,467,000	4.0	6,054,500	3.3	-18.6
Campania	13,163,500	2.3	10,817,000	1.9	-17.6
E.-Romagna	8,334,500	1.9	4,622,000	1.0	-44.7
Friuli V. Giulia	2,980,000	2.5	2,344,000	2.0	-21.4
Latium	14,021,000	2.5	11,134,500	1.9	-20.5
Liguria	3,266,500	2.2	2,568,500	1.7	-21.4
Lombardy	11,187,500	1.1	9,785,500	1.0	-12.8
Marche	2,898,000	2.0	2,350,000	1.6	-18.8
Molise	708,000	2.4	697,000	2.4	-1.1
Piedmont	6,791,500	1.6	6,423,500	1.5	-5.4
Sardinia	2,262,500	1.4	2,157,500	1.4	-4.2
Sicily	16,677,500	3.5	13,928,000	2.9	-16.2
Tuscany	7,931,500	2.2	6,055,500	1.7	-23.6
Umbria	1,003,000	1.2	90,000	0.1	-91.0
Veneto	6,591,500	1.4	1,043,500	0.2	-84.2
Italy	117,992,500	2.0	88,839,500	1.5	-24.7

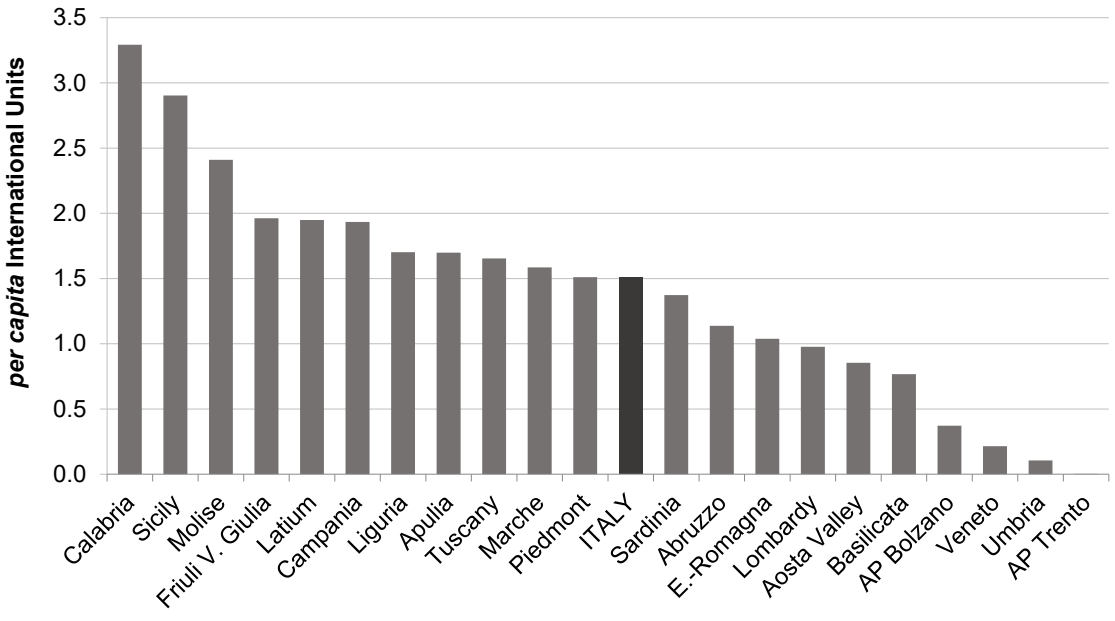

Figure 13. Total and regional demand (public and private) for antithrombin, expressed in International Units *per capita*, 2024 (adapted by the CNS on data from the Traceability information flow)

Figure 14 shows the difference between the regional *per capita* percentage and the national mean value for the year 2024.

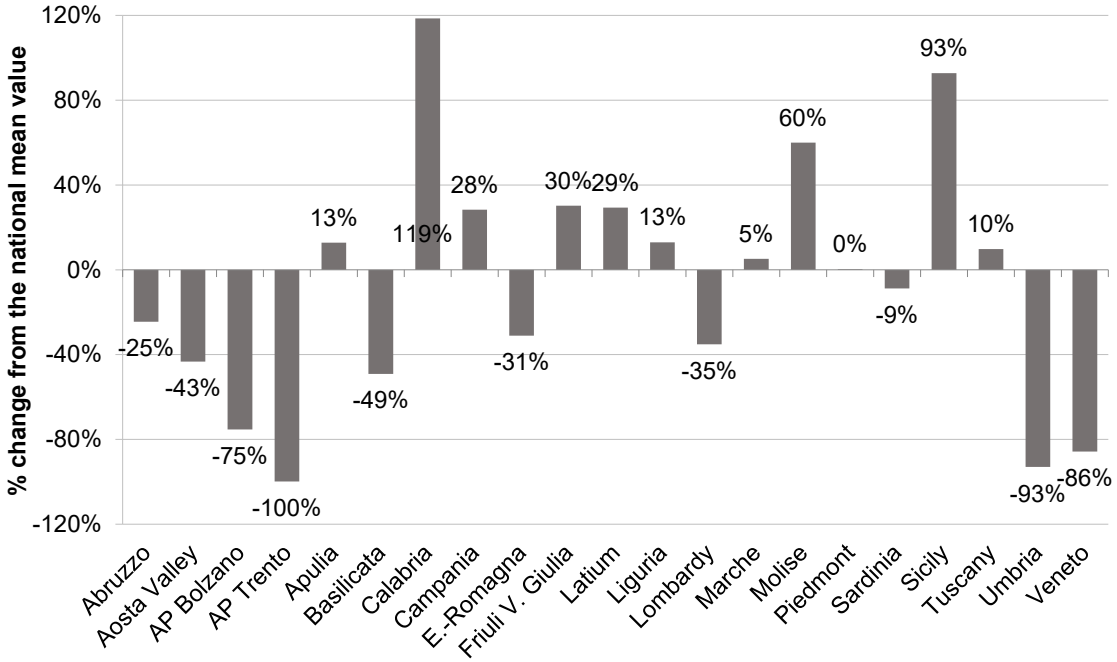

Figure 14. Percentage change from the national mean value of standardised regional demand for antithrombin in 2024 (adapted by the CNS on data from the Traceability information flow)

COAGULATION FACTOR VIII (ATC B02BD02), COAGULATION FACTOR VIII AND VON WILLEBRAND FACTOR IN COMBINATION (ATC B02BD06), VON WILLEBRAND FACTOR (ATC B02BD10), RECOMBINANT FACTOR VIII (ATC B02BD02)

Coagulation FVIII is used in the replacement therapy of haemophilia A, a rare, haemorrhagic, hereditary, x-linked or acquired recessive disorder caused by FVIII deficiency. Depending on the level of activity of the circulating FVIII, there are severe forms of haemophilia A (FVIII <1%), moderate (between 1 and 5%) and mild (>5%) (22).

Products containing FVIII are divided in plasma-derived concentrates (pdFVIII) and products obtained with genetic recombination techniques (rFVIII) (23). PdFVIII concentrates are obtained from plasma pools from thousands of donors. FVIII is initially separated from the plasma by cold precipitation (cryoprecipitation) and then further purified with different techniques such as ion exchange and affinity chromatography (24).

The number of FVIII units administered is expressed in IUs, according to the current international WHO standards (25) for human FVIII concentrates. One IU is equivalent to the amount of FVIII in 1 millilitre (mL) of normal human plasma. The calculation of the required dosage is based on empirical evidence that 1 IU of FVIII per kilogram of body weight increases the plasma activity of FVIII by 2.1 ± 0.4% of normal activity.

Many of the pdFVIII concentrates also contain von Willebrand Factor (vWF) with a different ratio compared to the FVIII content: following clinical trials supporting their efficacy, some of these drugs were approved for both the treatment of haemophilia and of von Willebrand disease (26).

The recombinant products obtained with genetic engineering techniques became part of clinical practice in Italy in the 1990s. The recombinant protein is synthesised by inserting the Regions encoding the human FVIII gene in Chinese hamster ovary cells (CHO) or in newborn hamster kidney cells (BHK) (23).

Tables 13-15 show the brand names of the preparations containing both plasma-derived and recombinant FVIII currently on the market in Italy and the relative amount of active ingredient contained expressed in IUs.

Table 13. Products containing plasma-derived coagulation Factor VIII currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
033657014	BERIATE*F 250IU+SOLV+SET	250	CSL BEHRING SpA	A
038541013	HAEMOCTIN*FL 250IU+FL 5mL+SIR	250	BIOTEST PHARMA GMBH	A
023564216	EMOCLOT*FL 500IU+FL 10mL+SET	500	KEDRION SpA	A
033657026	BERIATE*F 500IU+SOLV+SET	500	CSL BEHRING SpA	A
038541025	HAEMOCTIN*FL 500IU+FL 10mL+SIR	500	BIOTEST PHARMA GMBH	A
041649017	KLOTT*FL 500IU+FL 10mL+SET	500	KEDRION SpA	A
023564228	EMOCLOT*FL 1000IU+FL 10mL+SET	1000	KEDRION SpA	A
033657038	BERIATE*F 1000IU+SOLV+S	1000	CSL BEHRING SpA	A
038541037	HAEMOCTIN*FL 1000IU+FL 10mL+SIR	1000	BIOTEST PHARMA GMBH	A
041649029	KLOTT*FL 1000IU+FL 10mL+SET	1000	KEDRION SpA	A
033657040	BERIATE*FL 2000IU+FL 10mL	2000	CSL BEHRING SpA	A

Table 14. Products containing plasma-derived coagulation Factor VIII and von Willebrand Factor in combination, and Von Willebrand Factor currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
Factor VIII and von Willebrand Factor in combination				
033077088	ALPHANATE*INF 1F 250IU+SIR+AD	250	GRIFOLS ITALIA SpA	A
033866043	FANHDI*INF FL 250IU+SIR SOLV+S	250	GRIFOLS ITALIA SpA	A
037148018	TALATE*250IU/190IU+FL5mL+SIR	250	BAXALTA INN.Gmbh	A
040112017	OCTANATE*INIET FL 250IU+FL 5mL	250	OCTAPHARMA Italy SpA	A
042939013	VONCENTO*250IU/600IU+FL 5mL	250	CSL BEHRING SpA	C(nn)
044564019	PLITATE*INF FL 250IU+SIR SOLV+SET	250	GRIFOLS ITALIA SpA	C(nn)
023308152	EMOWIL*1F 500IU+F 10mL	500	KEDRION SpA	A
026600080	HAEMATEP*FL 500IU+FL 10mL+SET	500	CSL BEHRING SpA	A
033077090	ALPHANATE*INF 1F 500IU+SIR+AD	500	GRIFOLS ITALIA SpA	A
033866056	FANHDI*INF FL 500IU+SIR SOLV+S	500	GRIFOLS ITALIA SpA	A
037148020	TALATE*500IU/375IU+FL10mL+SIR	500	BAXALTA INN. Gmbh	A
039385036	WILATE*FL 500+500IU+FL 5mL+SIR	500	OCTAPHARMA Italy SpA	A
040112029	OCTANATE*INIET FL 500IU+FL 10mL	500	OCTAPHARMA Italy SpA	A
040112056	OCTANATE*INIET FL 5mL100IU/mL	500	OCTAPHARMA Italy SpA	A
042939025	VONCENTO*500IU/1200IU+FL 10mL	500	CSL BEHRING SpA	C(nn)
042939037	VONCENTO*500IU/1200IU+FL 5mL	500	CSL BEHRING SpA	C(nn)
044564021	PLITATE*INF FL 500IU+SIR SOLV+SET	500	GRIFOLS ITALIA SpA	C(nn)
023308188	EMOWIL*1F 1000IU+F 10mL	1000	KEDRION SpA	A
026600078	HAEMATEP*FL 1000IU+FL 15mL+SET	1000	CSL BEHRING SpA	A
033077102	ALPHANATE*INF 1F 1000IU+SIR+AD	1000	GRIFOLS ITALIA SpA	A
033866068	FANHDI*INF FL 1000IU+SIR SOLV+S	1000	GRIFOLS ITALIA SpA	A
037148032	TALATE*1000IU/750IU+FL10mL+SIR	1000	BAXALTA Italy Srl	A
039385024	WILATE*FL 900+800IU+FL 10mL+SIR	1000	OCTAPHARMA Italy SpA	A
039385048	WILATE*FL 1000+1000IU+FL 10mL+SI	1000	OCTAPHARMA Italy SpA	A
040112031	OCTANATE*INIET FL 1000IU+FL 10mL	1000	OCTAPHARMA Italy SpA	A
040112068	OCTANATE*INIET FL 5mL 200IU/mL	1000	OCTAPHARMA Italy SpA	A
042939049	VONCENTO*1000IU/2400IU+FL 10mL	1000	CSL BEHRING SpA	C(nn)
044564033	PLITATE*INF FL1000IU+SIR SOLV+SET	1000	GRIFOLS ITALIA SpA	C(nn)
033077114	ALPHANATE*INF 1F 1500IU+SIR+AD	1500	GRIFOLS ITALIA SpA	A
033866070	FANHDI*INF FL1500IU+SIR SOLV+S	1500	GRIFOLS ITALIASpA	A
044564045	PLITATE*INF FL1500IU+SIRSOLV+SET	1500	GRIFOLS ITALIA SpA	C(nn)
033077126	ALPHANATE *INF 1F 2000 IU+SIR+SET	2000	GRIFOLS ITALIA SpA	C
von Willebrand Factor				
037392026	WILFACTIN* 500IU+FL 5mL	500	LFB	C
037392014	WILFACTIN*1000IU+FL 10mL	1000	LFB	C
037392038	WILFACTIN*2000IU+FL 20mL	2000	LFB	C
von Willebrand Recombinant Factor				
046994012	VEYVONDI*650 UI+FL 5mL+DISP	650	BAXALTA INN. GmbH	C
046994024	VEYVONDI*1300 UI+ FL 10mL+DISP	1300	BAXALTA INN. GmbH	C

Table 15. Products containing recombinant coagulation Factor VIII and long-acting recombinant Factor VIII currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
028687010	RECOMBINATE*FL 250IU+FL 10mL	250	BAXALTA Italy Srl	A
028687046	RECOMBINATE*FL 250IU+FL 5mL	250	BAXALTA Italy Srl	A
028687073	RECOMBINATE*FL 250IU+FL 5mL	250	BAXALTA Italy Srl	A
028687109	RECOMBINATE*FL 250IU+FL 10mL	250	BAXALTA Italy Srl	A
034421014	REFACTOAF*IV 1FL 250IU+SIR 4mL	250	PFIZER ITALIA Srl	A

AIC code	Brand name	IU	Manufacturer	NHS class
034421091	REFACTOAF*IV 1SIR PRER 250IU	250	PFIZER ITALIA Srl	A
034955017	KOGENATE BAYER*250IU+1FL+1KI	250	BAYER SpA	A
034955043	KOGENATE BAYER*FL 250IU+SIR+1KI	250	BAYER SpA	A
034955070	KOGENATE BAYER*EV 250IU+SIR	250	BAYER SpA	A
034956019	HELIXATE NEXGEN*250IU+1FL+1KIT	250	CSL BEHRING SpA	A
036160012	ADVATE*FL 250IU+FL SOLV 5mL	250	BAXTER SpA	A
036160075	ADVATE*FL 250IU+FL SOLV 2mL	250	BAXALTA Italy Srl	A
036160113	ADVATE*FL 250IU+FL SOLV 5mL	250	BAXALTA Italy Srl	A
036160176	ADVATE*FL 250IU+FL SOLV 2mL	250	BAXALTA Italy Srl	A
043153016	NOVOEIGHT*EV FL 250IU+SIR 4mL	250	NOVO NORDISK SpA	A
043534015	NUWIQ*EV FL 250IU+SIR 2,5mL	250	KEDRION SpA	A
044725012	IBLIAS*FL POLV EV 250IU+FL 2,5mL	250	BAYER SpA	A
044726014	KOVALTRY*1FL POLV EV 250IU+SOLV	250	BAYER SpA	A
044726026	KOVALTRY*1FL POLV EV 250IU+SOLV	250	BAYER SpA	A
044726115	KOVALTRY* 1FL POLV EV 250 IU	250	BAYER AG	C(nn)
044726127	KOVALTRY* 1FL POLV EV 250 IU	250	BAYER AG	A
045255015	AFSTYLA 250IU+FL SOLV 2,5mL+SIR	250	CSL BEHRING GmbH	A
045273012	VIHUMA*EV 250IU+FL SOLV 2,5mL	250	OCTAPHARMA AB	C(nn)
028687022	RECOMBINATE*FL 500IU+FL 10mL	500	BAXALTA Italy Srl	A
028687059	RECOMBINATE*FL 500IU+FL 5mL	500	BAXALTA Italy Srl	A
028687085	RECOMBINATE*FL 500IU+FL 5mL	500	BAXALTA Italy Srl	A
028687111	RECOMBINATE*FL 500IU+FL 10mL	500	BAXALTA Italy Srl	A
034421026	REFACTOAF*IV 1FL 500IU+SIR 4mL	500	PFIZER ITALIA Srl	A
034421065	REFACTOAF*IV 1SIR PRER 500IU	500	PFIZER ITALIA Srl	A
034955029	KOGENATE BAYER*500IU+1FL+1KIT	500	BAYER SpA	A
034955056	KOGENATE BAYER*FL 500IU+SIR	500	BAYER SpA	A
034955082	KOGENATE BAYER*EV 500IU+SIR	500	BAYER SpA	A
034956021	HELIXATE NEXGEN*500IU+1FL+1KIT	500	CSL BEHRING SpA	A
036160024	ADVATE*FL 500IU+FL SOLV 5mL	500	BAXTER SpA	A
036160087	ADVATE*FL 500IU+FL SOLV 2mL	500	BAXALTA Italy Srl	A
036160125	ADVATE*FL 500IU+FL SOLV 5mL	500	BAXALTA Italy Srl	A
036160188	ADVATE*FL 500IU+FL SOLV 2mL	500	BAXALTA Italy Srl	A
043153028	NOVOEIGHT*EV FL 500IU+SIR 4mL	500	NOVO NORDISK SpA	A
043534027	NUWIQ*EV FL 500IU+SIR 2,5mL	500	KEDRION SpA	A
044725024	IBLIAS*FL POLV EV 500IU+FL 2,5mL	500	BAYER SpA	A
044726038	KOVALTRY*1FL POLV EV 500IU+SOLV	500	BAYER SpA	A
044726040	KOVALTRY*1FL POLV EV 500IU+SOLV	500	BAYER SpA	A
044726139	KOVALTRY*1FL POLV EV 500IU	500	BAYER AG	C(nn)
044726141	KOVALTRY*1FL POLV EV 500IU	500	BAYER AG	A
045255027	AFSTYLA 500IU+FL SOLV 2,5mL+SIR	500	CSL BEHRING GmbH	A
045273024	VIHUMA*EV500IU+FL SOLV 2,5mL	500	OCTAPHARMA AB	C(nn)
028687034	RECOMBINATE*FL 1000IU+FL 10mL	1000	BAXALTA Italy Srl	A
028687061	RECOMBINATE*FL 1000IU+FL 5mL	1000	BAXALTA Italy Srl	A
028687097	RECOMBINATE*FL 1000IU+FL 5mL	1000	BAXALTA Italy Srl	A
028687123	RECOMBINATE*FL 1000IU+FL 10mL	1000	BAXALTA Italy Srl	A
034421038	REFACTO AF*IV 1FL 1000IU+SIR 4mL	1000	PFIZER ITALIA Srl	A
034421077	REFACTO AF*IV 1SIR PRER 1000IU	1000	PFIZER ITALIA Srl	A
034955031	KOGENATE BAYER*1000IU+1FL+1KIT	1000	BAYER SpA	A
034955068	KOGENATE BAYER*FL 1000IU+SIR	1000	BAYER SpA	A
034955094	KOGENATE BAYER*EV 1000IU+SIR	1000	BAYER SpA	A
034956033	HELIXATE NEXGEN*1000IU+1FL+KIT	1000	CSL BEHRING SpA	A
036160036	ADVATE*FL 1000IU+FL SOLV 5mL	1000	BAXTER SpA	A
036160099	ADVATE*FL 1000IU+FL SOLV 2mL	1000	BAXALTA Italy Srl	A
036160137	ADVATE*FL 1000IU+FL SOLV 5mL	1000	BAXALTA Italy Srl	A
036160190	ADVATE*FL 1000IU+FL SOLV 2mL	1000	BAXALTA Italy Srl	A
043153030	NOVOEIGHT*EV FL 1000IU+SIR 4mL	1000	NOVO NORDISK SpA	A
043534039	NUWIQ*EV FL 1000IU+SIR 2,5mL	1000	KEDRION SpA	A

AIC code	Brand name	IU	Manufacturer	NHS class
044725036	IBLIAS*FL POLV EV 1000IU+2,5 mL	1000	BAYER SpA	A
044726053	KOVALTRY*FL POLV EV 1000IU+SOLV	1000	BAYER SpA	A
044726065	KOVALTRY*FL POLV EV 1000IU+SOLV	1000	BAYER SpA	A
044726154	KOVALTRY* 1FL POLV EV 1000 IU	1000	BAYER AG	C(nn)
044726166	KOVALTRY* 1FL POLV EV 1000 IU	1000	BAYER AG	A
045255039	AFSTYLA 1000IU+FL SOLV 2,5mL+SIR	1000	CSL BEHRING GmbH	A
045273036	VIHUMA*EV 1000IU+FL SOLV 2,5mL	1000	OCTAPHARMA AB	C(nn)
036160048	ADVATE*FL 1500IU+FL SOLV 5mL	1500	BAXTER SpA	A
036160101	ADVATE*FL 1500IU+FL SOLV 2mL	1500	BAXALTA Italy Srl	A
036160149	ADVATE*FL 1500IU+FL SOLV 5mL	1500	BAXALTA Italy Srl	A
036160202	ADVATE*FL 1500IU+FL SOLV 2mL	1500	BAXALTA Italy Srl	A
043153042	NOVOEIGHT*EV FL 1500IU+SIR 4mL	1500	NOVO NORDISK SpA	A
043534080	NUWIQ*EV FL 1500UI+SIR 2,5ML	1500	OCTAPHARMA AB	A
045255041	AFSTYLA 1500IU+FL SOLV 2,5mL+SIR	1500	CSL BEHRING GmbH	A
034421040	REFACTOAF*IV 1FL 2000IU+SIR 4mL	2000	PFIZER ITALIA Srl	A
034421089	REFACTOAF*IV 1SIR PRER 2000IU	2000	PFIZER ITALIA Srl	A
034955106	KOGENATE BAYER*EV 2000IU+SIR	2000	BAYER SpA	A
034955118	KOGENATE BAYER*EV 2000IU+SIR	2000	BAYER SpA	A
036160051	ADVATE*FL 2000IU+FL SOLV 5mL	2000	BAXTER SpA	A
036160152	ADVATE*FL 2000IU+FL SOLV 5mL	2000	BAXALTA Italy Srl	A
043153055	NOVOEIGHT*EV FL 2000IU+SIR 4mL	2000	NOVO NORDISK SpA	A
043534041	NUWIQ*EV FL 2000IU+SIR 2,5mL	2000	KEDRION SpA	A
044725048	IBLIAS*FL POLV EV 2000IU+FL 5mL	2000	BAYER SpA	A
044726077	KOVALTRY*FL POLV EV 2000IU+SOLV	2000	BAYER SpA	A
044726089	KOVALTRY*FL POLV EV 2000IU+SOLV	2000	BAYER SpA	A
045255054	AFSTYLA 2000IU+FL SOLV 2,5mL+SIR	2000	CSL BEHRING GmbH	A
045273048	VIHUMA*EV 2000IU+FL SOLV 2,5mL	2000	OCTAPHARMA AB	C(nn)
043534054	NUWIQ*EV FL 2500IU+SIR 2,5mL	2500	OCTAPHARMA AB	A
045255066	AFSTYLA 2500IU+FL SOLV 2,5mL+SIR	2500	CSL BEHRING GmbH	A
045273051	VIHUMA*EV 2500IU+FL SOLV 2,5mL	2500	OCTAPHARMA AB	C(nn)
034421053	REFACTO AF*IV 1SIR PRER 3000IU	3000	PFIZER ITALIA Srl	A
034955120	KOGENATE BAYER*EV 3000IU+SIR	3000	BAYER SpA	A
034955132	KOGENATE BAYER*EV 3000IU+SIR	3000	BAYER SpA	A
034956058	HELIXATE NEXGEN*3000IU+1FL+KIT	3000	CSL BEHRING SpA	A
036160063	ADVATE*FL 3000IU+FL SOLV 5mL	3000	BAXTER SpA	A
036160164	ADVATE*FL 3000IU+FL SOLV 5mL	3000	BAXALTA Italy Srl	A
043153067	NOVOEIGHT*EV FL 3000IU+SIR 4mL	3000	NOVO NORDISK SpA	A
043534066	NUWIQ*EV FL 3000IU+SIR 2,5mL	3000	OCTAPHARMA AB	A
044725051	IBLIAS*FL POLV EV 3000IU+FL 5mL	3000	BAYER SpA	A
044726091	KOVALTRY*FL POLV EV 3000IU+SOLV	3000	BAYER SpA	A
044726103	KOVALTRY*FL POLV EV 3000IU+SOLV	3000	BAYER SpA	A
045255078	AFSTYLA 3000IU+FL SOLV 2,5mL+SIR	3000	CSL BEHRING GmbH	A
045273063	VIHUMA*EV 3000IU+FL SOLV 2,5mL	3000	OCTAPHARMA AB	C(nn)
043534078	NUWIQ*EV FL 4000IU+SIR 2,5mL	4000	OCTAPHARMA AB	C
045273075	VIHUMA*EV 4000IU+FL SOLV 2,5mL	4000	OCTAPHARMA AB	C(nn)
044726178	KOVALTRY*30FL 250UI+ SIR 3mL	7500	BAYER AG	C(nn)
044726180	KOVALTRY*30FL 250UI+ SIR 5mL	7500	BAYER AG	C(nn)
044726192	KOVALTRY*30FL 500UI+ SIR 3mL	15000	BAYER AG	C(nn)
044726204	KOVALTRY*30FL 500UI+SIR 5mL	15000	BAYER AG	C(nn)
044726216	KOVALTRY*30FL 1000UI+SIR 3mL	30000	BAYER AG	C(nn)
044726228	KOVALTRY*30FL 1000UI+SIR 5mL	30000	BAYER AG	C(nn)
044726230	KOVALTRY*30FL 2000UI+SIR 5mL	60000	BAYER AG	C(nn)
044726242	KOVALTRY*30FL 3000UI+SIR 5mL	90000	BAYER AG	C(nn)
Extended half-life Recombinant Factor VIII				
044563017	ELOCTA*IV 1FL 250IU+SIR PRERI	250	SOBI Srl	A
045936010	ADYNOVI*EV 250 IU+FL 2 mL+DISP	250	BAXALTA INN. Gmbh.	A
045936022	ADYNOVI*EV 250 IU + FL 2 mL + DISP	250	BAXALTA INN. Gmbh.	A

AIC code	Brand name	IU	Manufacturer	NHS class
045936034	ADYNOVI*EV 250 IU + FL 5 mL + DISP	250	BAXALTA INN. Gmbh.	A
045936046	ADYNOVI*EV 250 IU + FL 5 mL + DISP	250	BAXALTA INN. Gmbh	A
047418013	JIVI* EV 250 IU + FL SOLV 2,5 mL + SIR	250	BAYER AG	A
044563029	ELOCTA*IV 1FL 500IU+SIR PRERI	500	SOBI Srl	A
045936059	ADYNOVI*EV 500IU + FL 2 mL + DISP	500	BAXALTA INN. Gmbh.	A
045936061	ADYNOVI*EV 500IU + FL 2 mL + DISP	500	BAXALTA INN. Gmbh	A
045936073	ADYNOVI*EV 500IU + FL 5 mL + DISP	500	BAXALTA INN. Gmbh.	C(nn)
045936085	ADYNOVI*EV 500IU + FL 5 mL + DISP	500	BAXALTA INN. Gmbh	A
047418025	JIVI* EV 500 IU + FL SOLV 2,5 mL + SIR	500	BAYER AG	A
048083012	ESPEROCT* EV 500 IU + FL 4 mL + SIR	500	NOVO NORDISK A/S	A
044563031	ELOCTA*IV 1FL 750IU+SIR PRERI	750	SOBI Srl	A
044563043	ELOCTA*IV 1FL 750UI+SIR PRERI	750	SOBI Srl	A
044563056	ELOCTA*IV 1FL 1000IU+SIR PRERI	1000	SOBI Srl	A
045936097	ADYNOVI*EV 1000 IU + FL 2 mL + DISP	1000	BAXALTA INN. Gmbh	C(nn)
045936109	ADYNOVI*EV 1000 IU + FL 2 mL + DISP	1000	BAXALTA INN. Gmbh	A
045936111	ADYNOVI*EV 1000 IU + FL 5 mL + DISP	1000	BAXALTA INN. Gmbh	C(nn)
045936123	ADYNOVI*EV 1000 IU + FL 5 mL + DISP	1000	BAXALTA INN. Gmbh	A
047418037	JIVI* EV 1000 IU + FL 2,5 mL + SIR	1000	BAYER AG	A
048083024	ESPEROCT* EV 1000 IU+ FL 4 mL+ SIR	1000	NOVO NORDISK A/S	A
044563068	ELOCTA*IV 1FL 1500IU+SIR PRERI	1500	SOBI Srl	A
048083036	ESPEROCT* EV 1500 IU+ FL 4 mL+ SIR	1500	NOVO NORDISK A/S	A
044563070	ELOCTA*IV 1FL 2000IU+SIR PRERI	2000	SOBI Srl	A
045936135	ADYNOVI*EV 2000 IU + FL 5 mL + DISP	2000	BAXALTA INN. Gmbh	C(nn)
045936147	ADYNOVI*EV 2000 IU + FL 5 mL + DISP	2000	BAXALTA INN. Gmbh	A
047418049	JIVI* EV 2000 IU + FL 2,5 mL + SIR	2000	BAYER AG	A
048083048	ESPEROCT* EV 2000 IU+ FL 4 mL+ SIR	2000	NOVO NORDISK A/S	A
044563082	ELOCTA*IV 1FL 3000IU+SIR PRERI	3000	SOBI Srl	A
045936150	ADYNOVI*EV3000UI+FL5mL+DISP	3000	BAXALTA INN. Gmbh	C(nn)
045936162	ADYNOVI*EV3000UI+FL5mL+DISPPRE	3000	BAXALTA INN. Gmbh	C(nn)
047418052	JIVI* EV 3000 IU + FL 2,5 mL + SIR	3000	BAYER AG	A
048083051	ESPEROCT* EV 3000 IU+ FL 4 mL+ SIR	3000	NOVO NORDISK A/S	A
044563094	ELOCTA*IV 1FL 4000IU+SIR PRERI	4000	SOBI Srl	C(nn)
048083063	ESPEROCT* EV 4000 UI+ FL4 mL+SIR	4000	NOVO NORDISK A/S	C(nn)
044563106	ELOCTA*IV 1FL 5000IU+SIR PRERI	5000	SOBI Srl	C(nn)
048083075	ESPEROCT* EV 5000 UI+ FL4 mL+SIR	5000	NOVO NORDISK A/S	C(nn)
044563118	ELOCTA*IV 1FL 6000IU+SIR PRERI	6000	SOBI Srl	C(nn)
047418064	JIVI* 30FL 250 UI + SOLV 2,5 mL+SIR	7500	BAYER AG	C(nn)
047418076	JIVI* 30FL 500 UI + SOLV 2,5 mL+SIR	15000	BAYER AG	C(nn)
047418088	JIVI* 30FL 1000 UI + SOLV 2,5 mL+SIR	30000	BAYER AG	C(nn)
047418090	JIVI* 30FL 2000 UI + SOLV 2,5 mL+SIR	60000	BAYER AG	C(nn)
047418102	JIVI* 30FL 3000 UI + SOLV 2,5 mL+SIR	90000	BAYER AG	C(nn)

Quantification and characterisation of demand

In Italy, the total demand for both plasma-derived and recombinant formulations FVIII, was equal to 535,819,650 IUs in 2024 (Table 16); of these, about a sixth (15.7% of the total, 84,025,500 IUs) were human plasma-derived (Figure 15). The tendency to use pdFVIII varied significantly from one Region to another ranging from 1.6% in Basilicata to 26% in Tuscany. In 2024, the total FVIII demand *per capita* (plasma-derived and recombinant) was about 9 IUs essentially unchanged from 2023.

The regional *per capita* demand shows significant fluctuations ranging from about 4 IUs in Friuli V. Giulia to about 14 IUs in Latium (Figure 16).

Table 16. Total demand (public and private) and total standardised demand for coagulation Factor VIII, expressed in International Units and International Units *per capita*, and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	16,462,750	12.9	14,411,500	11.4	-12.2
Aosta Valley	603,000	4.9	589,000	4.8	-2.1
AP Bolzano	3,210,500	6.0	3,527,000	6.6	9.2
AP Trento	3,805,500	7.0	3,757,250	6.9	-1.7
Apulia	46,253,000	11.8	49,787,750	12.8	8.1
Basilicata	3,019,000	5.6	2,821,000	5.3	-5.8
Calabria	16,235,250	8.8	18,152,500	9.9	12.3
Campania	59,102,500	10.5	57,659,750	10.3	-2.2
E.-Romagna	45,408,750	10.2	53,497,500	12.0	17.4
Friuli V. Giulia	4,772,000	4.0	5,093,500	4.3	6.7
Latium	80,397,250	14.1	79,657,250	13.9	-0.8
Liguria	9,332,000	6.2	11,121,000	7.4	19.1
Lombardy	76,526,750	7.7	72,250,250	7.2	-5.9
Marche	10,671,500	7.2	10,706,500	7.2	0.4
Molise	3,322,000	11.4	2,764,500	9.6	-16.4
Piedmont	31,435,750	7.4	29,222,000	6.9	-7.0
Sardinia	13,189,000	8.4	14,102,750	9.0	7.5
Sicily	44,459,500	9.2	43,944,000	9.2	-0.8
Tuscany	26,410,250	7.2	22,055,650	6.0	-16.5
Umbria	6,679,000	7.8	6,179,500	7.2	-7.1
Veneto	34,518,000	7.1	34,519,500	7.1	-0.1
Italy	535,813,250	9.1	535,819,650	9.1	0.0

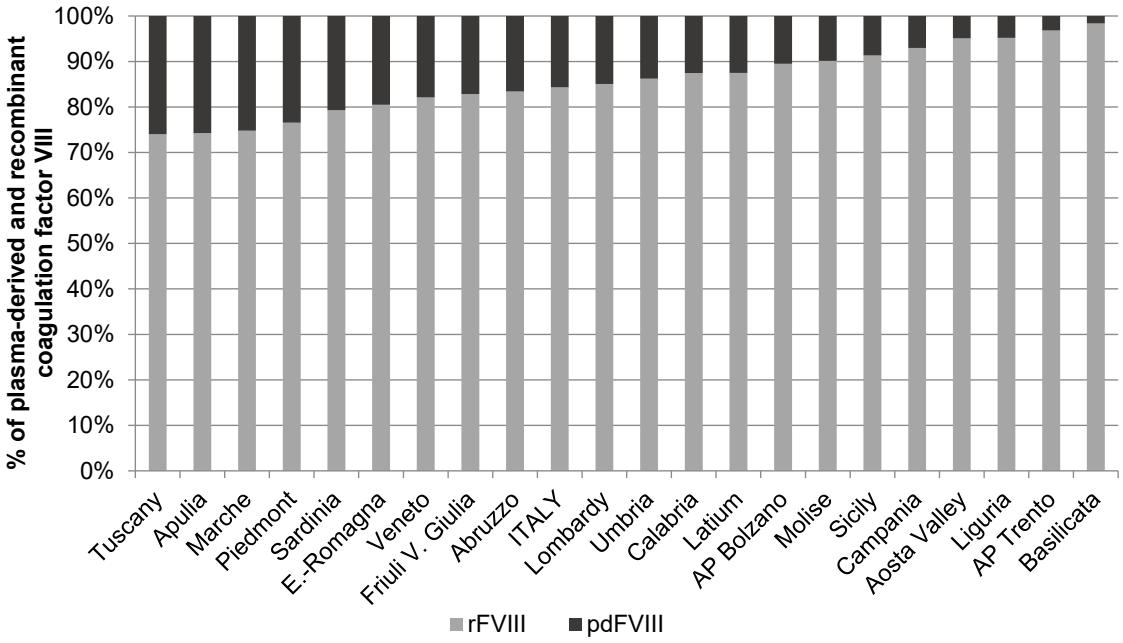

Figure 15. Percentage distribution of plasma-derived and recombinant coagulation Factor VIII, by Region, 2024 (adapted by the CNS on data from the Traceability information flow)

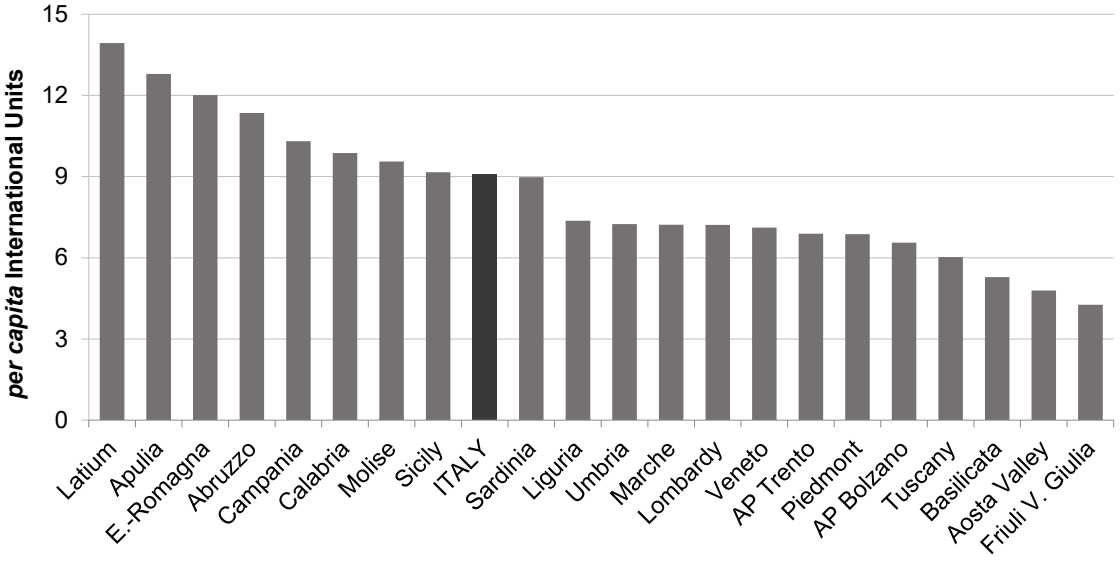

Figure 16. Total and regional demand (public and private) for coagulation Factor VIII, expressed in International Units *per capita*, 2024 (adapted by the CNS on data from the Traceability information flow)

The most significant decreases in standardised regional demand were observed in Tuscany, Molise and Abruzzo, where use decreased by -16.5% for the first, -16.4% for the second and -12.2% for the third. It is important to underline that for FVIII, strong fluctuations can occur due to the contingent needs of a few patients (immunotolerance treatments, surgeries, severe traumas, etc.). Eight Regions had a greater demand compared to the national average (Figure 17).

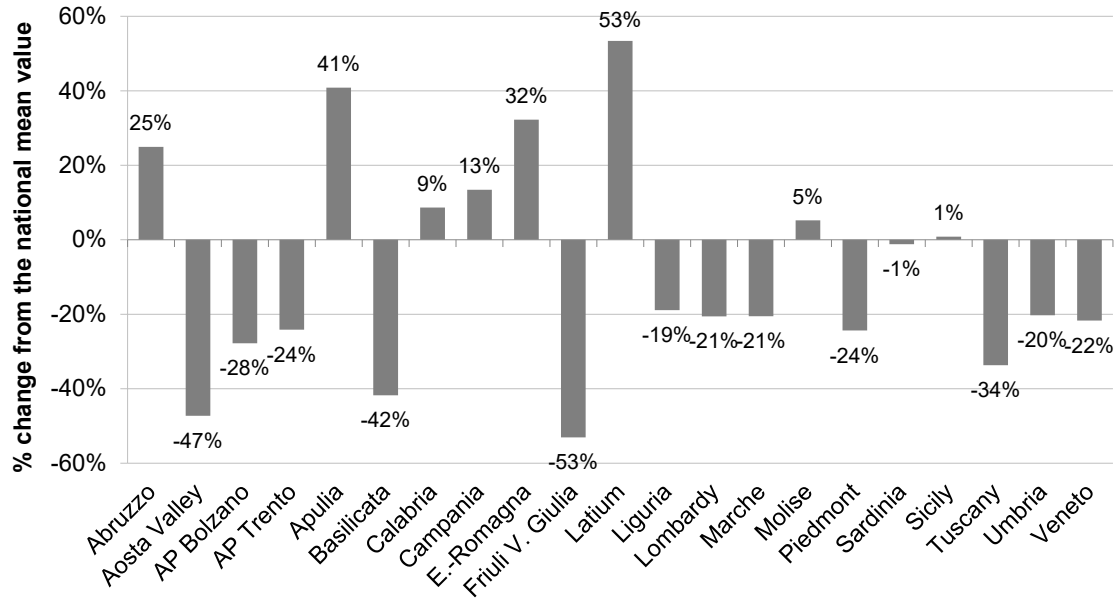

Figure 17. Percentage variation from the national mean value of standardised regional demand for coagulation Factor VIII in 2024 (adapted by the CNS on data from the Traceability information flow)

Plasma-derived Factor VIII (B02BD02), Plasma derived and Von Willebrand Factor in combination (B02BD06) and Von Willebrand Factor (B02BD10)

In 2024, the national demand for pdFVIII was about 15.7% - equivalent to 84,025,500 IUs - of the total demand. There is a downward trend of -5% compared to the 2023 value and a standardized total demand of 1.4 IU *per capita* (Table 17). *per capita* demand varied significantly with the highest volumes in Apulia (3.3 IUs *per capita*), Emilia-Romagna (2.3 IUs *per capita*), Abruzzo and Sardinia (1.9 IU *per capita*), Marche (1.8 IU *per capita*) and Latium (1.7 IUs *per capita*); the corresponding percentage variation between the aforementioned values and the Italian mean value were of +131, +65%, +32%, +31%, +28% respectively and +22% in the case of the last Region.

Table 17. Total demand (public and private) and total standardised demand for plasma-derived coagulation Factor VIII, expressed in International Units and International Units *per capita*, and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	3,927,500	3.1	2,394,000	1.9	-38.9
Aosta Valley	20,000	0.2	29,000	0.2	45.3
AP Bolzano	563,000	1.1	370,000	0.7	-34.7
AP Trento	114,000	0.2	120,000	0.2	4.8
Apulia	11,622,000	3.0	12,816,000	3.3	10.8
Basilicata	90,000	0.2	46,000	0.1	-48.5
Calabria	1,919,000	1.0	2,280,500	1.2	19.4
Campania	4,072,000	0.7	4,050,000	0.7	-0.3
E.-Romagna	5,351,750	1.2	10,449,500	2.3	94.6
Friuli V. Giulia	1,647,000	1.4	874,000	0.7	-47.0
Latium	11,402,500	2.0	9,954,500	1.7	-12.6
Liguria	313,000	0.2	536,000	0.4	71.1
Lombardy	12,380,250	1.2	10,786,000	1.1	-13.2
Marche	2,516,000	1.7	2,699,500	1.8	7.4
Molise	632,000	2.2	273,000	0.9	-56.6
Piedmont	8,499,000	2.0	6,850,500	1.6	-19.4
Sardinia	2,407,000	1.5	2,922,000	1.9	22.0
Sicily	4,129,000	0.9	3,818,000	0.8	-7.2
Tuscany	9,066,000	2.5	5,734,000	1.6	-36.7
Umbria	539,500	0.6	851,000	1.0	58.4
Veneto	7,240,000	1.5	6,172,000	1.3	-14.8
Italy	88,450,500	1.5	84,025,500	1.4	-5.0

The lowest volumes (below 1 IU *per capita*) were recorded in Molise, Sicily, Friuli V. Giulia, Campania, AP of Bolzano, Liguria, Aosta Valley, Basilicata, AP of Trento and Basilicata (Figures 18 and 19). The decrease recorded at a national level is due to twelve Italian Regions showing declining demand (range: -0.3%; -56.6%); in contrast, Calabria, Emilia-Romagna, Liguria, Marche, AP of Trento, Apulia, Sardinia, Umbria and Aosta Valley show increases ranging from 5% to 95%.

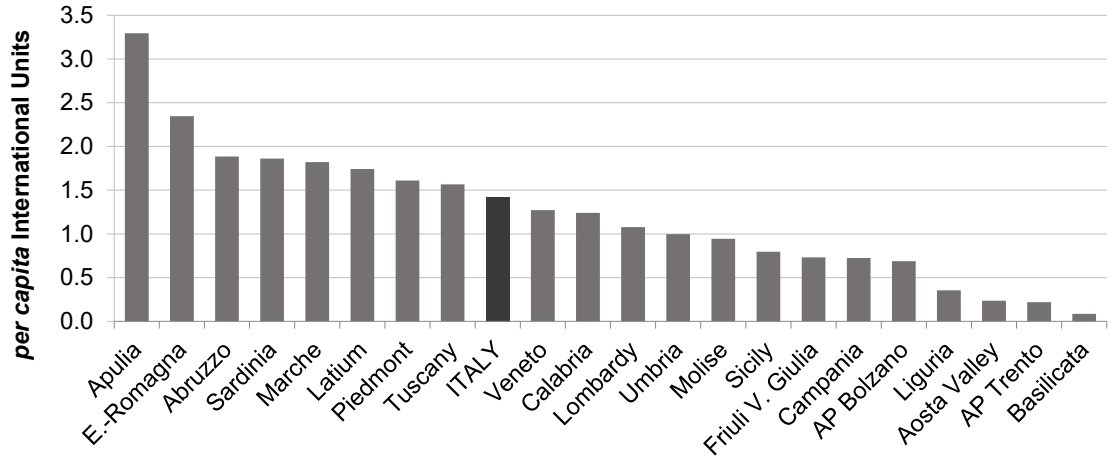

Figure 18. Total and regional demand (public and private) for plasma-derived coagulation Factor VIII, expressed in International Units *per capita*, 2024 (adapted by the CNS on data from the Traceability information flow)

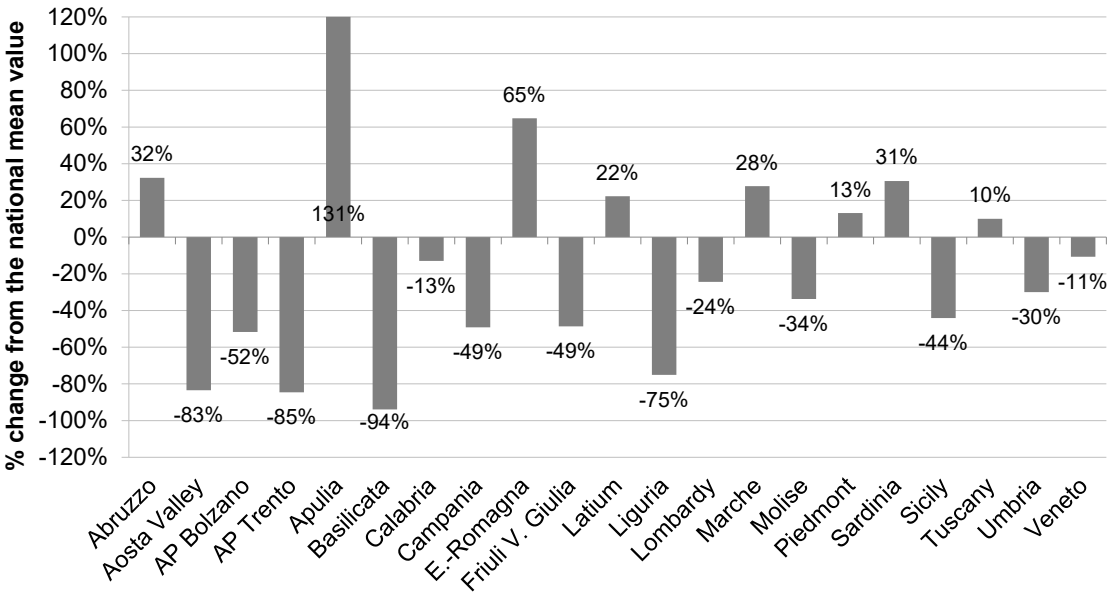

Figure 19. Percentage change from the national mean value of standardised regional demand for plasma-derived coagulation Factor VIII in 2024 (adapted by the CNS on data from the Traceability information flow)

Plasma-derived Factor VIII (B02BD02)

In 2024, the total demand for plasma-derived FVIII was 26,426,000 IUs. The mean national demand *per capita* was about 0.4 IUs, with a range amongst Regions of 0.003 IUs and 1.7 IUs (Table 18). The Regions with the highest *per capita* consumption of pdFVIII were Apulia (1.7 IUs), Piedmont (1.0 IUs) and Veneto (0.7 IUs). The lowest utilisation was observed in Molise (0.003 IUs *per capita*). No consumption was recorded in Aosta Valley, in the AP of Trento, Marche and in Campania. Figure 20 shows the percentage distribution of plasma-derived FVIII and plasma-derived FVIII/von Willebrand in combination by Region.

Table 18. Total demand (public and private) and total standardised demand for plasma-derived coagulation FVIII, expressed in International Units and International Units *per capita,* and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	290,000	0.2	60,000	0.0	-79.3
Aosta Valley	-	-	-	-	NA
AP Bolzano	430,000	0.8	340,000	0.6	-21.4
AP Trento	-	-	-	-	NA
Apulia	5,207,000	1.3	6,756,000	1.7	30.3
Basilicata	10,000	0.0	20,000	0.0	101.6
Calabria	203,000	0.1	380,000	0.2	88.0
Campania	-	-	-	-	NA
E.-Romagna	1,327,000	0.3	403,000	0.1	-69.7
Friuli V. Giulia	1,400,000	1.2	590,000	0.5	-57.9
Latium	4,821,000	0.8	183,000	0.0	-96.2
Liguria	90,000	0.1	200,000	0.1	122.0
Lombardy	8,208,000	0.8	6,102,000	0.6	-25.9
Marche	1,514,000	1.0	-	-	-100.0
Molise	218,000	0.8	1,000	0.0	-99.5
Piedmont	5,622,000	1.3	4,309,000	1.0	-23.4
Sardinia	318,000	0.2	458,000	0.3	44.7
Sicily	1,327,000	0.3	1,187,000	0.2	-10.2
Tuscany	5,409,000	1.5	1,917,000	0.5	-64.5
Umbria	50,000	0.1	130,000	0.2	161.0
Veneto	4,580,000	0.9	3,390,000	0.7	-26.0
Italy	41,024,000	0.7	26,426,000	0.4	-35.6

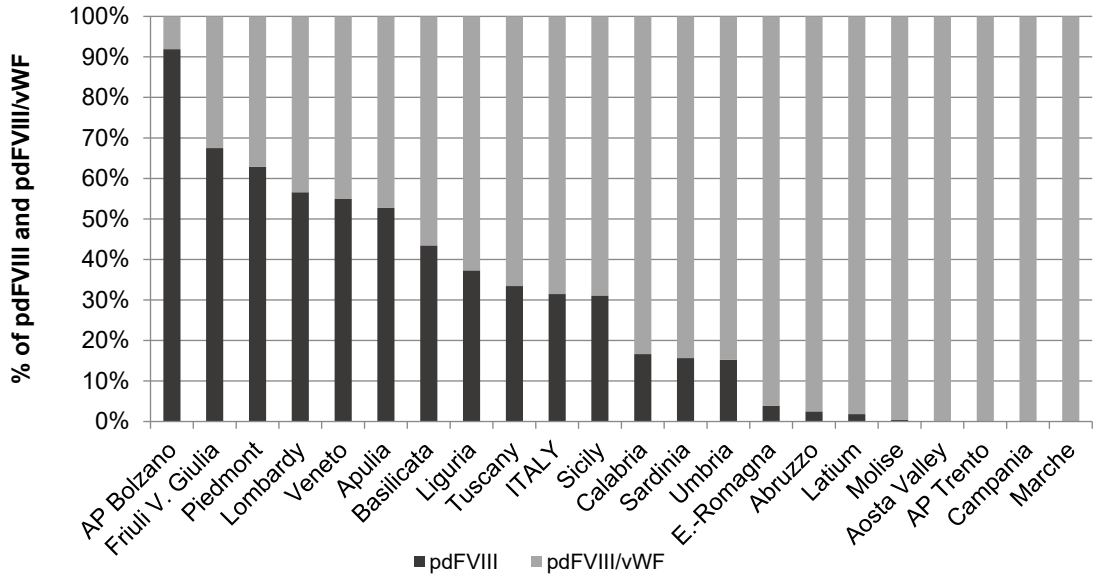

Figure 20. Percentage distribution of plasma-derived FVIII and plasma-derived FVIII/von Willebrand in combination, by Region, 2024 (adapted by the CNS on data from the Traceability information flow)

Coagulation Factor VIII and von Willebrand Factor in combination (ATC B02BD06) and Von Willebrand Factor (ATC B02BD10)

In 2024, the national demand for FVIII and von Willebrand Factor in combination was 57,599,500 IUs, about 68.5% of the total demand for pdFVIII. The mean national demand *per capita* was 1.0 IUs, with a range between Regions of 0.05 IUs (Basilicata) and 2.3 IUs (Emilia-Romagna) (Table 19).

Table 19. Total demand (public and private) and total standardised demand for FVIII and Von Willebrand Factor in combination, expressed in International Units and International Units *per capita,* and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	3,637,500	2.9	2,334,000	1.8	-35.7
Aosta Valley	20,000	0.2	29,000	0.2	45.3
AP Bolzano	133,000	0.2	30,000	0.1	-77.6
AP Trento	114,000	0.2	120,000	0.2	4.8
Apulia	6,415,000	1.6	6,060,000	1.6	-5.1
Basilicata	80,000	0.1	26,000	0.0	-67.2
Calabria	1,716,000	0.9	1,900,500	1.0	11.2
Campania	4,072,000	0.7	4,050,000	0.7	-0.3
E.-Romagna	4,024,750	0.9	10,046,500	2.3	148.8
Friuli V. Giulia	247,000	0.2	284,000	0.2	14.9
Latium	6,581,500	1.2	9,771,500	1.7	48.6
Liguria	223,000	0.1	336,000	0.2	50.5
Lombardy	4,172,250	0.4	4,684,000	0.5	11.9
Marche	1,002,000	0.7	2,699,500	1.8	169.7
Molise	414,000	1.4	272,000	0.9	-34.0
Piedmont	2,877,000	0.7	2,541,500	0.6	-11.7
Sardinia	2,089,000	1.3	2,464,000	1.6	18.5
Sicily	2,802,000	0.6	2,631,000	0.5	-5.8
Tuscany	3,657,000	1.0	3,817,000	1.0	4.4
Umbria	489,500	0.6	721,000	0.8	47.9
Veneto	2,660,000	0.5	2,782,000	0.6	4.5
Italy	47,426,500	0.8	57,599,500	1.0	21.5

The Regions with the highest *per capita* demand of FVIII and von Willebrand Factor in combination were Emilia-Romagna (2.3 IUs), Abruzzo and Marche (1.8 IUs) and Latium (1.7 IUs). The lowest utilization equal to 0.05 IUs *per capita* was observed in Basilicata (Figure 21).

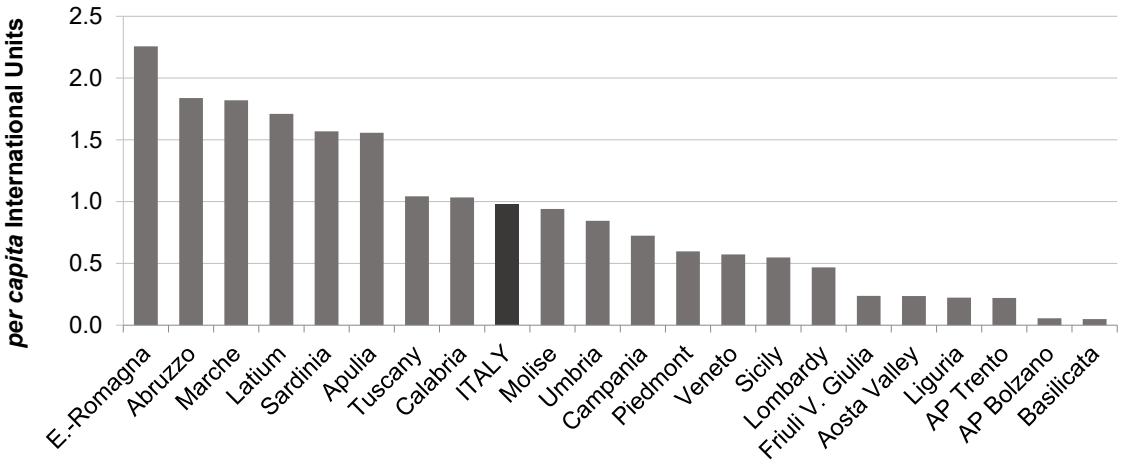

Figure 21. Total and regional demand (public and private) for pdFVIII and von Willebrand Factor in combination, expressed in International Units *per capita*, 2024 (adapted by the CNS on data from the Traceability information flow)

Recombinant Factor VIII

In 2024, the total demand for rFVIII was 451,794,150 IUs, with an increase of approximately +1% compared to 2023. The mean national demand *per capita* was about 8 IUs, with a range among different Regions of 3.5 IUs and 12.2 IUs (Table 20).

Table 20. Total demand (public and private) and total standardised demand for recombinant coagulation Factor VIII, expressed in International Units and International Units *per capita*, and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	12,535,250	9.8	12,017,500	9.5	-3.9
Aosta Valley	583,000	4.7	560,000	4.6	-3.7
AP Bolzano	2,647,500	5.0	3,157,000	5.9	18.5
AP Trento	3,691,500	6.8	3,637,250	6.7	-1.9
Apulia	34,631,000	8.9	36,971,750	9.5	7.2
Basilicata	2,929,000	5.4	2,775,000	5.2	-4.5
Calabria	14,316,250	7.8	15,872,000	8.6	11.4
Campania	55,030,500	9.8	53,609,750	9.6	-2.3
E.-Romagna	40,057,000	9.0	43,048,000	9.7	7.1
Friuli V. Giulia	3,125,000	2.6	4,219,500	3.5	35.0
Latium	68,994,750	12.1	69,702,750	12.2	1.1
Liguria	9,019,000	6.0	10,585,000	7.0	17.2
Lombardy	64,146,500	6.4	61,464,250	6.1	-4.5
Marche	8,155,500	5.5	8,007,000	5.4	-1.7
Molise	2,690,000	9.3	2,491,500	8.6	-6.9
Piedmont	22,936,750	5.4	22,371,500	5.3	-2.5
Sardinia	10,782,000	6.8	11,180,750	7.1	4.2
Sicily	40,330,500	8.4	40,126,000	8.4	-0.2
Tuscany	17,344,250	4.7	16,321,650	4.5	-5.9
Umbria	6,139,500	7.2	5,328,500	6.2	-12.9
Veneto	27,278,000	5.6	28,347,500	5.8	3.9
Italy	447,362,750	7.6	451,794,150	7.7	1.0

The Regions in which the highest *per capita* utilisation of rFVIII was observed were Latium (12.2 IUs), Emilia-Romagna and Campania (10 IUs) (Figure 22), with a percentage variation compared to the Italian mean value of +59%, +26% and +25%, respectively (Figure 23). The lowest utilisation – between 3.5 and 4.6 IUs *per capita* – was observed in Friuli V. Giulia, Tuscany and Aosta Valley.

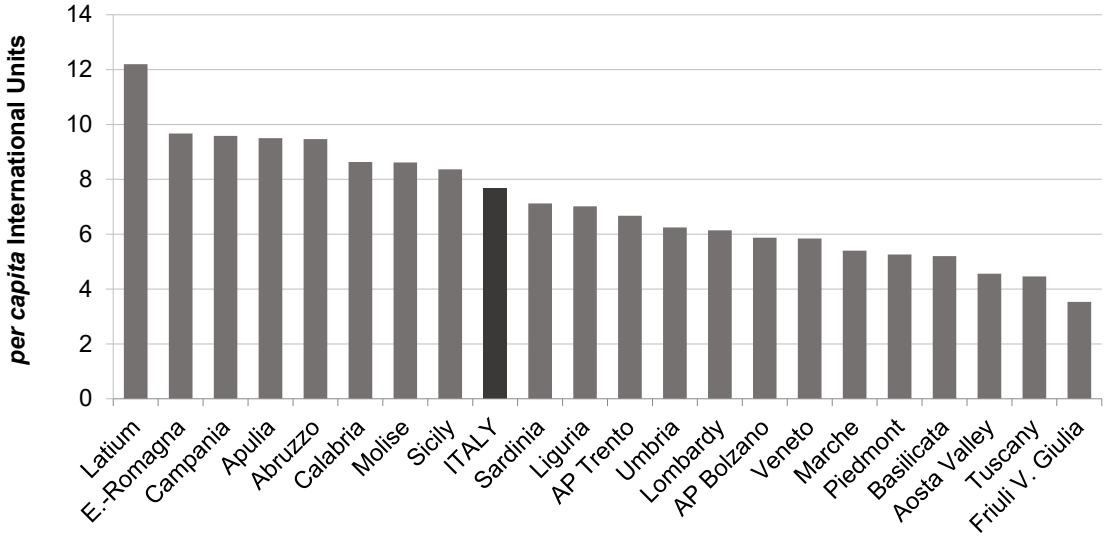

Figure 22. Total and regional demand (public and private) for recombinant coagulation Factor VIII, expressed in International Units *per capita*, 2024 (adapted by the CNS on data from the Traceability information flow)

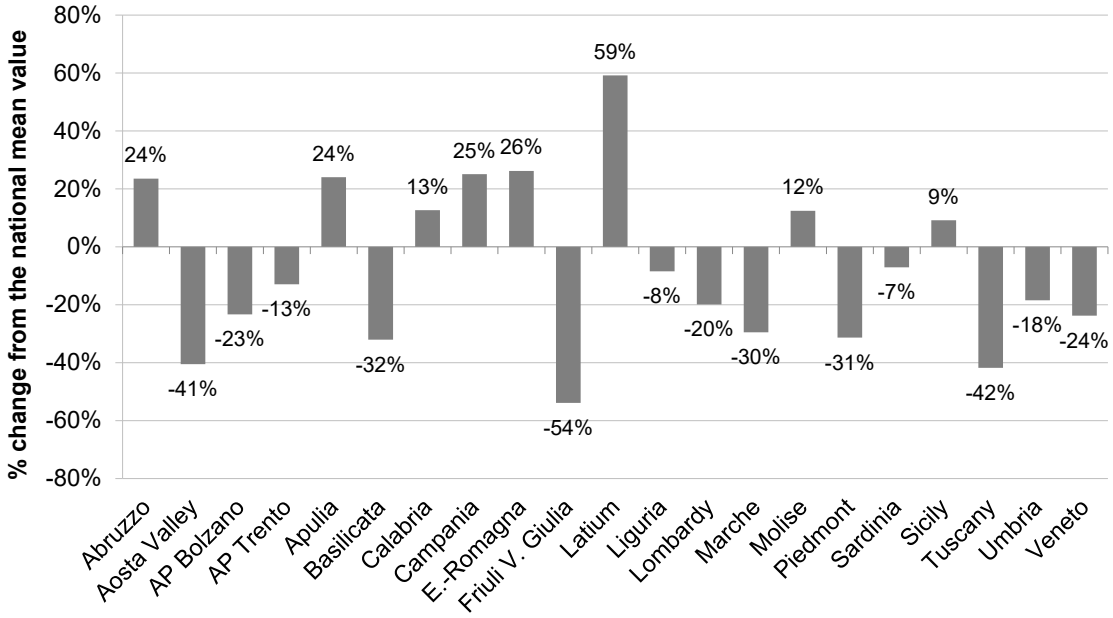

Figure 23. Percentage variation from the national mean value of standardised regional demand for recombinant coagulation Factor VIII in 2024 (adapted by the CNS on data from the Traceability information flow)

Extended half-life Recombinant Factor VIII

Part of the total demand for rFVIII is represented by drugs containing extended half-life molecules. In 2024, the demand for these products was equal to 302,192,750 IUs, about 67% of the total demand for rFVIII (Table 21) and recorded an increase of +13% compared to the previous year.

Table 21. Total demand (public and private) and total standardised demand for long-acting recombinant coagulation Factor VIII, expressed in International Units and International Units *per capita* and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	9,073,250	7.1	8,837,500	7.0	-2.4
Aosta Valley	546000	4.4	504000	4.1	-7.5
AP Bolzano	1,173,000	2.2	2,084,000	3.9	76.5
AP Trento	824500	1.5	805000	1.5	-2.8
Apulia	20,004,500	5.1	23,625,000	6.1	18.6
Basilicata	794,500	1.5	1,377,500	2.6	74.8
Calabria	6,764,000	3.7	9,186,500	5.0	36.4
Campania	31,356,500	5.6	34,553,750	6.2	10.5
E.-Romagna	27,412,000	6.2	33,591,750	7.5	22.1
Friuli V. Giulia	2,573,000	2.2	3,914,500	3.3	52.1
Latium	42,007,000	7.3	46,167,250	8.1	10.0
Liguria	7,316,000	4.9	8,639,000	5.7	18.0
Lombardy	35,009,250	3.5	40,670,250	4.1	15.8
Marche	6,260,500	4.2	6,001,000	4.0	-4.0
Molise	1,808,000,0	6.2	1,963,000,0	6.8	9.1
Piedmont	14,908,500	3.5	15,982,000	3.8	7.2
Sardinia	5157000	3.3	5656000	3.6	10.2
Sicily	19,256,000	4.0	21,121,000	4.4	10.1
Tuscany	10,979,750	3.0	11,458,750	3.1	4.4
Umbria	3,122,500	3.6	3,807,500	4.5	22.4
Veneto	20,652,500	4.3	22,247,500	4.6	7.7
Italy	266,998,250	4.5	302,192,750	5.1	13.2

The national demand *per capita* was about 5.1 IUs, with a range among Regions of 1.5 IUs in the AP of Trento and 8.1 IUs in Latium (+58% as compared to national mean value) (Figures 24 and 25).

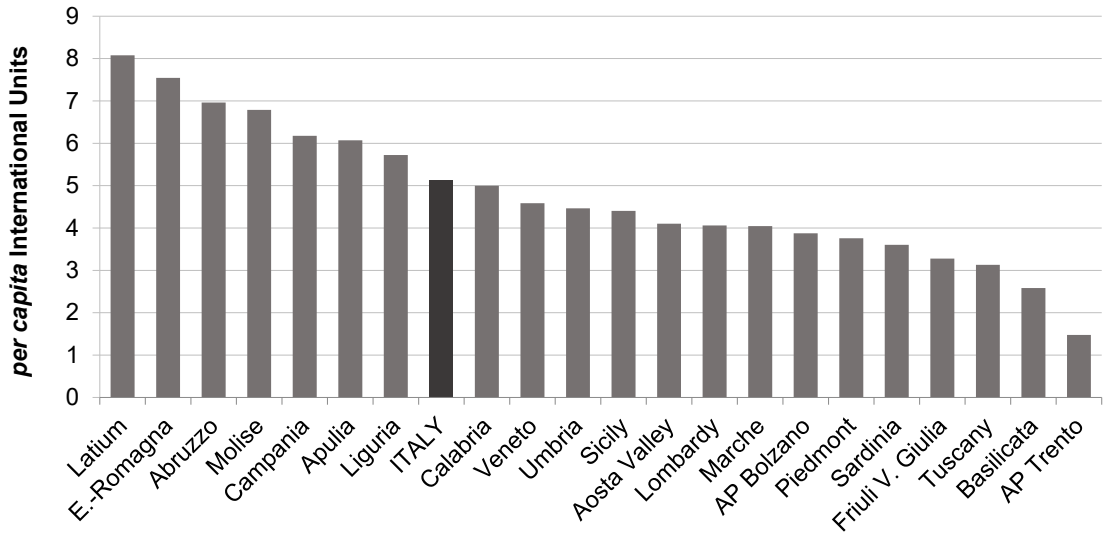

Figure 24. Total and regional demand (public and private) for extended half-life recombinant Factor VIII, expressed in International Units *per capita*, 2024 (adapted by the CNS on data from the Traceability information flow)

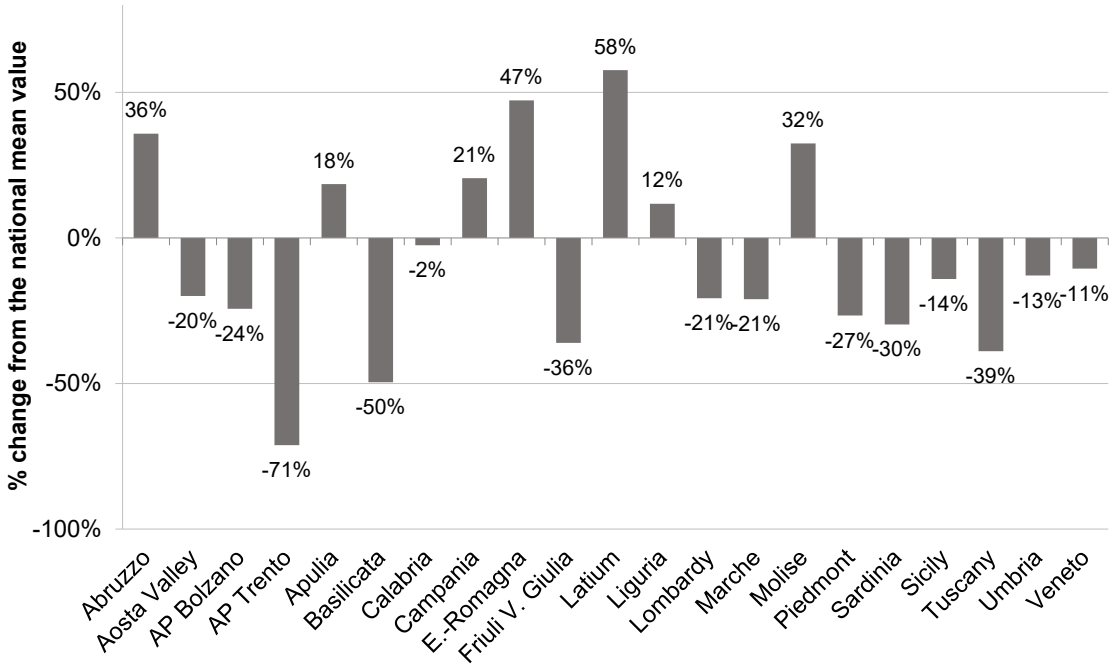

Figure 25. Percentage change from the national mean value of standardised regional demand for extended half-life recombinant Factor VIII in 2024 (adapted by the CNS on data from the Traceability information flow)

EMICIZUMAB (ATC B02BX06)

Emicizumab is a humanised monoclonal modified immunoglobulin G4 (IgG4) antibody produced using recombinant DNA technology in mammalian Chinese Hamster Ovary (CHO) cells.

Emicizumab is indicated for routine prophylaxis of bleeding episodes in patients with severe hemophilia A (congenital FVIII deficiency<1%) who have not developed factor VIII inhibitors with:

– severe disease (blood factor VIII level less than 1%)
– moderate disease (blood factor VIII level between 1% and 5%) with severe hemorrhagic phenotype.

The use of Emicizumab is also indicated in patients who have developed factor VIII inhibitors, which are antibodies in the blood that act against factor VIII drugs and prevent them from functioning properly. Emicizumab can be used in all age groups and is administered via subcutaneous way only (27).

Besides the well-known bypassing agents, activated Prothrombin Complex Concentrates (aPCCs) and recombinant activated Factor VII (rFVIIa), used to treat or prevent bleeding in haemophilia patients with inhibitors, Emicizumab is a monoclonal antibody which has been designed to function as FVIII normally does, bringing together 2 clotting Factors (IXa and X) as part of a chain of reactions needed for blood to clot.

Table 22 shows the brand names of preparations containing Emicizumab currently marketed in Italy and the amount of the contained active ingredients expressed in milligrams (mg).

Table 22. Products containing emicizuma currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	mg	Manufacturer	NHS class
046130062	HEMLIBRA*SC1 1FL 0.4 mL 30mg/mL	12	ROCHE GMBH	A
046130011	HEMLIBRA*SC1 FL 1mL 30 mg/mL	30	ROCHE GMBH	A
046130023	HEMLIBRA*SC 1FL 0.4 mL 150mg/mL	60	ROCHE GMBH	A
046130035	HEMLIBRA *SC 1 FL 0.7 mL 150mg/mL	105	ROCHE GMBH	A
046130047	HEMLIBRA*SC 1FL 1mL 150 mg/mL	150	ROCHE GMBH	A
046130050	HEMLIBRA*SC 1FL 2mL 150 mg/mL	300	ROCHE GMBH	C

Quantification and characterisation of the demand

Table 23 shows the total and per 1,000 population demand for drugs containing Emicizumab for the year 2024, at national and regional levels and the percentage change from the previous year.

The total national demand for Emicizumab formulation shows a strong increase for the year 2024 and its was 2,889,243 mg, with an increase of +17% compared to the year 2023. For the first time, demand has been recorded in all Regions and APs. The national demand (mg per 1,000 population) was about 49 mg (Table 23), showing a regional range from 3.1 mg in the AP of Trento to a maximum of 87 mg in Aosta Valley (Figure 26).

Table 23. Total demand (public and private) and total standardised demand for Emicizumab expressed in mg and mg per 1,000 population for the year 2023 and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	mg	mg per 1,000 pop	mg	mg per 1,000 pop	
Abruzzo	56,130	44.1	68,100	53.6	21.6
Aosta Valley	10,710,0	87.0	10,710,0	87.2	0.2
AP Bolzano	24,615	46.1	30,600	56.9	23.5
AP Trento	-	-	1,680,0	3.1	NA
Apulia	83,040	21.3	95,400	24.5	15.4
Basilicata	14,340	26.7	11,580	21.7	-18.6
Calabria	106,575	57.7	119,430	65.0	12.6
Campania	223,500	39.8	328,200	58.7	47.3
E.-Romagna	132,180	29.8	140,205	31.5	5.7
Friuli V. Giulia	41,280	34.6	44,490	37.2	7.7
Latium	142,845	25.0	206,370	36.1	44.6
Liguria	46,485	30.8	46,080	30.5	-1.0
Lombardy	519,495	52.1	591,771	59.1	13.5
Marche	66,000	44.5	77,010	51.9	16.8
Molise	16,350,0	56.3	18,840,0	65.1	15.8
Piedmont	309,240	72.7	324,060	76.2	4.8
Sardinia	2,475,0	1.6	10,005,0	6.4	306.2
Sicily	165,210	34.3	191,217	39.9	16.1
Tuscany	247,905	67.7	288,135	78.7	16.3
Umbria	48,465	56.6	42,705	50.1	-11.5
Veneto	216,135	44.6	242,655	50.0	12.2
Italy	2,472,975	41.9	2,889,243	49.0	16.9

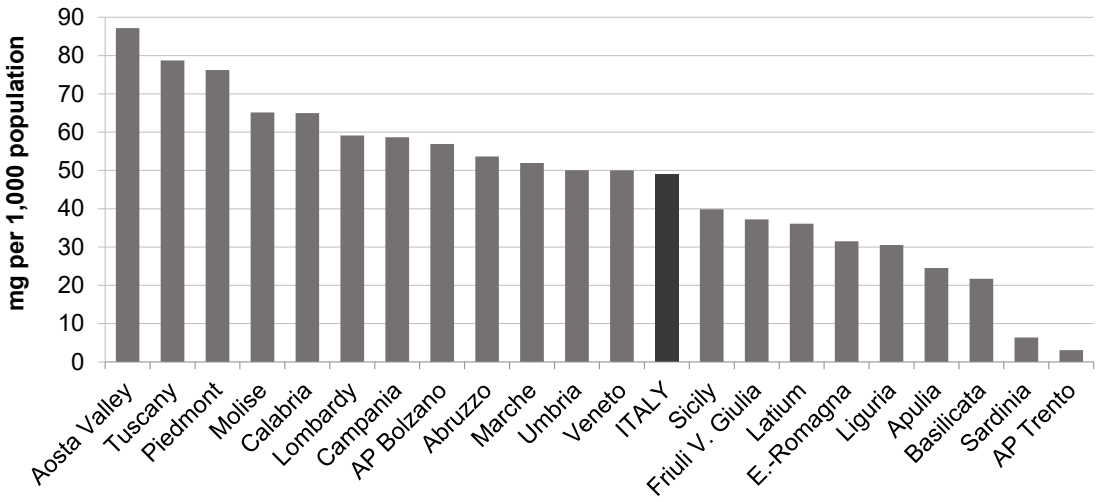

Figure 26. Total and regional demand (public and private) for Emicizumab expressed in mg per 1,000 population 2024 (adapted by the CNS on data from the Traceability information flow)

Figure 27 shows the variations in percentage of each Region compared to the national average. The Regions where the highest value was recorded are Aosta Valley (+78%) and Tuscany (+61%).

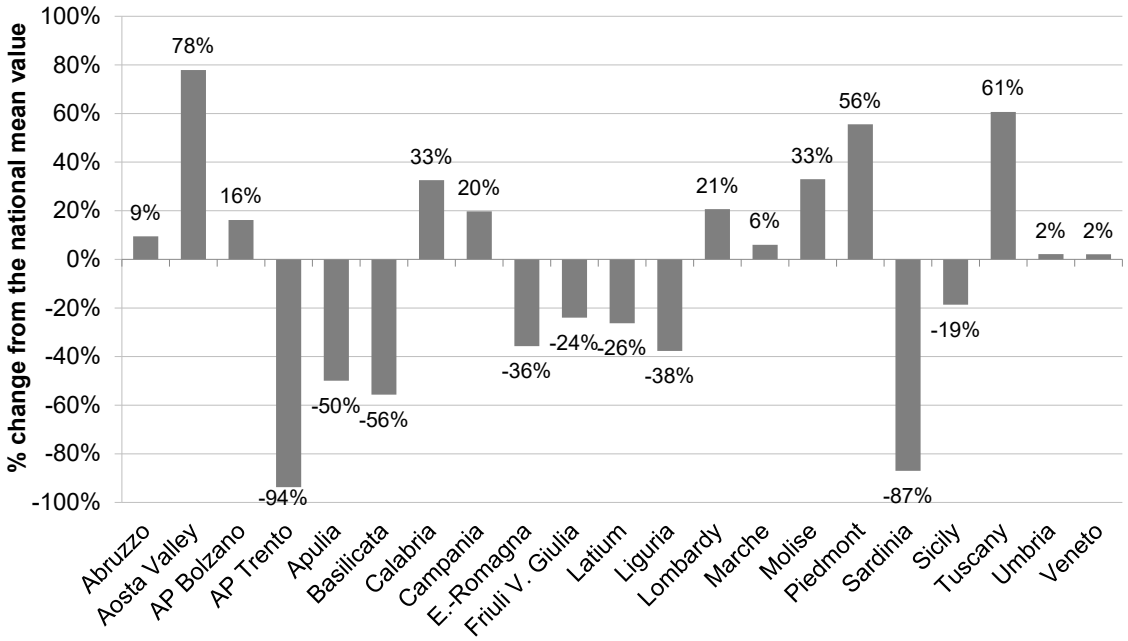

Figure 27. Percentage change from the national mean value of standardised regional demand for Emicizumab in 2024 (adapted by the CNS on data from the Traceability information flow)

COAGULATION FACTOR IX (ATC B02BD04), RECOMBINANT COAGULATION FACTOR IX (ATC B02BD04)

Coagulation FIX is used in the replacement therapy of haemophilia B, also called Christmas disease, a rare, haemorrhagic, hereditary, x-linked or acquired recessive disorder, with an estimated prevalence of 2-3/100,000 male subjects (28) and caused by a FIX deficiency. Depending on the level of activity of the circulating factor, there are severe forms of haemophilia B (FIX <1%), moderately severe (between 1 and 5%) and mild (> 5%) (29). FIX coagulation concentrates are divided in plasma-derived concentrates and products obtained with genetic recombination techniques (29). Tables 24 and 25 show the brand names of preparations containing pdFIX and rFIX currently marketed in Italy and the related amount of active ingredient contained and expressed in IUs.

Table 24. Products containing plasma-derived coagulation Factor IX currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
025841089	AIMAFIX*FL 500IU+FL 10mL+SET	500	KEDRION SpA	A
028142026	MONONINE*EV F 500IU+F 5mL+KIT	500	CSL BEHRING SpA	A
029250065	ALPHANINE*EV 500IU+SIR 10mL+A	500	GRIFOLS ITALIA SpA	A
039072020	HAEMOBIONINE*1FL 500IU	500	BIOTEST ITALIA Srl	A
040092013	OCTANINE*FL 500IU+FL 5mL	500	OCTAPHARMA Italy SpA	A
041799026	IXED*FL 500IU+FL 10mL+SET	500	KEDRION SpA	A
038324024	FIXNOVE*FL 600IU+FL 10mL	600	BAXALTA Italy Srl	A
025841103	AIMAFIX*FL 1000IU+FL 10mL+SET	1000	KEDRION SpA	A
028142038	MONONINE*EV F 1000IU	1000	CSL BEHRING SpA	A
029250077	ALPHANINE “1000 IU/10 mL	1000	GRIFOLS ITALIA SpA	A
039072032	HAEMOBIONINE*1FL 1000IU	1000	BIOTEST ITALIA Srl	A
040092025	OCTANINE*FL 1000IU+FL	1000	OCTAPHARMA Italy SpA	A
041799038	IXED*FL 1000IU+FL 10mL+SET	1000	KEDRION SpA	A
038324036	FIXNOVE*FL 1200IU+FL 10mL	1200	BAXALTA Italy Srl	A
029250089	ALPHANINE “1500 IU/10 mL	1500	GRIFOLS ITALIA SpA	A

Table 25. Products containing recombinant coagulation Factor IX and long-acting recombinant Factor IX currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
033535016	BENEFIX*IV 1FL 250IU	250	PFIZER ITALIA Srl	A
033535042	BENEFIX*IV 1FL 250IU+SIR 5mL+SE	250	PFIZER ITALIA Srl	A
043796010	RIXUBIS*IV 1FL 250IU 5mL	250	BAXTER SpA	A
033535028	BENEFIX*IV 1FL 500IU	500	PFIZER ITALIA Srl	A
033535055	BENEFIX*IV 1FL 500IU+SIR 5mL+SE	500	PFIZER ITALIA Srl	A
043796022	RIXUBIS*IV 1FL 500IU 5mL	500	BAXTER SpA	A
033535030	BENEFIX*IV 1FL 1000IU	1000	PFIZER ITALIA Srl	A
033535067	BENEFIX*IV 1FL 1000IU+SIR 5mL+S	1000	PFIZER ITALIA Srl	A
043796034	RIXUBIS*IV 1FL 1000IU 5mL	1000	BAXTER SpA	A
033535093	BENEFIX*IV 1FL 1500IU+SIR5mL+S	1500	PFIZER EUROPE MA EEIG	A
033535079	BENEFIX*IV 1FL 2000IU+SIR 5mL+S	2000	PFIZER ITALIA Srl	A
043796046	RIXUBIS*IV 1FL 2000IU 5mL	2000	BAXTER SpA	A
033535081	BENEFIX*IV 1FL 3000IU+SIR 5mL+S	3000	PFIZER ITALIA Srl	A
043796059	RIXUBIS*IV 1FL 3000IU 5mL	3000	BAXTER SpA	A

AIC code	Brand name	IU	Manufacturer	NHS class
Extended half- recombinant Factor IX life				
044888016	ALPROLIX*1FL 250IU+1SIR 5mL	250	SOBI Srl	A
044891012	IDELVION*EV FL 250IU+FL 2,5mL	250	CSL BEHRING SpA	A
044888028	ALPROLIX*1FL 500IU+1SIR 5mL	500	SOBI Srl	A
044891024	IDELVION*EV FL 500IU+FL 2,5mL	500	CSL BEHRING SpA	A
045488018	REFIXIA*EV FL 500 IU+ FL 4 mL+SIR	500	NOVO NORDISK A/S	C
044888030	ALPROLIX*1FL 1000IU+1SIR 5mL	1000	SOBI Srl	A
044891036	IDELVION*EV FL 1000IU+FL 2,5mL	1000	CSL BEHRING SpA	A
045488020	REFIXIA*EV FL 1000IU+ FL 4mL+SIR	1000	NOVO NORDISK A/S	C
045488032	REFIXIA*EV FL 2000 IU+FL 4mL+SIR	1500	NOVO NORDISK A/S	C
044888042	ALPROLIX*1FL 2000IU+1SIR 5mL	2000	SOBI Srl	A
044891048	IDELVION*EV FL 2000IU+FL 2,5mL	2000	CSL BEHRING SpA	A
044888055	ALPROLIX*1FL 3000IU+1SIR 5mL	3000	SOBISrl	A
045488044	REFIXIA*EV FL 3000UI+FL 4mL+SIR	3000	NOVO NORDISK A/S	C(nn)
044891051	IDELVION*EV FL 3500IU+FL 5 ML	3500	CSL BEHRING SpA	C(nn)

Quantification and characterisation of the demand

Table 26 illustrates the total and *per capita* demand for plasma-derived and recombinant FIX for the two-year period 2023-2024, at national and regional levels.

Table 26. Total demand (public and private) and total standardised demand for coagulation Factor IX, expressed in International Units and International Units *per capita*, and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	2,174,000	1.7	2,691,500	2.1	24.1
Aosta Valley	-	-	-	-	NA
APBolzano	236,000	0.4	234,000	0.4	-1.5
APTrento	744,000	1.4	715,000	1.3	-4.3
Apulia	5,447,500	1.4	5,258,000	1.4	-3.1
Basilicata	250,500	0.5	260,250	0.5	4.7
Calabria	1,705,500	0.9	1,560,500	0.8	-8.1
Campania	7,512,000	1.3	7,478,200	1.3	-0.2
E.-Romagna	4,749,500	1.1	5,178,000	1.2	8.7
Friuli V. Giulia	946,000	0.8	1,059,000	0.9	11.9
Latium	5,862,700	1.0	6,199,600	1.1	5.9
Liguria	2,194,000	1.5	1,739,000	1.2	-20.8
Lombardy	11,117,150	1.1	11,719,500	1.2	5.0
Marche	1,788,800	1.2	1,739,300	1.2	-2.7
Molise	136,800	0.5	50,000	0.2	-63.3
Piedmont	4,374,750	1.0	4,230,500	1.0	-3.3
Sardinia	6,000	0.0	18,000	0.0	201.5
Sicily	4,542,500	0.9	4,728,500	1.0	4.5
Tuscany	6,853,900	1.9	6,878,200	1.9	0.4
Umbria	632,500	0.7	833,500	1.0	32.3
Veneto	3,709,000	0.8	4,461,000	0.9	20.2
Italy	64,983,100	1.1	67,031,550	1.1	3.2

* The values inserted as "0.0" do not identify the absence of quantities distributed, but consumption that would have required an excessive number of decimals to be quantified.

The total demand for FIX formulations recorded in 2024 was 67,031,550 IUs (Table 26); about 5.6% of the aforementioned amount (3,738,300 IUs) was plasma-derived. Demand was essentially in line with the previous year for FIXpd (+1.1%) and increased for FIXr (+3.3%), mainly due to long half-life formulations, which recorded a +12.1% increase in the two-year period considered.

In 2024, the standardised demand for plasma-derived and recombinant FIX was 1.1 IUs *per capita*, with significantly different regional trends: these ranged from a minimum – close to zero – in Sardinia (-99% compared to the Italian mean value), to a maximum in Abruzzo (2.1 IUs), Tuscany (1.9 IUs), Apulia (1.4 IUs), AP of Trento and Campania with 1.3 IUs *per capita* (+87%, +65%, +19%, +18% and +15% compared to the national mean value, respectively) (Figures 28 and 29). No consumption in Aosta Valley was registered.

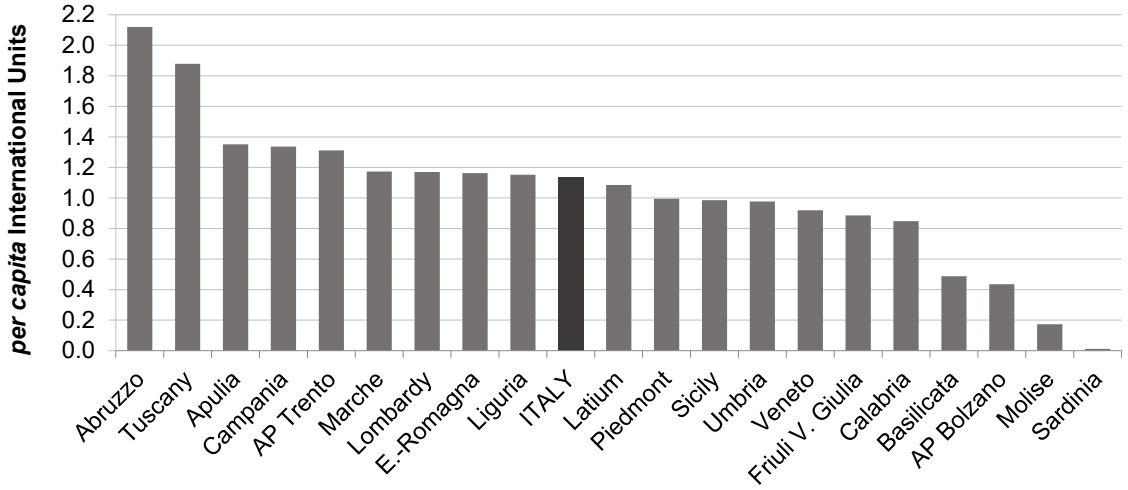

Figure 28. Total and regional demand (public and private) for coagulation Factor IX, expressed in International Units *per capita*, 2024 (adapted by the CNS on data from the Traceability information flow)

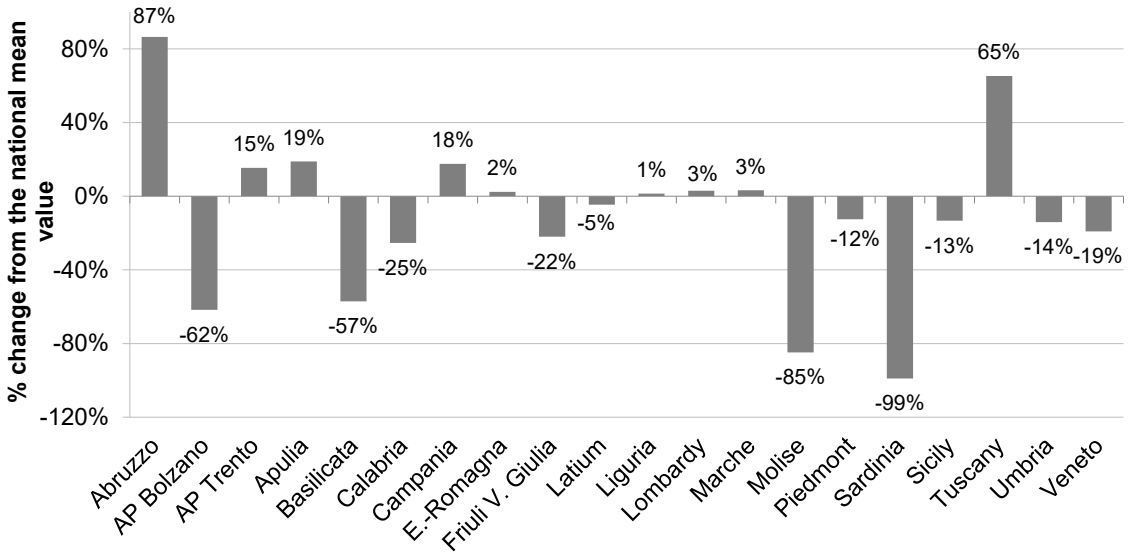

Figure 29. Percentage variation from the national mean value of standardised regional demand for coagulation Factor IX (International Units *per capita*) in 2024 (adapted by the CNS on data from the Traceability information flow)

In eleven Regions there were percentage increases in demand (range: 0.4-201.5%) which is instead decreasing in nine Regions (range: -63; -0.2%) (Table 26).

In Sardinia, AP of Trento, Friuli V.Giulia, Basilicata and Abruzzo rFIX was used exclusively, while in Campania, Liguria, Tuscany, Emilia-Romagna, Veneto, Piedmont, Apulia and Calabria, the rFIX demand reached volumes of above 95% (Figure 30).

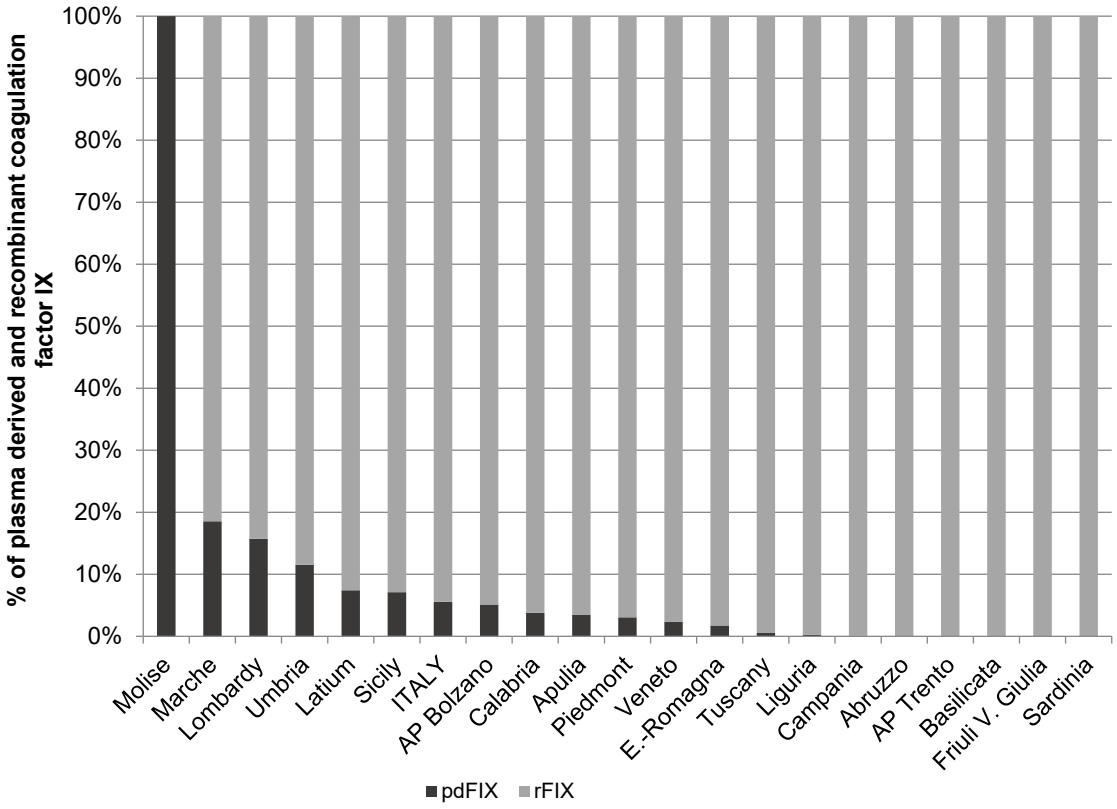

Figure 30. Distribution expressed in % of Factor IX per type, by Region, 2024 (adapted by the CNS on data from the Traceability information flow)

Plasma-derived Factor IX

In 2024, total demand for FIXpd (expressed in absolute terms and ***per capita***) was substantially in line with that recorded in 2023 (+1.1%), with an absolute value of 3,738,300 IU, equal to 0.1 IU *per capita* (Table 27).

The Regions with the highest *per capita* demand were Lombardy, Molise and Marche with 0.2 IUs; in Abruzzo, Basilicata, Friuli V.Giulia, AP of Trento, Sardinia and Aosta Valley there was no reported consumption of pdFIX (Figures 31 and 32).

Table 27. Total demand (public and private) and total standardised demand for plasma-derived coagulation Factor IX, expressed in International Units and International Units *per capita*, and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	-	-	-	-	NA
Aosta Valley	-	-	-	-	NA
AP Bolzano	6,000	0.0	12,000	0.0	98.7
AP Trento	-	-	-	-	NA
Apulia	-	-	184,000	0.0	100.0
Basilicata	-	-	-	-	NA
Calabria	54,000	0.0	59,000	0.0	9.7
Campania	36,000	0.0	7,200	0.0	-79.9
E.-Romagna	43,000	0.0	91,000	0.0	110.9
Friuli V. Giulia	-	-	-	-	NA
Latium	715,200	0.1	460,600	0.1	-35.5
Liguria	4,000	0.0	4,000	0.0	-0.1
Lombardy	1,603,400	0.2	1,843,500	0.2	14.6
Marche	574,800	0.4	322,800	0.2	-43.8
Molise	136,800	0.5	50,000	0.2	-63.3
Piedmont	94,000	0.0	130,000	0.0	38.3
Sardinia	-	-	-	-	NA
Sicily	130,000	0.0	336,000	0.1	159.4
Tuscany	104,400	0.0	37,200	0.0	-64.4
Umbria	175,500	0.2	96,000	0.1	-45.1
Veneto	22,500	0.0	105,000	0.0	366.4
Italy	3,699,600	0.1	3,738,300	0.1	1.1

* The amounts of pdFIX contained in Factor X P Behring® are not included.

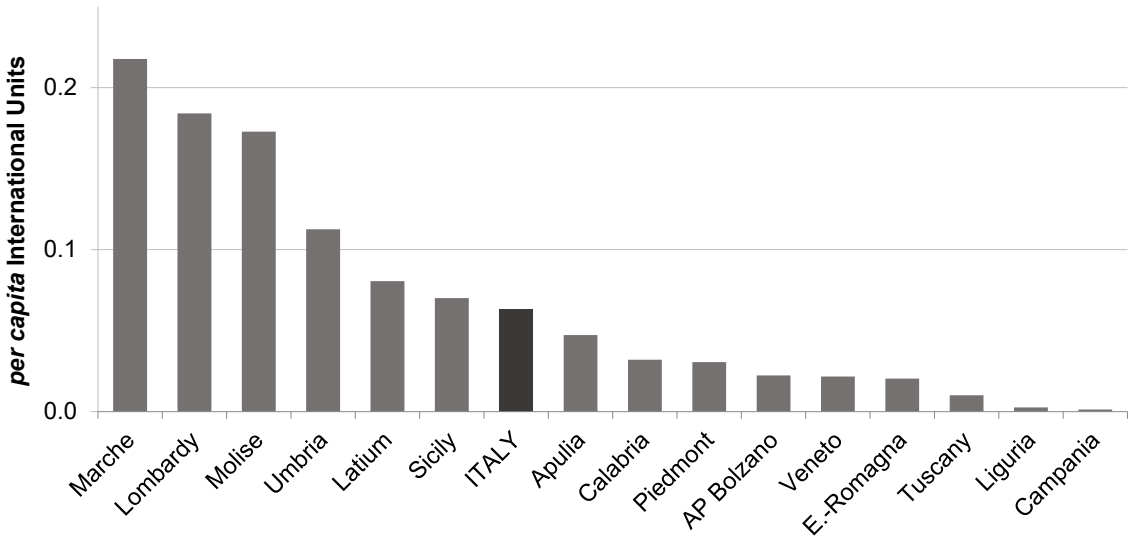

Figure 31. Total and regional demand (public and private) for plasma-derived coagulation Factor IX, expressed in International Units *per capita*, 2024 (adapted by the CNS on data from the Traceability information flow)

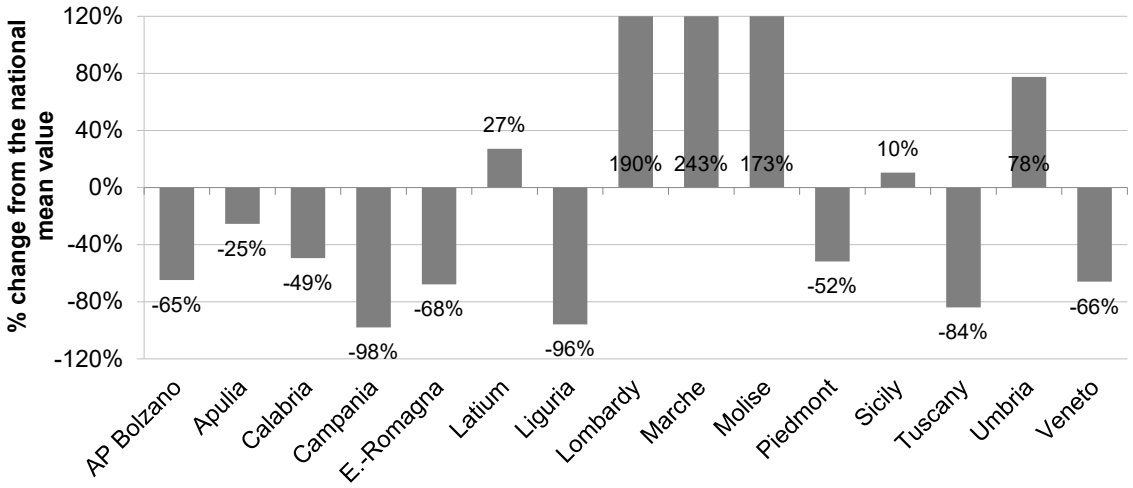

Figure 32. Percentage change from the national mean value of standardised regional demand for plasma-derived coagulation Factor IX in 2024 (adapted by the CNS on data from the Traceability information flow)

Recombinant Factor IX

The total demand for rFIX showed, in the period 2023-2024, an increase of +3.3%, registering a value of 63,293,250 IUs in 2024, equal to 1.1 IU *per capita* (Table 28).

Table 28. Total demand (public and private) and total standardised demand for recombinant coagulation Factor IX, expressed in International Units and International Units *per capita*, and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	2,174,000	1.7	2.691.500	2.1	24.1
Aosta Valley	-	-	-	-	NA
AP Bolzano	230,000	0.4	222.000	0.4	-4.1
AP Trento	744,000	1.4	715.000	1.3	-4.3
Apulia	5,447,500	1.4	5.074.000	1.3	-6.4
Basilicata	250,500	0.5	260.250	0.5	4.7
Calabria	1,651,500	0.9	1.501.500	0.8	-8.7
Campania	7,476,000	1.3	7.471.000	1.3	0.2
E.-Romagna	4,706,500	1.1	5.087.000	1.1	7.7
Friuli V. Giulia	946,000	0.8	1.059.000	0.9	11.9
Latium	5,147,500	0.9	5.739.000	1.0	11.6
Liguria	2,190,000	1.5	1.735.000	1.1	-20.9
Lombardy	9,513,750	1.0	9.876.000	1.0	3.4
Marche	1,214,000	0.8	1.416.500	1.0	16.8
Molise	-	-	-	-	NA
Piedmont	4,280,750	1.0	4.100.500	1.0	-4.2
Sardinia	6,000	0.0	18.000	0.0	201.5
Sicily	4,412,500	0.9	4.392.500	0.9	-0.1
Tuscany	6,749,500	1.8	6.841.000	1.9	1.4
Umbria	457,000	0.5	737.500	0.9	62.0
Veneto	3,686,500	0.8	4.356.000	0.9	18.1
Italy	61,283,500	1.0	63.293.250	1.1	3.3

The Regions with the highest *per capita* demand (Figure 33) were Abruzzo, Tuscany, Campania, the AP of Trento and Apulia with 2.1 IU for the first one, 1.9 IU for the second one, 1.3 IU for the last three (+98%, +74%, +24%, +22% and +22% compared to the national average) (Figure 34).

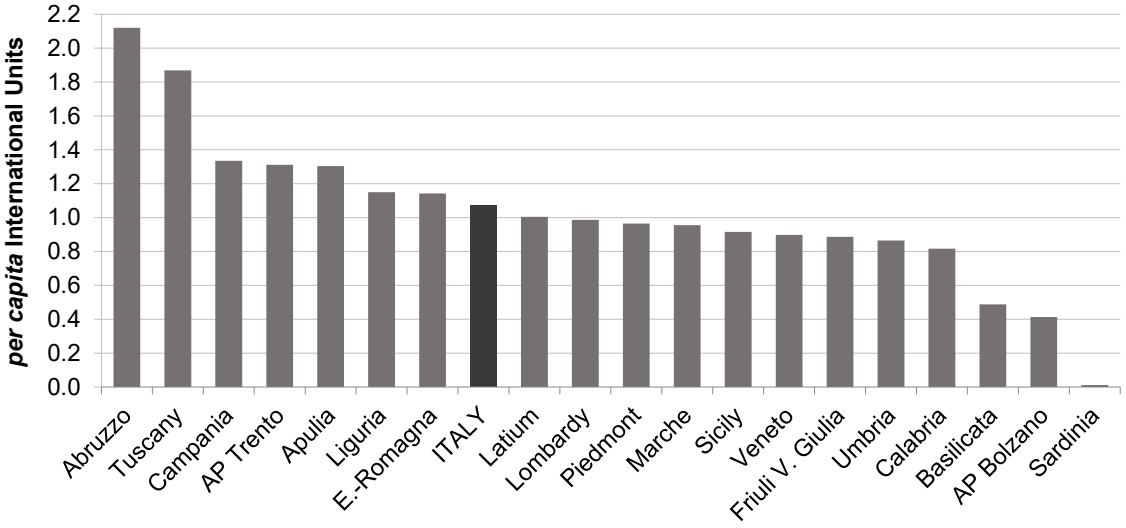

Figure 33. Total and regional demand (public and private) for recombinant coagulation Factor IX, expressed in International Units *per capita*, 2024 (adapted by the CNS on data from the Traceability information flow)

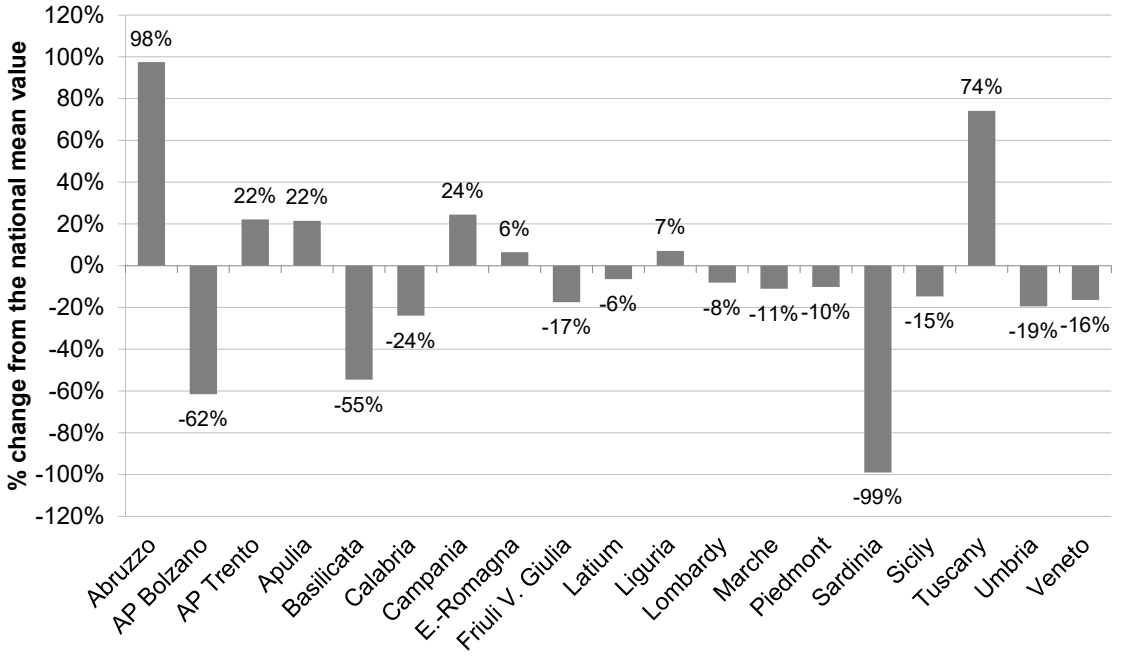

Figure 34. Percentage variation from the national mean value of standardised regional demand for recombinant coagulation Factor IX in 2024 (adapted by the CNS on data from the Traceability information flow)

In Aosta Valley and Molise there was no reported consumption of rFIX in 2024. In 2024 there was an increase in *per capita* demand, compared to 2023, which is particularly evident in Sardinia (+201.5%) and in Umbria (+62%); instead a significant decrease occurred in Liguria (-21%).

Extended half- recombinant Factor IX life

Out of 63.3 million IUs of rFIX demand, extended half-life recombinant Factor IX molecules recorded a total demand of 51,408,500 IUs, about 81% of the total (Table 29).

Table 29. Total demand (public and private) and total standardised demand for long-acting recombinant coagulation Factor IX, expressed in International Units and International Units *per capita* and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	1,914,500	1.5	2,220,500	1.7	16.3
Aosta Valley	-	-	-	-	NA
AP Bolzano	230,000,0	0.4	220,000,0	0.4	-5.0
AP Trento	53,000,0	0.1	179,000,0	0.3	236.4
Apulia	4,628,500	1.2	4,926,000	1.3	6.9
Basilicata	139,500	0.3	164,250	0.3	18.7
Calabria	1,194,500	0.6	1,063,500	0.6	-10.6
Campania	4,727,500	0.8	5,900,000	1.1	25.2
E.-Romagna	4,088,000	0.9	4,605,250	1.0	12.3
Friuli V. Giulia	944,000	0.8	1,057,000	0.9	11.9
Latium	3,173,500	0.6	4,478,000	0.8	41.2
Liguria	2,090,000	1.4	1,731,000	1.1	-17.3
Lombardy	8,037,000	0.8	8,763,000	0.9	8.6
Marche	1,125,000	0.8	1,245,500	0.8	10.8
Molise	-	-	-	-	NA
Piedmont	3,594,750	0.8	3,835,500	0.9	6.7
Sardinia	-	-	-	-	NA
Sicily	3,131,500	0.7	3,283,500	0.7	5.2
Tuscany	3,230,000	0.9	3,077,000	0.8	-4.7
Umbria	442,000	0.5	706,500	0.8	60.5
Veneto	3,146,500	0.6	3,953,000	0.8	25.6
Italy	45,889,750	0.8	51,408,500	0.9	12.1

The mean national demand *per capita* was about 0.9 IU, with a range among Regions of 0.3 IU and 1.7 IU. In Molise, Sardinia and in the Aosta Valley there was no consumption for these drugs in 2024 (Figure 35 and 36).

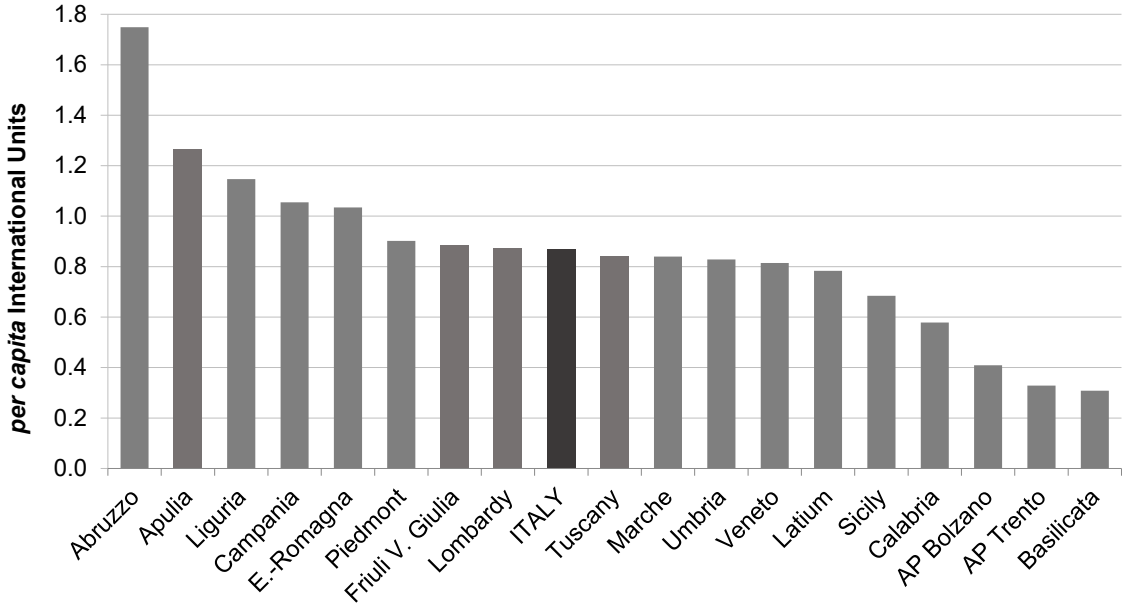

Figure 35. Total and regional demand (public and private) for extended half-life recombinant Factor IX, expressed in International Units *per capita*, 2024 (adapted by the CNS on data from the Traceability information flow)

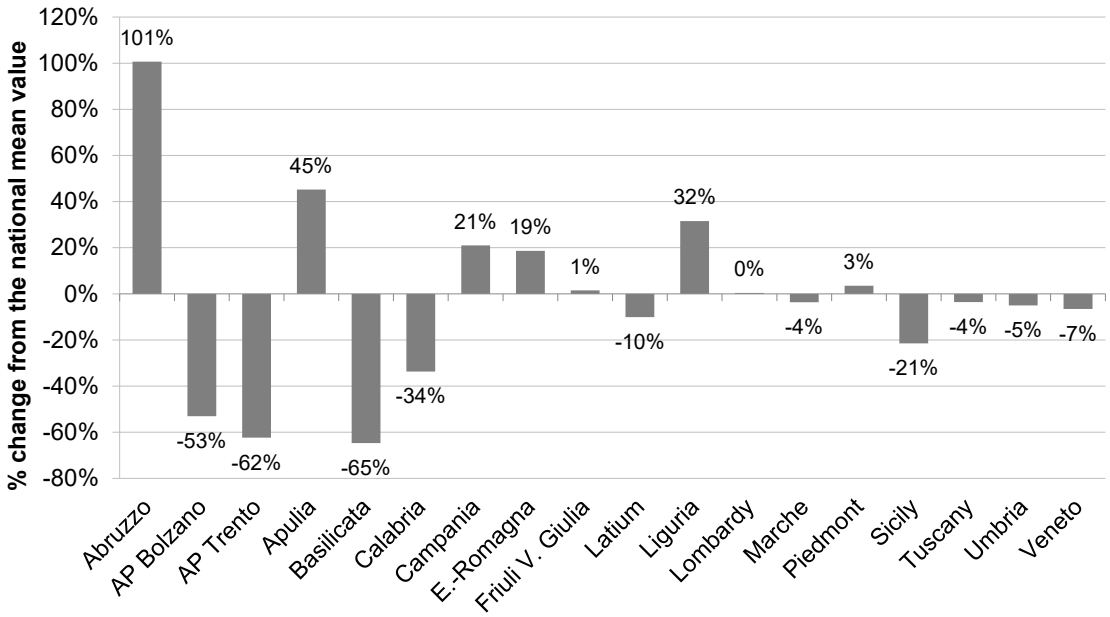

Figure 36. Percentage variation from the national mean value of standardised regional demand for extended half-life recombinant Factor IX in 2024 (adapted by the CNS on data from the Traceability information flow)

3-FACTOR PROTHROMBIN COMPLEX CONCENTRATES (ATC B02BD) AND 4-FACTOR PROTHROMBIN COMPLEX CONCENTRATES (ATC B02BD01)

Prothrombin Complex Concentrates (PCCs) are plasma-derived therapeutic medicinal products useful for the urgent temporary reversal of prothrombin complex factors deficiency (19).

Three or four-factor PCCs can be obtained through different production processes. 3F-PCCs contain Factor II (FII), Factor IX (FIX) and Factor X (FX), and 4F-PCCs contain FII, FVII, FIX, and FX with pro-coagulant action, as well as natural and physiological coagulation inhibitors such as protein C, protein S and traces of protein, heparin and vitronectin (30). As with all the other PDMPs, PCCs undergo viral inactivation, which can be physical (heat), or chemical (solvent-detergent use) and virus removal by nanofiltration (31). Tables 30 and 31 show the brand names of preparations containing 3F-PCCs and 4F-PCCs currently on the market in Italy and their relative amount of the active ingredients contained expressed in IUs.

Table 30. Products containing 3-factor prothrombin complex concentrates currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
023309103	UMANCOMPLEX D.I.*FL 500IU+F20mL	500	KEDRION SpA	A
041850013	KEDCOM*FL 500IU+FL 20mL+SET	500	KEDRION SpA	H
023288032	PROTROMPLEX TIM3*F 600IU+20mL	600	BAXTER AG	A

Table 31. Products containing 4-factor prothrombin complex concentrates currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
049861014	COFACT*FL 250 UI + FL SOLV 10mL	250	Prothya Biosolutions Netherlands B.V.	H
038844015	CONFIDEX*500IU+1FL SOLV 20mL	500	CSL BEHRING GMBH	H
039240015	PRONATIV*500IU+FL SOLV 20mL	500	OCTAPHARMA Italy	H
049861026	COFACT*FL 500 UI + FL SOLV 20mL	500	Prothya Biosolutions Netherlands B.V.	H
043304029	PROPLEX*FL 500UI+FL SOLV 17mL	500	BAXALTA Italy Srl	C(nn)
049861038	COFACT*500 UI + SOLV 2ML+DISP	500	Prothya Biosolutions Netherlands B.V.	C(nn)
043304017	PROPLEX*FL 600IU/20mL+FL SOLV	600	BAXALTA Italy Srl	H
038844027	CONFIDEX 1000*FL POLV+FL 40mL	1000	CSL BEHRING SpA	H
039240027	PRONATIV*1000IU+FL SOLV 20mL	1000	OCTAPHARMA Italy	H

Quantification and characterisation of the demand

Table 32 shows the total demand and the standardised one (expressed in IUs *per capita*) for 3F-PCCs in the two-year period 2023-2024, at both national and regional level.

In 2024 there was a decrease in the total demand (-7.3%) compared to 2023; it stood at 31,091,000 IUs, equal to 0.5 IU *per capita*. There were considerable differences in the use of 3F-PCCs from one Region to another with standardised values ranging from 0.2 IUs (Basilicata,

Abruzzo and Latium) to 0.8 IU (Molise and Piedmont), with a percentage deviation from the national average of +54% and +43% for the latter two, respectively (Figures 37 and 38).

Table 32. Total demand (public and private) and total standardised demand for 3 factor-prothrombin complex concentrates, expressed in International Units and International Units *per capita*, and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	361,000	0.3	268,500	0.2	-25.4
AostaValley	10,000	0.1	-	0.0	-100.0
APBolzano	251,000	0.5	175,000	0.3	-30.7
APTrento	250,000	0.5	187,500	0.3	-25.3
Apulia	1,775,500	0.5	2,532,000	0.7	43.2
Basilicata	419,500	0.8	82,500	0.2	-80.2
Calabria	742,000	0.4	689,000	0.4	-6.7
Campania	1,558,500	0.3	1,814,000	0.3	16.7
E.-Romagna	3,367,500	0.8	3,231,500	0.7	-4.3
Friuli V. Giulia	261,000	0.2	500,000	0.4	91.5
Latium	1,751,700	0.3	1,388,000	0.2	-20.7
Liguria	998,500	0.7	619,000	0.4	-38.1
Lombardy	7,209,500	0.7	6,120,000	0.6	-15.4
Marche	614,200	0.4	518,500	0.3	-15.5
Molise	155,000	0.5	235,500	0.8	52.7
Piedmont	3,213,500	0.8	3,207,500	0.8	-0.2
Sardinia	692,000	0.4	838,500	0.5	21.8
Sicily	2,813,500	0.6	3,220,000	0.7	14.8
Tuscany	2,094,000	0.6	1,818,500	0.5	-13.1
Umbria	397,500	0.5	381,000	0.4	-3.8
Veneto	4,601,000	0.9	3,264,500	0.7	-29.1
Italy	33,536,400	0.6	31,091,000	0.5	-7.3

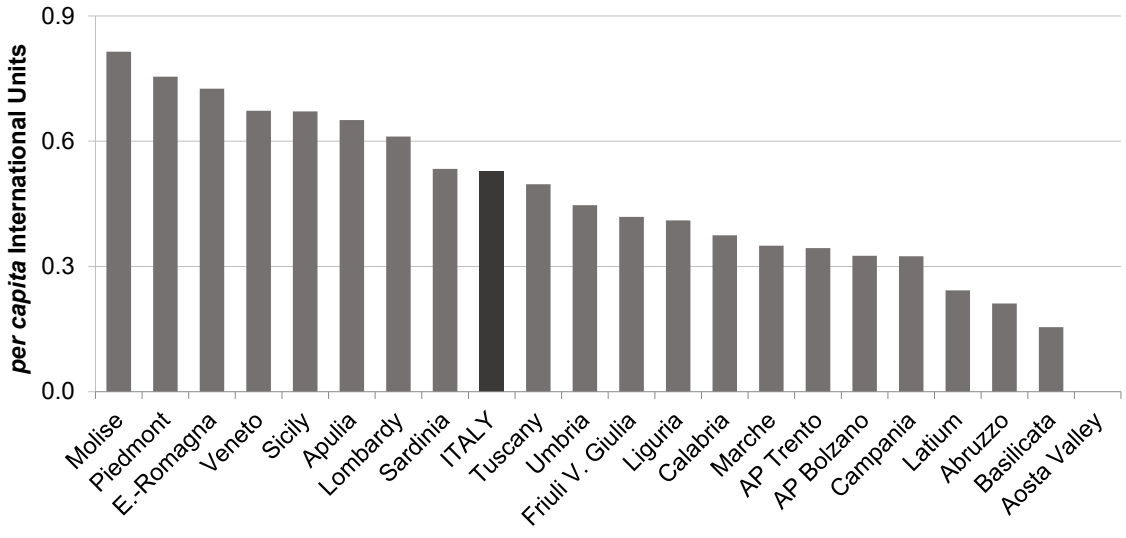

Figure 37. Total and regional demand (public and private) for 3-factor prothrombin complex concentrates, expressed in International Units *per capita*, 2024 (adapted by the CNS on data from the Traceability information flow)

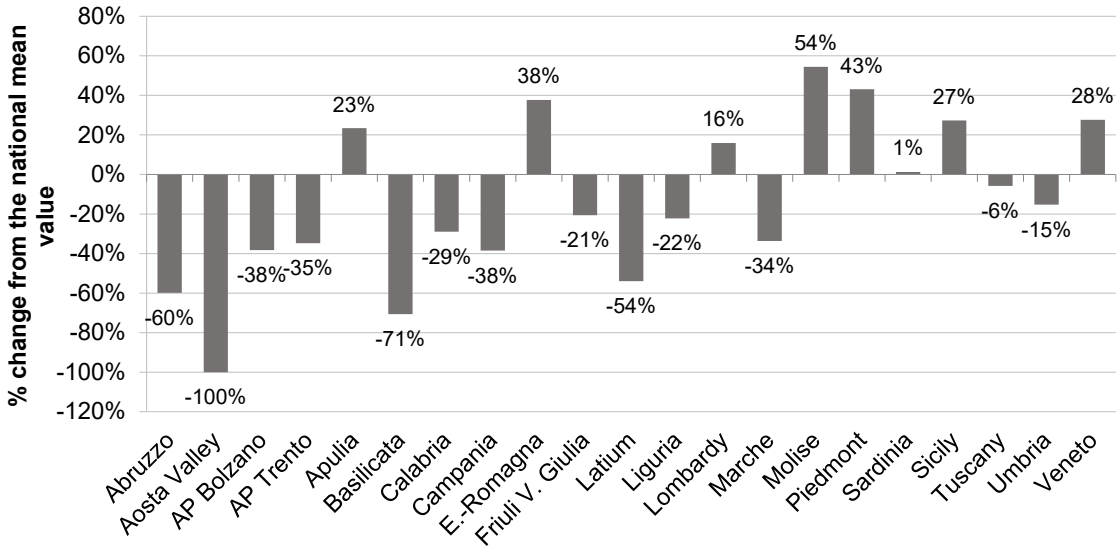

Figure 38. Percentage variation from the national mean value of standardised regional demand for 3-factor prothrombin complex concentrates in 2024 (adapted by the CNS on data from the Traceability information flow)

In 2024, the national demand for 4F-PCCs was 25,109,600 IUs, equal to 44,7% of the overall demand for PCCs, with a standardised demand of 0.4 IU *per capita* and with an increase of 6.4% compared to the previous year (Table 33).

Table 33. Total demand (public and private) and total standardised demand for 4-factor prothrombin complex concentrates, expressed in International Units and International Units *per capita*, and variations in percentage between 2023-2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	978,500	0.8	603,000	0.5	-38.2
Aosta Valley	100,500	0.8	83,500	0.7	-16.7
AP Bolzano	1,099,000	2.1	697,500	1.3	-36.9
AP Trento	135,000	0.2	120,000	0.2	-11.5
Apulia	370,100	0.1	307,500	0.1	-16.6
Basilicata	293,000	0.5	335,000	0.6	15.3
Calabria	414,500	0.2	242,500	0.1	-41.2
Campania	2,820,300	0.5	2,305,500	0.4	-18.0
E.-Romagna	2,391,800	0.5	2,549,200	0.6	6.2
Friuli V. Giulia	-	-	959,500	0.8	100.0
Latium	2,978,300	0.5	4,039,600	0.7	35.8
Liguria	1,260,000	0.8	1,038,500	0.7	-17.7
Lombardy	2,196,000	0.2	2,192,600	0.2	-0.5
Marche	799,700	0.5	932,500	0.6	16.7
Molise	-	-	-	-	NA
Piedmont	1,774,300	0.4	2,401,300	0.6	35.3
Sardinia	1,296,500	0.8	1,606,500	1.0	24.5
Sicily	619,300	0.1	376,900	0.1	-38.9
Tuscany	2,097,400	0.6	1,966,500	0.5	-6.2
Umbria	635,500	0.7	359,000	0.4	-43.3
Veneto	1,348,000	0.3	1,993,000	0.4	47.8
Italy	23,607,700	0.4	25,109,600	0.4	6.4

Also for 4F-PCCs, there were considerable differences regarding its utilisation from one Region to another.

The Region with the highest demand in 2024 is the AP of Bolzano with 1.3 IU *per capita*, followed by Sardinia and Friuli V. Giulia with 1.0 IU and 0.8 IU *per capita* respectively (Figure 39). Figure 40 shows percentage variations compared to the Italian mean values of the standardised regional demand for 4F-PCCs as recorded by the drug Traceability system in 2024.

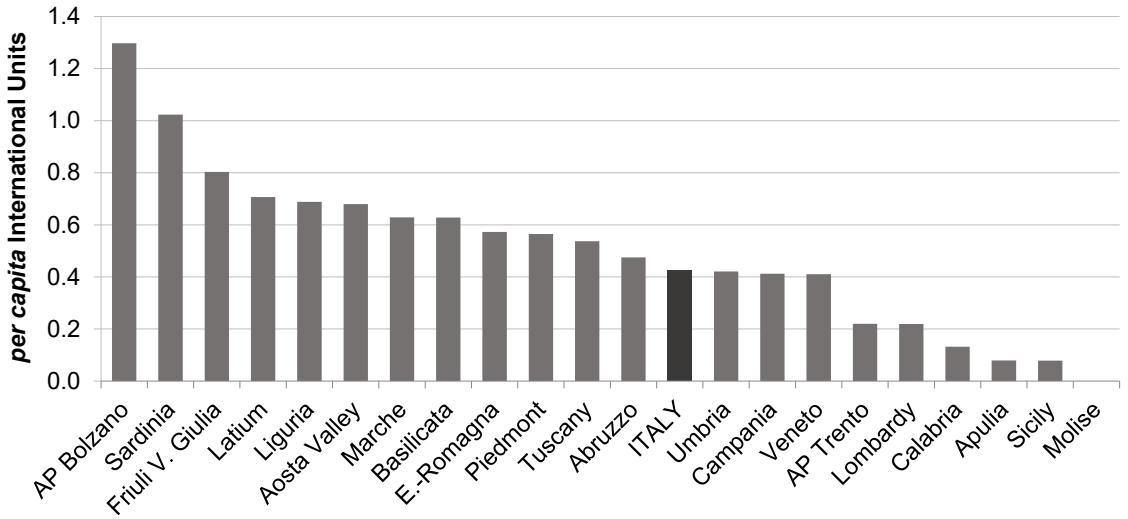

Figure 39. Total and regional demand (public and private) for 4-factor prothrombin complex concentrates, expressed in International Units *per capita*, 2024 (adapted by the CNS on data from the Traceability information flow)

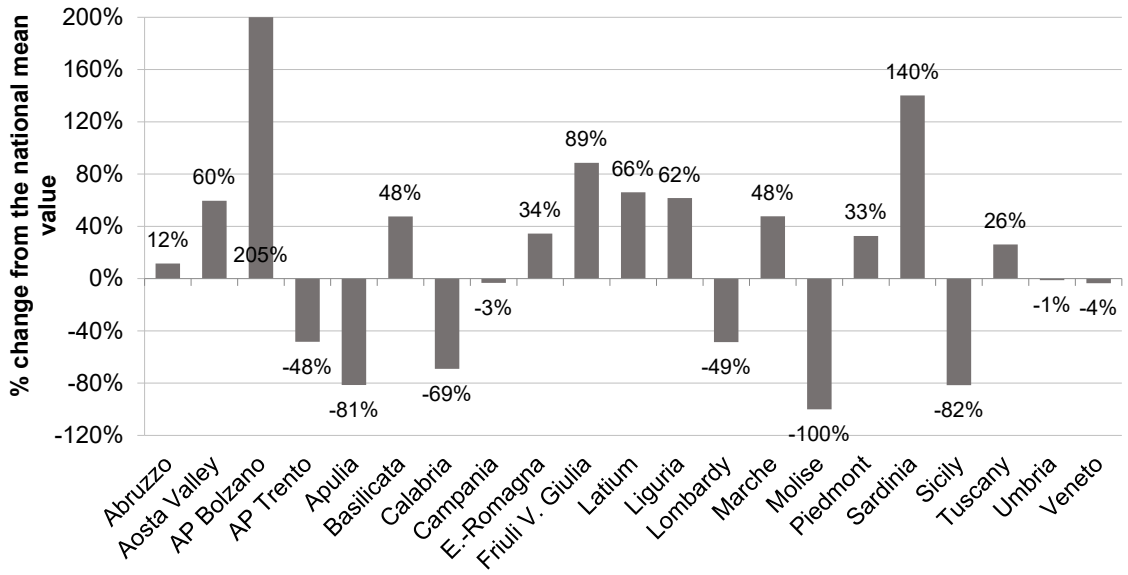

Figure 40. Percentage variation from the national mean value of standardised regional demand for 4-factor prothrombin complex concentrates in 2024 (adapted by the CNS on data from the Traceability information flow)

FIBRINOGEN (ATC B02BB01)

Fibrinogen is one of the most present coagulation factors in plasma, with an average concentration of about 2-4 g/L. It is converted into fibrin by thrombin and is the maincomponent of the coagulation phase. Fibrin, therefore, can be considered both a structural protein and a coagulation factor. In order to provide adequate structural support, the plasma concentration of fibrinogen must be relatively high. A deficiency of fibrinogen thus implies a lower capacity of the blood to coagulate, with a consequent increase in the tendency to bleeding (32).

The utilisation of Fibrinogen is indicated in the following clinical conditions:

i. hypofibrinogenaemia or congenital afibrinogenaemia; ii. congenital dysfibrinogenaemia with a tendency to haemorrhage; iii. occasionally in acquired hypofibrinogenaemia, but only after carefully evaluating other therapeutic options (33) (fresh frozen plasma and cryoprecipitate).

Table 34 shows the brand names of medicinal products containing fibrinogen currently available on the Italian market and the amount of the active ingredients they contain expressed in grams (g).

Table 34. Products containing fibrinogen currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	g	Manufacturer	NHS class
*E00178010	HAEMOCOMPLETTAN P 1F 1g	1	CSL BEHRING SpA	H
040170019	RIASTAP FL POLV 1g 20mg/mL	1	CSL BEHRING SpA	C
040170021	RIASTAP*F POLV 1g20mg/mL+DISP	1	CSL BEHRING SpA	C
048798019	FIBRYGA*FLPOLV 1g 100Mm+F50mL	1	OCTAPHARMA Italy SpA	A
044380018	FIBRICLOTTE*FL POLV 1,5g 100mL	1.5	LFB	C(nn)

* Medicinal products imported under the provisions of DM of 11 February 1997 (8) and DM of 11 May 2001 (10).

Quantification of the demand

Table 35 shows the total demand and the total standardised demand (g per 1,000 population) for fibrinogen over the two-year period 2023-2024 at regional and national level.

In 2024, total fibrinogen demand showed a significant increase (+10.2%) compared to the previous year. Its volume of 73,693 g, with a standardised demand of 1.2 g per 1,000 population, confirmed the rapid upward trend. All Regions, with the exception of Abruzzo, Marche, AP of Bolzano and Umbria contributed to this growth to different extents.

Figure 41 shows the regional and national standardised demand for fibrinogen in 2024. The Regions with the highest demand per 1,000 population were Veneto (2.3 g), then the AP of Bolzano and Umbria (1.7 g), Friuli V. Giulia (1.6 g) and Abruzzo (1,5 g). The lowest demand, between 0.4 g and 0.9 g per 1,000 population, was recorded in Molise, Aosta Valley and Sicily.

Table 35. Total demand (public and private) and total standardised demand for fibrinogen, expressed in grams and grams per 1,000 population, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow and Product Quality and Pharmacrime Office - AIFA)

Region	2023		2024		% Var 2023-2024
	g	g per 1,000 pop	g	g per 1,000 pop	
Abruzzo	1,959	1.5	1,875	1.5	-4.1
Aosta Valley	63	0.5	89	0.7	41.6
AP Bolzano	1,450	2.7	920	1.7	-37.0
AP Trento	690	1.3	760	1.4	9.7
Apulia	3,941	1.0	4,082	1.0	4.0
Basilicata	494	0.9	576	1.1	17.7
Calabria	1,849	1.0	1,871	1.0	1.6
Campania	5,233	0.9	6,571	1.2	25.9
E.-Romagna	5,122	1.2	5,625	1.3	9.5
Friuli V. Giulia	1,680	1.4	1,948	1.6	15.9
Latium	4,999	0.9	7,241	1.3	45.0
Liguria	1,727	1.1	1,815	1.2	5.0
Lombardy	9,389	0.9	10,672	1.1	13.3
Marche	1,808	1.2	1,512	1.0	-16.3
Molise	6	0.0	126	0.4	2010.3
Piedmont	3,469	0.8	4,077	1.0	17.5
Sardinia	2,041	1.3	2,204	1.4	8.5
Sicily	3,955	0.8	4,421	0.9	12.2
Tuscany	4,433	1.2	4,503	1.2	1.6
Umbria	1,660	1.9	1,460	1.7	-11.7
Veneto	10,933	2.3	11,346	2.3	3.7
Italy	66,899	1.1	73,693	1.2	10.2

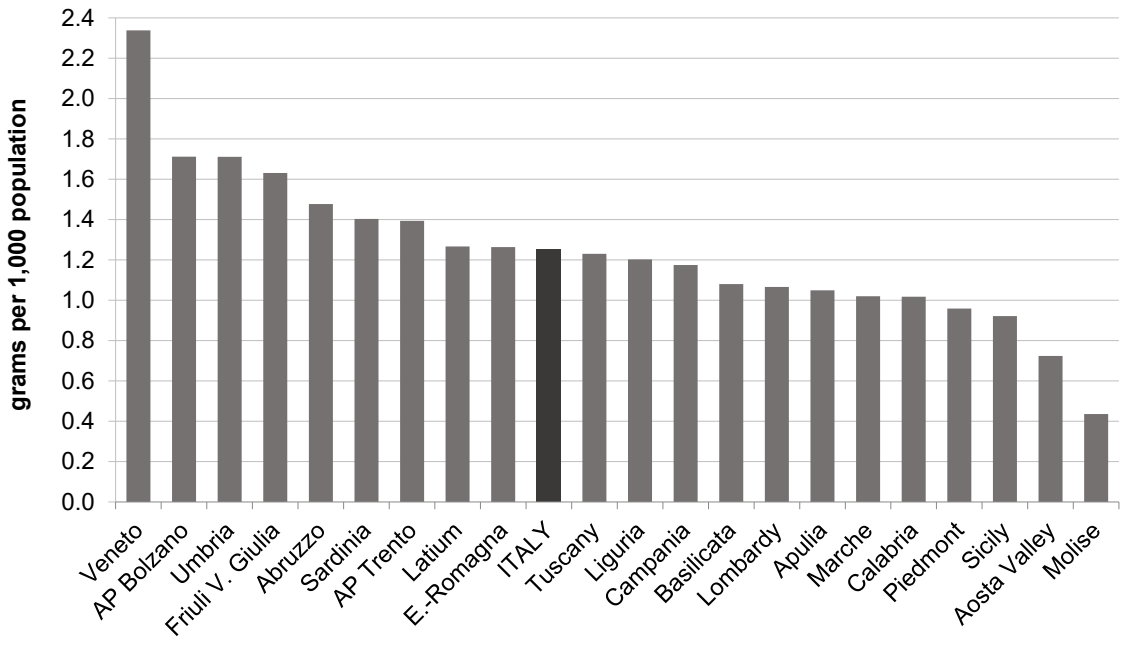

Figure 41. Total and regional demand (public and private) for fibrinogen, expressed in grams per 1,000 population, 2024 (adapted by the CNS on data from the Traceability information flow)

PART B
Other plasma-derived medicinal products

HEPATITIS B IMMUNOGLOBULINS FOR INTRAVENOUS AND SUBCUTANEOUS USE (ATC J06BB04)

The tables below show the brand names of medicinal products containing hepatitis B immunoglobulins for intravenous (IV) (Table 36) and subcutaneous (SC) / intramuscular (IM) use (Table 37) currently on the market in Italy and the amount of the active ingredient they contain expressed in IUs.

Table 36. Products containing hepatitis B immunoglobulins for intravenous use currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
035561012	NEOHEPATECT*IV 1F 100IU 2mL	100	BIOTEST PHARMA GMBH	H
026415048	VENBIG*1F 500IU+F 10mL+SET	500	KEDRION SpA	H
035561024	NEOHEPATECT*IV 1F 500IU 10mL	500	BIOTEST PHARMA GMBH	H
038059010	KEYVENB“500IU/10mL+SET	500	KEDRION SpA	H
038059034	KEYVENB“50IU/mL” F. CON 500IU	500	KEDRION SpA	H
041985019	VEBIKED"50IU/mL"FL CON 500IU	500	KEDRION SpA	C(nn)
038445019	NIULIVA*250 IU/mL 1SIR 2.4 mL	600	GRIFOLS ITALIA SpA	H
038445021	NIULIVA*INF 1SIR 4mL“250IU/mL	1000	INSTITUTO GRIFOLS S.A.	H
035561036	NEOHEPATECT*IV FL 2000IU 40mL	2000	BIOTEST PHARMA GMBH	H
026415051	VENBIG*F 2500IU/50mL+F 45mL+SET	2500	KEDRION SpA	H
038059022	KEYVENB“2500IU/45mL+SET	2500	KEDRION SpA	H
038059046	KEYVENB“50IU/mL” F 2500IU	2500	KEDRION SpA	H
041985021	VEBIKED"50IU/mL" FL 2500IU+SET	2500	KEDRION SpA	C(nn)
035561048	NEOHEPATECT*IV FL 5000IU 100mL	5000	BIOTEST ITALIA Srl	H
038445033	NIULIVA*INF 1FL 20mL 250IU/mL	5000	GRIFOLS ITALIA SpA	H
038445045	NIULIVA“250IU/mL” 1F. 40mL	10000	INSTITUTO GRIFOLS S.A.	H

Table 37. Products containing hepatitis B immunoglobulins for subcutaneous/intramuscular use currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
023782028	UMAN BIG “180 IU/1mL SOLUZ. INIET”	180	KEDRION SpA	A
025653015	IMMUNOHBS*IM 1F 1mL 180IU	180	KEDRION SpA	A
042002016	KEDHBS 180 IU/1mL - 1FL 1mL	180	KEDRION SpA	A
023782016	UMANBIG*IM 1FL 3mL 540IU	540	KEDRION SpA	A
025653027	IMMUNOHBS*IM 1F 3mL 540IU	540	KEDRION SpA	A
042002028	KEDHBS 540 IU/3mL - 1FL 3mL	540	KEDRION SpA	A
035320011	IGANTIBE*IM 1F 3mL 600IU/3mL	600	INSTITUTO GRIFOLS S.A.	A
025653054	IMMUNOHBS*IM 1SIR 1000IU 3mL	1000	KEDRION SpA	A
035320023	IGANTIBE*IM 1F 5mL 1000IU/5mL	1000	INSTITUTO GRIFOLS S.A.	A
042002030	KEDHBS 1000 IU/3mL 1SIR 3mL	1000	KEDRION SpA	A
039644012	ZUTECTRA*SC 5SIR 1mL 500IU	2500	BIOTEST PHARMA GMBH	A

Quantification of the demand

Tables 38 and 39 show respectively the total demand and the total standardised demand (expressed in IUs *per capita*) of hepatitis B IG formulations for IV and for SC/IM use for the two-year period 2023-2024, at national and at regional level. The national demand for hepatitis B IGs for IV use, showed a downward trend (-12%) already observed in previous years (34).

The total demand in 2024 was almost 11,2 million IUs (0.2 IU *per capita*) (Table 38).

Table 38. Total demand (public and private) and total standardised demand for hepatitis B immunoglobulins for intravenous use, expressed in International Units and International Units *per capita*, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow).

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	18,000	0.0	-	-	-100.0
Aosta Valley	-	-	-	-	NA
AP Bolzano	-	-	-	-	NA
AP Trento	-	-	-	-	NA
Apulia	1,546,500	0.4	809,000	0.2	-47.5
Basilicata	2,000	0.0	-	-	-100.0
Calabria	115,500	0.1	75,500	0.0	-34.3
Campania	2,479,000	0.4	2,045,000	0.4	-17.3
E.-Romagna	1,497,500	0.3	1,885,000	0.4	25.5
Friuli V. Giulia	-	-	-	-	NA
Latium	1,065,000	0.2	1,059,000	0.2	-0.5
Liguria	180,000	0.1	312,500	0.2	73.4
Lombardy	1,195,500	0.1	1,715,000	0.2	42.9
Marche	121,000	0.1	209,000	0.1	72.9
Molise	-	-	-	-	NA
Piedmont	547,500	0.1	375,000	0.1	-31.5
Sardinia	629,000	0.4	528,000	0.3	-15.6
Sicily	490,000	0.1	302,500	0.1	-38.1
Tuscany	901,000	0.2	716,000	0.2	-20.5
Umbria	-	-	4,000,0	0.0	100.0
Veneto	1,977,000	0.4	1,206,500	0.2	-39.0
Italy	12,764,500	0.2	11,242,000	0.2	-11.9

Emilia-Romagna and Campania (0.4 IU *per capita*) and Sardinia (0.3 IU *per capita*) are the Regions with the highest demand together accounting for more than 40 percent of national demand.

On the other hand, the national demand for antihepatitis B SC/IM IG, shows a slight decrease, equal to -2.5% of the demand recorded in 2023; the total consumption for 2024 is approximately 58.4 million IUs (1.0 IUs *per capita*) (Table 39) and accounted 84% of the total demand for antihepatitis B IGs.

Table 39. Total demand (public and private) and total standardised demand for hepatitis B immunoglobulins for subcutaneous/intramuscular use, expressed in International Units and International Units *per capita*, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow).

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	560,000	0.4	625,460	0.5	12.0
Aosta Valley	207,800	1.7	211,760	1.7	2.1
AP Bolzano	90,620	0.2	156,660	0.3	71.8
AP Trento	177,320	0.3	198,420	0.4	11.5
Apulia	6,376,640	1.6	5,813,980	1.5	-8.4
Basilicata	248,300	0.5	426,540	0.8	73.2
Calabria	1,347,240	0.7	1,569,940	0.9	17.0
Campania	18,322,120	3.3	17,241,100	3.1	-5.6
E.-Romagna	4,113,820	0.9	4,132,440	0.9	0.1
Friuli V. Giulia	288,200	0.2	392,380	0.3	36.1
Latium	2,343,740	0.4	2,242,580	0.4	-4.2
Liguria	526,020	0.3	626,460	0.4	19.0
Lombardy	8,353,780	0.8	8,252,940	0.8	-1.6
Marche	695,740	0.5	689,840	0.5	-0.7
Molise	202,480	0.7	150,180	0.5	-25.5
Piedmont	4,480,820	1.1	4,462,860	1.0	-0.4
Sardinia	2,994,300	1.9	3,082,260	2.0	3.4
Sicily	2,956,000	0.6	3,247,340	0.7	10.2
Tuscany	2,628,320	0.7	2,124,340	0.6	-19.1
Umbria	319,720	0.4	283,900	0.3	-10.9
Veneto	2,634,340	0.5	2,433,320	0.5	-7.7
Italy	59,867,320	1.0	58,364,700	1.0	-2.5

TETANUS IMMUNOGLOBULINS (ATC J06BB02)

Table 40 shows drugs containing tetanus IGs currently available on the Italian market and the amount of the active ingredient they contain, expressed in IUs.

Table 40. Products containing tetanus immunoglobulins currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024).

AIC code	Brand name	IU	Manufacturer	NHS class
022488047	TETANUSGAMMA*IM 1SIR 250IU 2mL	250	KEDRION SpA	A
022488062	TETANUSGAMMA*IM SIR 250IU 1mL	250	KEDRION SpA	A
022601088	TETABULIN*IM 1SIR 250IU 1mL	250	BAXTER SpA	A
022635041	GAMMATET P*IM 1F 250IU 1mL	250	CSL BEHRING SpA	A
022635066	GAMMATET P*IM 1SIR 250IU 1mL	250	CSL BEHRING SpA	A
033863010	IGANTET*IM 1SIR 1mL 250IU	250	GRIFOLS ITALIA SpA	A
022488050	TETANUSGAMMA*IM 1SIR 500IU 2mL	500	KEDRION SpA	A
022601090	TETABULIN*IM 1SIR 500IU 2mL	500	BAXTER SpA	A
022635054	GAMMATET P*IM 1F 500IU 2mL	500	CSL BEHRING SpA	A
022635078	GAMMATET P*IM 1SIR 500IU 2mL	500	CSL BEHRING SpA	A
033863022	IGANTET*IM 1SIR 2mL 500IU	500	GRIFOLS ITALIA SpA	A
-*	TETAGAM P 250 IU/1 mL	250	CSL BEHRING SpA	-

*Medicinal products imported under the provisions of DM of 11 February 1997 (8) and DM of 11 May 2001 (10).

Quantification of the demand

In 2024 the total demand for tetanus IGs was 124,856,500 IUs (2.1 IUs *per capita*), showing an increase of +2% compared to 2023 (Table 41).

The Regions with the highest demand, expressed as standardised volume for the resident population, were Campania (4.4 IUs *per capita*), Basilicata (4.3 IUs *per capita*), Abruzzo (3.6 IUs *per capita*) and Calabria (3.1 IUs *per capita*).

In 2024, most Regions will see a decline in demand, in some cases quite significant, as in the case of AP of Bolzano (-35%) and Aosta Valley (-27%), while the increase in demand recorded in Friuli V. Giulia and Basilicata (respectively +153% and +38%) is particularly evident.

For the year 2024, there were no imports of anti-tetanus IGs under the provisions of the DM of 11 February 1997 and the DM of 11 May 2001, as it had happened in the previous years, when they were listed under the heading “Not Specified Region”.

Table 41. Total demand (public and private) and total standardised demand, expressed in International Units and International Units *per capita*, for tetanus immunoglobulins and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow and Product Quality and Pharmacrime Office - AIFA)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	4,994,250	3.9	4,600,000	3.6	-7.7
Aosta Valley	326,750	2.7	238,000	1.9	-27.0
AP Bolzano	631,500	1.2	413,750	0.8	-34.9
AP Trento	458,250	0.8	455,000	0.8	-1.1
Apulia	6,604,750	1.7	6,988,000	1.8	6.3
Basilicata	1,673,500	3.1	2,295,500	4.3	38.3
Calabria	6,043,500	3.3	5,770,500	3.1	-4.1
Campania	22,826,000	4.1	24,709,000	4.4	8.6
E.-Romagna	6,366,250	1.4	6,189,750	1.4	-3.1
Friuli V. Giulia	26,250	0.0	66,500	0.1	153.3
Latium	10,833,000	1.9	11,405,000	2.0	5.4
Liguria	3,704,000	2.5	3,433,000	2.3	-7.4
Lombardy	15,884,250	1.6	15,741,750	1.6	-1.2
Marche	4,114,250	2.8	4,303,250	2.9	4.7
Molise	886,500	3.1	837,250	2.9	-5.1
Piedmont	4,754,250	1.1	4,620,750	1.1	-2.8
Sardinia	4,012,000	2.5	3,950,250	2.5	-1.1
Sicily	12,831,000	2.7	13,011,750	2.7	1.8
Tuscany	10,876,000	3.0	10,802,000	3.0	-0.6
Umbria	2,166,500	2.5	2,008,500	2.4	-6.9
Veneto	2,570,500	0.5	3,017,000	0.6	17.3
Italy	122,583,250	2.1	124,856,500	2.1	1.9

ANTI-D (RH) IMMUNOGLOBULINS (ATC J06BB01)

Table 42 shows the brand names of medicinal products containing the anti-D (Rh) IGs currently available on the Italian market and the amount of active ingredient they contain, expressed in IUs.

Table 42. Products containing anti-D (Rh) immunoglobulins currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
039596010	RHESONATIV*1F 1mL 625IU/mL	625	OCTAPHARMA Italy SpA	A
022547020	IMMUNORHO*IM 1FL 200mcg+1F 2mL	1000	KEDRION SpA	A
036161014	RHOPHYLAC*1SIR 200 mcg/2mL	1000	CSL BEHRING GmbH	C
039596022	RHESONATIV*1F 2mL 625IU/mL	1250	OCTAPHARMA Italy SpA	A
022547018	IMMUNORHO*IM 1FL 300mcg+1F 2mL	1500	KEDRION SpA	A
022547044	IMMUNORHO*IM 1SIR 2mL 300mcg	1500	KEDRION SpA	A
033867021	IGAMAD*IM 1SIR 1500IU/2mL	1500	GRIFOLS ITALIA SpA	A
036161026	RHOPHYLAC*1SIR 300mcg/2mL	1500	CSL BEHRING GmbH	C
036161038	RHOPHYLAC*5SIR 300mcg/2mL	7500	CSL BEHRING GmbH	C
039596034	RHESONATIV*10F 2mL 625IU/mL	12500	OCTAPHARMA Italy SpA	A

Quantification of the demand

The national demand for anti-D IGs between 2023 and 2024 showed a decrease (-12%) and stood at 93,692,625 IUs in 2024 (1.6 IUs *per capita*), with the highest peak in the AP of Bolzano and the lowest level in Friuli V. Giulia (3.6 and 0.2 IUs *per capita*, respectively) (Table 43).

Table 43. Total demand (public and private) and total standardised demand for anti-D (Rh) immunoglobulins, expressed in International Units and in International Units *per capita* and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Abruzzo	2,298,000	1.8	2,262,000	1.8	-1.3
Aosta Valley	268,500	2.2	225,000	1.8	-16.0
AP Bolzano	1,996,250	3.7	1,951,250	3.6	-2.9
AP Trento	1,504,500	2.8	1,318,750	2.4	-12.7
Apulia	6,315,000	1.6	5,415,000	1.4	-13.9
Basilicata	948,000	1.8	793,500	1.5	-15.6
Calabria	2,644,500	1.4	2,553,000	1.4	-3.0
Campania	6,862,000	1.2	7,224,000	1.3	5.6
E.-Romagna	10,093,750	2.3	7,740,750	1.7	-23.6
Friuli V. Giulia	135,000	0.1	249,000	0.2	84.4
Latium	8,739,000	1.5	7,117,500	1.2	-18.5
Liguria	2,577,000	1.7	2,391,000	1.6	-7.3
Lombardy	21,551,125	2.2	19,789,750	2.0	-8.5

Region	2023		2024		% Var 2023-2024
	IU	IU *per capita*	IU	IU *per capita*	
Marche	2,656,500	1.8	2,647,500	1.8	-0.2
Molise	298,500	1.0	371,125	1.3	24.9
Piedmont	8,139,375	1.9	8,004,000	1.9	-1.7
Sardinia	1,287,000	0.8	1,033,500	0.7	-19.3
Sicily	7,559,500	1.6	6,458,000	1.3	-14.3
Tuscany	8,309,250	2.3	6,948,500	1.9	-16.3
Umbria	1,668,000	1.9	1,458,000	1.7	-12.2
Veneto	10,278,000	2.1	7,741,500	1.6	-24.7
Italy	106,128,750	1.8	93,692,625	1.6	-11.7

CYTOMEGALOVIRUS IMMUNOGLOBULINS (ATC J06BB09)

Table 44 shows the brand names of medicinal products containing cytomegalovirus immunoglobulins (anti-CMV IGs) currently available on the Italian market and the amount of the active ingredients they contain expressed in U (Unit of the Paul-Erlich Institute and in References preparation).

Table 44. Products containing cytomegalovirus immunoglobulins currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	U	Manufacturer	NHS class
26167015	CYTOTECT BIOTEST*EV 10mL 500U	500	BIOTEST PHARMA GmbH	H
26167027	CYTOTECT BIOTEST*EV 20mL 1000U	1000	BIOTEST PHARMA GmbH	H
26167041	CYTOTECT BIOTEST*EV 10mL1000U	1000	BIOTEST PHARMA GmbH	H
46731016	CYTOMEGATECT*EV10mL100U	1000	BIOTESTPHARMAGmbH	H
26167039	CYTOTECT BIOTEST*EV 50mL 2500U	2500	BIOTEST PHARMA GmbH	H
26167054	CYTOTECTBIOTEST*EV50mL 5000U	5000	BIOTESTPHARMAGmbH	H
46731028	CYTOMEGATECT*EV50mL 100U	5000	BIOTESTPHARMAGmbH	H

Quantification of the demand

Table 45 shows the total demand and the total standardised demand (U *per capita*) for CMV IGs for the two-year period 2023-2024, at national and regional levels.

Table 45. Total demand (public and private) and total standardised demand for cytomegalovirus immunoglobulins products, expressed in References preparation Unit of the Paul-Erlich Institute and in References preparation Unit of the Paul-Erlich Institute *per capita*, and variations in percentages between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	U	U *per capita*	U	U *per capita*	
Abruzzo	73,000	0.1	109,000	0.1	49.7
Aosta Valley	15,000	0.1	-	-	-100.0
AP Bolzano	-	-	31,000	0.1	100.0
AP Trento	-	-	6,000,0	0.0	100.0
Apulia	799,000	0.2	697,000	0.2	-12.4
Basilicata	95,000	0.2	-	-	-100.0
Calabria	670,000	0.4	379,000	0.2	-43.2
Campania	1,204,000	0.2	1,517,000	0.3	26.3
E.-Romagna	1,056,000	0.2	1,496,000	0.3	41.2
Friuli V. Giulia	510,000	0.4	690,000	0.6	35.3
Latium	627,000	0.1	810,000	0.1	29.3
Liguria	55,000	0.0	88,000	0.1	59.8
Lombardy	860,000	0.1	778,000	0.1	-9.9
Marche	127,000	0.1	188,000	0.1	48.2

Region	2023		2024		% Var 2023-2024
	U	U *per capita*	U	U *per capita*	
Molise	-	-	-	-	NA
Piedmont	3,598,000	0.8	2,559,000	0.6	-28.9
Sardinia	48,000,0	0.0	86,000	0.1	80.0
Sicily	1,355,000	0.3	654,000	0.1	-51.6
Tuscany	986,000	0.3	1,391,000	0.4	41.1
Umbria	219,000	0.3	194,000	0.2	-11.1
Veneto	2,469,000	0.5	3,371,000	0.7	36.5
Italy	14,766,000	0.3	15,044,000	0.3	1.9

During the period under examination, the CMV IGs national demand increased by 2% compared to the previous year and stood at 15,044,000 U. However, the national average showed strong fluctuations, trends varied from one Region to another; Veneto was the Region with the highest standardized demand (0.7 U *per capita*), followed by Piedmont and Friuli V. Giulia (0.6 U *per capita*).

VARICELLA/ZOSTER IMMUNOGLOBULINS FOR INTRAVENOUS USE (ATC J06BB03)

Human immunoglobulins with specific anti-human herpesvirus 3 antibodies (varicella-zoster virus 1) (Var IGs) are used in post-exposure prophylaxis of varicella zoster and for the treatment of severe varicella-zoster infections or complications, in immunocompromised patients or infants at risk. These human immunoglobulins are obtained from selected plasma donors with high titers of anti-varicella antibodies (35-37).

Table 46 shows the brand names of medicinal products containing Var IGs currently available on the Italian market and the amount of the active ingredients they contain, expressed in IUs.

Table 46. Products containing specific varicella/zoster immunoglobulins for intravenous use currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
026978027*	VARITECT 25 IU/mL 1F 5mL	125	BIOTEST PHARMA GmbH	H
026978015*	VARITECT 25 IU/mL 1F 20mL	500	BIOTEST PHARMA GmbH	H

* Medicinal products imported under the provisions of DM of 11 February 1997 (8) and DM of 11 May 2001 (10).

Quantification of the demand

Table 47 shows the total demand and the total standardised demand (IUs per 1,000 population) of specific IG anti-Var zoster (IV) in the two-year period 2023-2024, at national and regional levels. The national demand for IG anti-Var over the time interval examined, showed a strong decrease (-58.5%). Total demand in 2024 was 41,250 IUs (0.7 IUs per 1,000 population).

Table 47. Total demand (public and private) and total standardised demand for products containing varicella/zoster immunoglobulins for intravenous use, expressed in International Units and International Units per 1,000 population and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Product Quality and Pharmacrime Office - AIFA)

Region	2023		2024		% Var 2023-2024
	IU	IU per 1,000 pop	IU	IU per 1,000 pop	
Abruzzo	1,000	0.8	-	0.0	-100.0
Aosta Valley	-	0.0	-	0.0	NA
AP Bolzano	2,750	5.1	2,500	4.7	-9.7
AP Trento	500	0.9	-	0.0	-100.0
Apulia	3,375	0.9	-	0.0	-100.0
Basilicata	-	0.0	-	0.0	NA
Calabria	-	0.0	-	0.0	NA
Campania	1,125	0.2	-	0.0	-100.0
Emilia-Romagna	9,875	2.2	-	0.0	-100.0
Friuli V. Giulia	18,500	15.5	3,500	2.9	-81.1

Region	2023		2024		% Var 2023-2024
	IU	IU per 1,000 pop	IU	IU per 1,000 pop	
Latium	5,875	1.0	250	0.0	-95.7
Liguria	625	0.4	-	0.0	-100.0
Lombardy	10,375	1.0	7,250	0.7	-30.4
Marche	29,125	19.6	12,000	8.1	-58.8
Molise	-	0.0	-	0.0	NA
Piedmont	4,000	0.9	9,625	2.3	140.6
Sardinia	-	0.0	250	0.2	NA
Sicily	-	0.0	-	0.0	NA
Tuscany	2,125	0.6	750	0.2	-64.7
Umbria	4,000	4.7	-	0.0	-100.0
Veneto	6,125	1.3	5,125	1.1	-16.4
Italy	99,375	1.7	41,250	0.7	-58.5

RABIES IMMUNOGLOBULINS (ATC J06BB05)

Human immunoglobulins with rabies-specific antibodies (rabies IGs) are used for post-exposure prophylaxis in cases of scratches, bites or other injuries caused by rabid or potentially rabid animals. They are obtained from selected plasma donors with high titers of anti-rabies antibodies (38).

Table 48 shows the brand names of drugs containing rabies IGs currently on the market in Italy and the amount of active ingredient they contain, expressed in IUs.

Table 48. Products containing rabies immunoglobulins currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
- *	BERIRAB P 150IU/mL 2mL	300	CSL BEHRING GmbH	-
- *	BERIRAB P 150IU/mL 5mL	750	CSL BEHRING GmbH	-

* Medicinal products imported under the provisions of the DM of 11 February 1997 (8) and the DM of 11 May 2001 (10).

Quantification of the demand

In 2024, the total demand for anti-rabies IG, recorded in only thirteen Regions, showed a significant increase compared to 2023 (+44%) and, therefore, the total demand amounted to 362,100 IUs (6.1 IUs per thousand population units) (Table 49).

Table 49. Total demand (public and private) and total standardised demand for rabies immunoglobulin, expressed in International Units and International Units per 1,000 population, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from theProduct Quality and Pharmacrime Office – AIFA)

Region	2023		2024		% Var 2023-2024
	IU	IU per 1,000 pop.	IU	IU per 1,000 pop.	
Abruzzo	900	0.7	-	-	-100.0
Aosta Valley	1,500	12.2	1,500	12.2	0.2
AP Bolzano	5,250	9.8	16,800	31.3	218.0
AP Trento	-	-	-	-	NA
Apulia	5,400	1.4	2,400	0.6	-55.4
Basilicata	-	-	-	-	NA
Calabria	-	-	-	-	NA
Campania	-	-	-	-	NA
E.-Romagna	24,000	5.4	38,100	8.6	58.2
Friuli V. Giulia	61,800	51.7	37,800	31.6	-38.9
Latium	3,000	0.5	4,200	0.7	40.1
Liguria	-	-	-	-	NA
Lombardy	63,150	6.3	113,700	11.4	79.4
Marche	7,500	5.1	8,400	5.7	12.1
Molise	-	-	-	-	NA
Piedmont	17,700	4.2	33,300	7.8	88.1
Sardinia	-	-	-	-	NA

Region	2023		2024		% Var 2023-2024
	IU	IU per 1,000 pop.	IU	IU per 1,000 pop.	
Sicily	1,800	0.4	2,100	0.4	17.1
Tuscany	29,850	8.2	44,400	12.1	48.8
Umbria	-	-	3,300	3.9	100.0
Veneto	28,950	6.0	56,100	11.6	93.7
Italy	250,800	4.3	362,100	6.1	44.4

LOCAL HAEMOSTATIC AGENTS-COMBINATIONS (ATC B02BC - ATC B02BC30)

Table 50 shows the brand names of drugs containing local haemostatics – combinations currently on the market in Italy and the amount of the active ingredients expressed in mL and in the number of gelatin sponges they contain.

Table 50. Products containing local haemostatics-combinations currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	mL	Manufacturer	NHS class
035941018	BERIPLAST P*FL POLV 0,5mL+FL	0.5	CSL BEHRING GmbH	C
035941020	BERIPLAST P*FL POLV 1mL+FL+SET	1	CSL BEHRING GmbH	C
035941032	BERIPLAST P*FL POLV 3mL+FL+SET	3	CSL BEHRING GmbH	C
039546015	ARTISS SOL. ADESIVO TISSUTALE	1	BAXTER SpA	H
039546078	ARTISS*1SIR 1mL+1mL	1	BAXTER SpA	C
025243179	TISSEEL 2mL ADESIVO TISSUTALE	2	BAXTER SpA	H
039546027	ARTISS SOL. ADESIaVO TISSUTALE	2	BAXTER SpA	C
039546080	ARTISS*1SIR 2mL+2mL	2	BAXTER SpA	C
039591019	EVICEL*2FL 1mL 90mg/mL+1200IU	2	OMRIX BIOPHARMA	H
042046019	SILKETAL 2,5mL ADESIVO TISSUTALE	2.5	KEDRION SpA	C
044152015	KOLFIB*FL POLV SOLV 2,5mL	2.5	KEDRION SpA	C
025243181	TISSEEL 4mL ADESIVO TISSUTALE	4	BAXTER SpA	H
039591021	EVICEL*2FL 2mL 90mg/mL+1200IU	4	OMRIX BIOPHARMA	H
039546039	ARTISS SOL. ADESIVO TISSUTALE	5	BAXTER SpA	C
039546092	ARTISS*1SIR 5mL+5mL	5	BAXTER SpA	C
042046021	SILKETAL 5mL ADESIVO TISSUTALE	5	KEDRION SpA	C
044152027	KOLFIB*FL POLV SOLV 5mL	5	KEDRION SpA	C
025243193	TISSEEL 10mL ADESIVO TISSUTALE	10	BAXTER SpA	H
039591033	EVICEL*2FL 5mL 90mg/mL+1200IU	10	OMRIX BIOPHARMA	H
042046033	SILKETAL 10mL ADESIVO TISSUTALE	10	KEDRION SpA	C
044152039	KOLFIB*FL POLV SOLV 10mL	10	KEDRION SpA	C
		sponges		
036557015	TACHOSIL*1SPUGNA 9,5cmx4,8cm	1	TAKEDA Italy SpA	C
036557039	TACHOSIL*1MATRICE 3 cmx2,5 cm	1	TAKEDA Gmbh	C
036557054	TACHOSIL*1MATRICE 4,8cmx4,8cm	1	TAKEDA Italy SpA	C
043011016	EVARREST*1BUST 8,1mg+40IU/cm^2	1	OMRIX BIOPHARMA	C
036557027	TACHOSIL*2SPUGNE 4,8cmx4,8cm	2	TAKEDA Italy SpA	C
043011028	EVARREST*2BUST 8,1mg+40IU/cm^2	2	OMRIX BIOPHARMA	C
036557041	TACHOSIL*5MATRICI 3 cm X 2,5 cm	5	TAKEDA Gmbh	C

Quantification of demand

The various products with an ATC code related to local haemostatics–combinations despite not always having the same composition, they can still be considered equivalent, their active ingredient is expressed in mL and mL per 1,000 population (Table 51). However, in the case of those products in the form of “medicated gelatin sponges” that cannot be expressed in mL no standardisation is performed and demand is calculated according to the number of packs sold (Table 52).

Table 51. Total demand (public and private) and total standardised demand for local haemostatics- combinations, expressed in millilitres and in millilitres per 1,000 population, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	mL	mL per 1,000 pop	mL	mL per 1,000 pop	
Abruzzo	13,066	10.3	14,740	11.6	13.1
Aosta Valley	334	2.7	386	3.1	15.8
AP Bolzano	3,095	5.8	3,238	6.0	4.0
AP Trento	3,334	6.1	2,752	5.0	-17.8
Apulia	35,558	9.1	34,676	8.9	-2.1
Basilicata	3,673	6.8	3,656	6.9	0.3
Calabria	4,444	2.4	6,298	3.4	42.3
Campania	68,443	12.2	76,827	13.7	12.6
Emilia-Romagna	39,312	8.9	37,950	8.5	-3.8
Friuli V. Giulia	4,996	4.2	4,290	3.6	-14.2
Latium	42,899	7.5	44,469	7.8	3.8
Liguria	7,518	5.0	8,418	5.6	11.9
Lombardy	74,526	7.5	79,646	8.0	6.5
Marche	4,580	3.1	6,360	4.3	39.0
Molise	8,060	27.7	9,454	32.7	17.9
Piedmont	22,226	5.2	23,403	5.5	5.3
Sardinia	13,822	8.8	16,444	10.5	19.6
Sicily	29,992	6.2	34,932	7.3	16.9
Tuscany	28,316	7.7	27,316	7.5	-3.5
Umbria	4,694	5.5	4,756	5.6	1.7
Veneto	29,940	6.2	29,810	6.1	-0.5
Italy	442,828	7.5	469,821	8.0	6.1

Table 52. Total demand (public and private) for local haemostatics-combinations, expressed in number of gelatin sponges, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023	2024	% Var 2023-2024
Abruzzo	1,357	1,850	36.3
Aosta Valley	210	241	14.8
AP Bolzano	481	582	21.0
AP Trento	262	194	-26.0
Apulia	1,688	1,908	13.0
Basilicata	825	752	-8.8
Calabria	1,960	2,410	23.0
Campania	5,846	9,068	55.1
Emilia-Romagna	2,383	3,093	29.8
Friuli V. Giulia	1,137	909	-20.1
Latium	2,861	2,813	-1.7
Liguria	505	545	7.9
Lombardy	7,934	9,199	15.9
Marche	1,530	1,496	-2.2
Molise	-	-	NA
Piedmont	3,996	3,906	-2.3
Sardinia	521	349	-33.0
Sicily	2,944	2,628	-10.7
Tuscany	2,936	2,811	-4.3
Umbria	982	1,303	32.7
Veneto	2,819	2,927	3.8
Italy	43,177	48,984	13.4

In 2024, the total demand for local haemostatics-combinations reached a volume of about 469,821 mL (8.0 mL per 1,000 population), recording a noticeble increase (+6%) compared to their volume in 2023 (Table 51). In 2024, the total demand for local haemostatics–combinations, expressed in number of gelatin sponges, also appeared to increase compared to the previous year (+13.4%), it amounted to 48,984 sponges (Table 52).

COAGULATION FACTOR VII (ATC B02BD05)

Table 53 shows the brand names of medicinal products containing FVII currently available on the Italian market and the amount of the active ingredients they contain expressed in IUs.

Table 53. Products containing Factor VII currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
024748042	PROVERTINUM TIM3*IV FL 600IU	600	BAXTER AG	A

Quantification of the demand

In 2024, the total demand and the total standardised national demand for FVII was approximately 6.6 million IUs, showing a slightly increase over 2023 (+2.2%) (Table 54).

Table 54. Total demand (public and private demand) and total standardised demand for Factor VII expressed in International Units and International Units per 1,000 population, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU per 1,000 pop	IU	IU per 1,000 pop	
Abruzzo	837,000	657.7	961,200	757.1	15.1
Aosta Valley	-	-	-	-	NA
AP Bolzano	-	-	-	-	NA
AP Trento	-	-	-	-	NA
Apulia	462,000	118.2	517,800	133.1	12.6
Basilicata	52,200	97.1	28,800	54.0	-44.4
Calabria	35,400	19.2	19,800	10.8	-43.8
Campania	442,800	78.9	729,000	130.3	65.1
E.-Romagna	282,000	63.5	459,000	103.1	62.2
Friuli V. Giulia	-	-	-	-	NA
Latium	1,936,200	338.5	1,455,000	254.6	-24.8
Liguria	26,400	17.5	45,600	30.2	72.6
Lombardy	1,418,400	142.2	1,378,800	137.7	-3.1
Marche	-	-	15,600	10.5	100.0
Molise	339,600	1168.5	300,000	1037.3	-11.2
Piedmont	239,400	56.3	247,200	58.1	3.3
Sardinia	-	-	10,200,0	6.5	100.0
Sicily	397,200	82.5	395,400	82.4	-0.1
Tuscany	34,800	9.5	87,000	23.8	150.1
Umbria	1,200	1.4	-	-	-100.0
Veneto	2,400	0.5	-	-	-100.0
Italy	6,507,000	110.3	6,650,400	112.8	2.2

The largest decreases were recorded in Umbria and Veneto (-100%), Basilicata and Calabria (-44%). An increase in the consumption of FVII was recorded in particular in Tuscany (+150%), in Sardinia and Marche (+100%) and in Liguria (+73%). In 2024, there was no utilisation of FVII in several Regions.

RECOMBINANT ACTIVATED FACTOR VII (EPTACOG ALFA ACTIVATED) (ATC B02BD08)

Table 55 shows the brand names of medicinal products containing rFVIIa currently available on the Italian market and the amount of the active ingredients they contain, expressed in milligrams (mg).

Table 55. Products containing recombinant activated Factor VII currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	mg	Manufacturer	NHS class
029447048	NOVOSEVEN*IV 1mg(50KIU)+1,1mL	1	NOVO NORDISK SpA	H
029447087	NOVOSEVEN*IV 1mg(50KIU)+1mL	1	NOVO NORDISK SpA	H
050298013	CEVENFACTA*EV 1 mg +Sol 1,1 mL	1	LFB	A
029447012	NOVOSEVEN*IV 1,2mg(60KIU)+2,2mL	1.2	NOVO NORDISK SpA	H
029447051	NOVOSEVEN*IV 2mg(100KIU)+2,1mL	2	NOVO NORDISK SpA	H
029447099	NOVOSEVEN*IV 2mg(100KIU)+2mL	2	NOVO NORDISK SpA	H
050298025	CEVENFACTA*EV 2 mg +Sol 2,2 mL	2	LFB	A
029447024	NOVOSEVEN*IV 2,4mg(120 KIU)	2.4	NOVO NORDISK SpA	H
029447036	NOVOSEVEN*IV 4,8 mg(240 KIU)	4.8	NOVO NORDISK SpA	H
029447063	NOVOSEVEN*IV 5mg(250KIU)+5,2mL	5	NOVO NORDISK SpA	H
029447101	NOVOSEVEN*IV 5mg(250KIU)+5mL	5	NOVO NORDISK SpA	H
050298037	CEVENFACTA*EV 5 mg +Sol 5,2 mL	5	LFB	A
029447075	NOVOSEVEN*IV8mg (400KIU)+8,1mL	8	NOVO NORDISK SpA	H
029447113	NOVOSEVEN*IV 8mg(400KIU)+8mL	8	NOVO NORDISK SpA	H

Quantification of the demand

Table 56 shows the total demand (mg) and the total standardised demand (mg per 1,000 population) of rFVIIa over the two-year period 2023-2024, at national and regional level. The total demand for rFVIIa recorded in 2024 was 36,878 mg (0.6 mg per 1,000 population) with a marked increase compared to 2023 (+16%).

Table 56. Total demand (public and private) and total standardised demand for recombinant activated Factor VII expressed in milligrams and in milligrams per 1,000 population and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	mg	mg per 1,000 pop	mg	mg per 1,000 pop	
Abruzzo	495	0.4	549	0.4	11.2
Aosta Valley	26,0	0.2	20,0	0.2	-22.9
AP Bolzano	73	0.1	-	-	-100.0
AP Trento	9	0.0	33	0.1	265.2
Apulia	2,213	0.6	4,005	1.0	81.8
Basilicata	22	0.0	384	0.7	1659.7
Calabria	923	0.5	1,287	0.7	40.0
Campania	2,371	0.4	2,490	0.4	5.3

Region	2023		2024		% Var 2023-2024
	mg	mg per 1,000 pop	mg	mg per 1,000 pop	
E.-Romagna	2,753	0.6	4,060	0.9	47.0
Friuli V. Giulia	1,406	1.2	943	0.8	-33.0
Latium	2,037	0.4	3,432	0.6	68.7
Liguria	331	0.2	1,490	1.0	349.7
Lombardy	3,654	0.4	2,995	0.3	-18.3
Marche	529	0.4	507	0.3	-4.1
Molise	80	0.3	46	0.2	-42.2
Piedmont	1,416	0.3	4,581	1.1	223.5
Sardinia	1,975	1.3	1,350	0.9	-31.3
Sicily	1,862	0.4	1,795	0.4	-3.3
Tuscany	4,755	1.3	5,006	1.4	5.3
Umbria	253	0.3	262	0.3	4.0
Veneto	4,587	0.9	1,643	0.3	-64.2
Italy	31,770	0.5	36,878	0.6	16.1

FACTOR VIII INHIBITOR BYPASSING ACTIVITY (ATC B02BD03)

Table 57 shows the brand names of medicinal products containing Factor VIII inhibitor bypassing activity currently available on the Italian market and the amount of the active ingredients they contain, expressed in FEIBA Units (FUs).

Table 57. Products containing Factor VIII inhibitor bypassing activity currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	FU	Manufacturer	NHS class
024744043	FEIBA*IV FL 500IU+F 20mL	500	BAXALTA Italy Srl	A
024744068	FEIBA*FL 500FU+BAXJECT II HF	500	BAXALTA Italy Srl	A
024744056	FEIBA TIM3*IV FL 1000IU+F 20mL	1000	BAXTER AG	A
024744070	FEIBA*FL 1000FU+BAXJECT II HF	1000	BAXTER AG	A

Quantification of the demand

Table 58 shows the total demand and the total standardised demand (FUs *per capita*) of Factor VIII inhibitor bypassing activity, or aPCCs, over the two-year period 2023-2024 at regional and national level.

Table 58. Total demand (public and private) and total standardised demand for Factor VIII inhibitor bypassing activity, expressed in FEIBA Units and FEIBA Units *per capita*, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	FU	FU *per capita*	FU	FU *per capita*	
Abruzzo	1,618,000	1.3	198,000	0.2	-87.7
Aosta Valley	-	-	-	-	NA
AP Bolzano	-	-	-	-	NA
AP Trento	-	-	-	-	NA
Apulia	364,000	0.1	161,000	0.0	-55.6
Basilicata	-	-	-	-	NA
Calabria	847,000	0.5	37,000	0.0	-95.6
Campania	656,000	0.1	84,000	0.0	-87.2
E.-Romagna	334,000	0.1	830,000	0.2	147.7
Friuli V. Giulia	348,000	0.3	-	0.0	-100.0
Latium	400,000	0.1	819,000	0.1	105.0
Liguria	130,000	0.1	10,000	0.0	-92.3
Lombardy	2,917,000	0.3	1,354,000	0.1	-53.7
Marche	87,000	0.1	122,000	0.1	40.4
Molise	-	-	-	-	NA
Piedmont	98,000	0.0	202,000	0.0	106.1
Sardinia	646,000	0.4	571,000	0.4	-11.2
Sicily	36,000	0.0	107,000	0.0	198.3
Tuscany	12,000	0.0	-	-	-100.0
Umbria	-	-	-	-	NA
Veneto	292,000	0.1	212,000	0.0	-27.4
Italy	8,785,000	0.1	4,707,000	0.1	-46.4

In 2024, national demand for aPCCs fell sharply compared to the previous year (-46.4%), almost halving in value, with some regional variability. Its total volume was 4,707,000 FUs (0.1 FUs *per capita*).

ALPHA-1-PROTEINASE INHIBITOR (ATC B02AB02)

The alpha-1-proteinase inhibitor (also known as alpha-1-antitrypsin or alpha-1-antiproteinase) is normally present in human plasma at concentrations that range from 0.7 to 2.3 g/L. The alpha-1-proteinase inhibitor is also present in some extravascular spaces, in particular the pulmonary alveoli, where it fulfills its main function. In fact, it modulates the action of enzymes produced by neutrophils (elastase) thus avoiding damage to lung tissue. Alpha-1-antitrypsin is indicated for replacement therapy in subjects with inherited deficiency (39). Table 59 shows the brand names of medicinal products containing alpha-1-proteinase inhibitor currently available on the Italian market and the relative quantity of active ingredient they contain, expressed in milligrams (mg).

Table 59. Products containing alpha-1-proteinase inhibitor currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	mg	Manufacturer	NHS class
037709019	PROLASTIN*EV 1F 1g/40mL+F40mL	1000	GRIFOLS ITALIA SpA	H
044479018	RESPREEZA*EV 1FL 20mL+SOL 1g	1000	CSL BEHRING GmbH	H
046292013	PLITALFA*EV 1F 1000MG/40ML	1000	GRIFOLS Italia SpA	C(nn)
037709021	PROLASTIN*EV 4F 1g/40mL+F40mL	4000	INST. GRIFOLS S.A.	C(nn)
044479020	RESPREEZA*EV 1FL 76mL + 4g+SET	4000	CSL BEHRING GmbH	C(nn)
044479032	RESPREEZA*EV 1FL 95mL+ 5g+ SET	5000	CSL BEHRING GmbH	H

Quantification of the demand

In 2024, the total demand for alpha-1-antitrypsin was 95,110 g (1.6 g per 1,000 population) recording a significant upward trend compared to the previous year (+15%) (Table 55).

Table 60. Total demand (public and private) and total standardised demand for alpha-1-proteinase inhibitor, expressed in grams and grams per 1,000 population, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	g	g per 1,000 pop	g	g per 1,000 pop	
Abruzzo	2,477	1.9	2,551	2.0	3.2
Aosta Valley	450	3.7	669	5.4	49.0
AP Bolzano	3,833	7.2	4,434	8.2	15.0
AP Trento	666	1.2	1,245	2.3	86.2
Apulia	2,887	0.7	4,021	1.0	39.9
Basilicata	-	-	-	-	NA
Calabria	1,627	0.9	2,139	1.2	32.0
Campania	9,911	1.8	10,491	1.9	6.1
E.-Romagna	7,842	1.8	6,068	1.4	-22.9
Friuli V.Giulia	2,490	2.1	3,423	2.9	37.4
Latium	5,580	1.0	7,835	1.4	40.6
Liguria	3,255	2.2	4,226	2.8	29.7

Region	2023		2024		% Var 2023-2024
	g	g per 1,000 pop	g	g per 1,000 pop	
Lombardy	11,574	1.2	11,695	1.2	0.7
Marche	787	0.5	702	0.5	-10.7
Molise	70	0.2	84	0.3	20.6
Piedmont	7,508	1.8	9,114	2.1	21.4
Sardinia	6,853	4.3	8,296	5.3	21.6
Sicily	5,528	1.1	6,950	1.4	26.2
Tuscany	3,795	1.0	4,301	1.2	13.4
Umbria	1,580	1.8	2,286	2.7	45.2
Veneto	4,217	0.9	4,580	0.9	8.5
Italy	82,930	1.4	95,110	1.6	14.7

In particular in the AP of Trento, Aosta Valley and Umbria the demand exceeded the value recorded in the previous year (+86%, +49% and +45%, respectively). The highest regional standardized demand is in the AP of Bolzano (8.2 grams per 1,000 population) and in Aosta Valley and Sardinia (5 grams per 1,000 population).

PLASMA-DERIVED C1-ESTERASE INHIBITOR (ATC B06AC01)

Human C1 esterase inhibitor is a heat-labile plasma protein that inhibits the uncontrolled activation of the classical complement pathway (in particular that of C1 esterase), the deficiency of which is responsible for hereditary angio-oedema. The mean concentration of the C1 inhibitor in plasma is approximately 0.2 g/L (40). Table 61 shows the brand names of medicinal products containing human C1 esterase inhibitor currently on the Italian market and the amount of the active ingredients they contain expressed in IUs.

Table 61. Products containing human C1 esterase inhibitor currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
039056015	BERINERT*IV FL 500IU+FL 10mL	500	CSL BEHRING SpA	A
039056027	BERINERT*IV FL 1500IU+FL 10mL	1500	CSL BEHRING SpA	A
042017018	CINRYZE*EV 2FL 500IU+2FL	1000	SHIRE ITALIA SpA	A
039056039	BERINERT*IV FL 2000IU + FL 4mL+ SET	2000	CSL BEHRING GMBH	C
039056041	BERINERT*IV FL 3000IU + FL 6mL+ SET	3000	CSL BEHRING GMBH	C

Quantification of the demand

In 2024, the total demand for C1 esterase inhibitor was 28,563,500 IUs (484 IUs per 1,000 population), and showed a clear increase compared to the previous year (+40%) (Table 62).

Table 62. Total demand (public and private) and total standardised demand for C1 esterase inhibitor, expressed in International Units and International Units per 1,000 population, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU per 1,000 pop	IU	IU per 1,000 pop	
Abruzzo	480,000	377.2	565,000	445.0	18.0
Aosta Valley	10,500	85.3	19,000	154.6	81.3
AP Bolzano	61,000	114.2	167,000	310.7	172.0
AP Trento	105,500	194.3	48,500	89.0	-54.2
Apulia	1,307,500	334.6	1,681,000	432.1	29.1
Basilicata	20,000	37.2	1,500	2.8	-92.4
Calabria	475,500	257.5	440,000	239.3	-7.1
Campania	1,851,500	330.1	2,309,000	412.8	25.1
E.-Romagna	782,000	176.2	1,231,500	276.6	57.0
Friuli V. Giulia	25,500	21.4	21,500	18.0	-15.7
Latium	3,870,500	676.6	6,427,500	1124.7	66.2
Liguria	55,500	36.8	416,500	276.0	649.7
Lombardy	3,267,500	327.5	5,070,500	506.4	54.6
Marche	524,000	353.0	1,213,000	818.1	131.7

Region	2023		2024		% Var 2023-2024
	IU	IU per 1,000 pop	IU	IU per 1,000 pop	
Molise	8,000	27.5	7,000	24.2	-12.1
Piedmont	1,373,000	323.0	1,484,000	349.0	8.1
Sardinia	671,500	425.5	490,000	312.0	-26.7
Sicily	3,099,500	643.8	4,552,000	948.9	47.4
Tuscany	684,500	186.9	852,000	232.8	24.5
Umbria	304,500	355.6	356,000	417.3	17.4
Veneto	1,408,500	290.4	1,211,000	249.6	-14.1
Italy	20,386,000	345.5	28,563,500	484.4	40.2

An exceptional variability in standardised regional demands was observed, with maximum volumes in Latium, Sicily, Marche and Lombardy (1,125, 949, 818 and 506 IUs per 1,000 population, respectively) and minimum volumes in Basilicata, Friuli V.Giulia, Molise and in the AP of Trento (range: 2.8 – 89 IUs per 1,000 population). Most Regions showed an increase from the previous year, in some cases even a particularly marked one, as in the case of Liguria (+650%); exceptions were Basilicata, Calabria, Friuli V. Giulia, Molise, Sardinia, Veneto and the AP of Trento, where, on the other hand, decreases in demand were recorded in the two-year period under consideration.

COAGULATION FACTOR X (ATC B02BD13)

Congenital Factor X deficiency (or Stuart-Prower Factor deficiency) is an inherited haemorrhagic disorder characterised by the decreased activity of the Factor X (FX) antigen, which causes severe or moderate bleeding. The prevalence of homozygous forms is estimated at 1/1,000,000. No gender differences have been reported. Haemorrhagic episodes are usually treated with 3F-PCCs or fresh frozen plasma (41).

Table 63 shows the brand names of medicinal products containing pdFX currently on the Italian market and the amount of the active ingredients they contain, expressed in IUs.

Table 63. Products containing coagulation Factor X currently available on the Italian market (adapted by the CNS on data from Farmadati and the Product Quality and Pharmacrime Office- AIFA, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
*	FACTOR X P BEHRING 1FL	600-1200§	CSL BEHRING SpA	-
044840015	COAGADEX 100IU/mL- IV 2,5 mL	250	BIO PROD. LAB. LTD	C
044840027	COAGADEX 100IU/mL- IV 5 mL	500	BIO PROD. LAB. LTD	C(nn)

* Medicinal products imported under the provisions of the DM of 11 February 1997 (8) and of the DM of 11 May 2001 (10).
§ The average quantity of active ingredient contained was used in the definition of the demand.

Quantification of the demand

Products containing FX concentrates are used exclusively in only four Regions; in 2024 the national demand was 176,300 IUs (3.0 IUs per 1,000 population) (Table 64).

Table 64. Total demand (public and private) and total standardised demand for coagulation Factor X expressed in International Units and International Units per 1,000 population, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from Product Quality and Pharmacrime Office-AIFA)

Region	2023		2024		% Var 2023-2024
	IU	IU per 1,000 pop	IU	IU per 1,000 pop	
Abruzzo	-	-	-	-	NA
Aosta Valley	-	-	-	-	NA
AP Bolzano	-	-	-	-	NA
AP Trento	-	-	-	-	NA
Apulia	-	-	-	-	NA
Basilicata	-	-	-	-	NA
Calabria	42,000	22.7	100,000	54.4	139.1
Campania	-	-	-	-	NA
E.-Romagna	-	-	-	-	NA
Friuli V. Giulia	-	-	1,000	0.8	100.0
Latium	-	-	-	-	NA
Liguria	-	-	-	-	NA
Lombardy	36,000	3.6	70,800	7.1	96.0

Region	2023		2024		% Var 2023-2024
	IU	IU per 1,000 pop	IU	IU per 1,000 pop	
Marche	-	-	-	-	NA
Molise	-	-	-	-	NA
Piedmont	-	-	4,500	1.1	100.0
Sardinia	-	-	-	-	NA
Sicily	-	-	-	-	NA
Tuscany	-	-	-	-	NA
Umbria	-	-	-	-	NA
Veneto	-	-	-	-	NA
Italy	78,000	1.3	176,300	3.0	126.1

COAGULATION FACTOR XI (ATC B02BD)

Factor XI (FXI), also known as plasma thromboplastin antecedent (PTA) or Rosenthal Factor, is a plasma glycoprotein responsible for activating FIX (42).

Congenital FXI deficiency causes an inherited recessive autosomal haemorrhagic disorder characterised by reduced FXI levels and activity, which causes moderate bleeding generally following trauma or surgery. The prevalence of homozygous forms is estimated at 1/1,000,000; in specific ethnic groups there is a significantly higher prevalence of severe forms (43).

Table 65 shows the brand names of medicinal products containing FXI currently on the Italian market and the amount of active ingredient they contain, expressed in IUs.

Table 65. Products containing recombinant coagulation Factor XI currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Name of medicinal product	IU	Manufacturer	NHS class
-*	HEMOLEVEN 100IU/mL 10mL	1000	LFB	-

* Medicinal product registered abroad and imported under the provisions of Ministerial Decree 11 February 1997 (8) and Ministerial Decree 11 May 2001 (10).

Quantification of the demand

In 2024, the demand for FXI was 11,000 IUs (0.2 IU per 1,000 population), showing a decrease compared to 2023 (-8%) (Table 66). Demand was detected only in two Italian Regions: Friuli V. Giulia and Piedmont.

Table 66. Total demand (public and private) and total standardised demand for coagulation Factor XI expressed in International Units and International Units per 1,000 population, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from theProduct Quality and Pharmacrime Office-AIFA)

Region	2023		2024		% Var 2023-2024
	IU	IU per 1,000 pop	IU	IU per 1,000 pop	
Abruzzo	-	-	-	-	NA
Aosta Valley	-	-	-	-	NA
AP Bolzano	-	-	-	-	NA
AP Trento	-	-	-	-	NA
Apulia	-	-	-	-	NA
Basilicata	-	-	-	-	NA
Calabria	-	-	-	-	NA
Campania	-	-	-	-	NA
E.-Romagna	2,000	0.5	-	-	-100.0
Friuli V. Giulia	6,000	5.0	9,000	7.5	50.0
Latium	-	-	-	-	NA
Liguria	2,000	1.3	-	-	-100.0
Lombardy	-	-	-	-	NA
Marche	-	-	-	-	NA
Molise	-	-	-	-	NA

Region	2023		2024		% Var 2023-2024
	IU	IU per 1,000 pop	IU	IU per 1,000 pop	
Piedmont	2,000	0.5	2,000	0.5	0.0
Sardinia	-	-	-	-	NA
Sicily	-	-	-	-	NA
Tuscany	-	-	-	-	NA
Umbria	-	-	-	-	NA
Veneto	-	-	-	-	NA
Italy	12,000	0.2	11,000	0.2	-8.3

COAGULATION FACTOR XIII (ATC B02BD07)

Plasma-derived coagulation Factor XIII (pdFXIII), also called fibrin stabilising factor, plasma protransglutaminase or Laki-Lorand Factor, plays a fundamental role in coagulation processes and is used in the replacement therapy for congenital FXIII deficiency, an autosomal-recessive disorder, whose prevalence is estimated at around 1/2,000,000 (44).

Depending on the level of FXIII activity, severe (FXIII<1%), moderate (between 1 and 4%) and mild (FXIII>5%) forms are distinguished. Should products containing pdFXIII be not available, fresh frozen plasma is used as an alternative (44).

Since 2014, products obtained with recombinant genetic techniques (rFXIII) have been available (45,46). However, only since 2016 has their utilisation been recorded and then only in certain Regions.

Table 67 and Table 68 show the brand names of medicinal products containing pdFXIII and rFXIII, respectively, currently available on the Italian market and the amount of the active ingredients they contain, expressed in IUs.

Table 67. Products containing plasma-derived coagulation Factor XIII distributed in Italy (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
024644015*	FIBROGAMMIN 1FL 250IU	250	CSL BEHRING GmbH	H
042605016	CLUVIAT FL 250IU	250	CSL BEHRING GmbH	H
024644027*	FIBROGAMMIN 1FL 1250IU	1250	CSL BEHRING GmbH	H
042605028	CLUVIAT FL 1250IU	1250	CSL BEHRING GmbH	H

* Medicinal products imported under the provisions of DM of 11 February 1997 (8) and DM of 11 May 2001 (10).

Table 68. Products containing recombinant coagulation Factor XIII currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
043034014	NOVOTHIRTEEN*EV FL 2500IU	2500	NOVO NORDISK SpA	H

Quantification of the demand

In 2024, the total demand for FXIII was 1,143,000 IUs (19.4 IUs per 1,000 population) and less than half, equal to 568,000 IUs (9.6 IUs per 1,000 population), was for pdFXIII. The latter recorded an increase of +17% compared to 2023 (Table 69). The highest demand for Factor XIII of plasma origin was maximum in the AP of Trento and Emilia-Romagna (118 IUs and 40 IUs per 1,000 population respectively).

In 2024, there was no utilisation of FXIII in some Regions (Friuli V. Giulia, Molise, Sardinia, Sicily, Umbria and Aosta Valley).

In Abruzzo, Basilicata and Campania recombinant coagulation Factor XIII was used exclusively (Table 70). In Latium, Marche, the AP of Bolzano, the AP of Trento, Apulia and Tuscany instead pdFXIII was used exclusively.

Table 69. Total demand (public and private) and total standardised demand for plasma-derived coagulation Factor XIII expressed in International Units and International Units per 1,000 population, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow and theProduct Quality and Pharmacrime Office-AIFA)

Region	2023		2024		% Var 2023-2024
	IU	IU per 1,000 pop	IU	IU per 1,000 pop	
Abruzzo	-	-	-	-	NA
Aosta Valley	-	-	-	-	NA
AP Bolzano	8,750	16.4	16,250	30.2	84.5
AP Trento	38,500	70.9	64,250	117.9	66.2
Apulia	12,500	3.2	3,000	0.8	-75.9
Basilicata	-	-	-	-	NA
Calabria	-	-	2,500,0	1.4	100.0
Campania	-	-	-	-	NA
E.-Romagna	138,500	31.2	176,750	39.7	27.2
Friuli V. Giulia	-	-	-	-	NA
Latium	40,500	7.1	42,000	7.3	3.8
Liguria	41,750	27.7	40,000	26.5	-4.3
Lombardy	30,000	3.0	26,000	2.6	-13.6
Marche	39,750	26.8	50,250	33.9	26.5
Molise	-	-	-	-	NA
Piedmont	25,000	5.9	24,250	5.7	-3.0
Sardinia	-	-	-	-	NA
Sicily	2,500	0.5	-	-	-100.0
Tuscany	32,500	8.9	25,500	7.0	-21.5
Umbria	2,500,0	2.9	-	-	-100.0
Veneto	73,500	15.2	97,250	20.0	32.2
Italy	486,250	8.2	568,000	9.6	16.9

Table 70. Total demand (public and private) and total standardised demand for recombinant coagulation Factor XIII expressed in International Units and International Units per 1,000 population, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow and the Product Quality and Pharmacrime office, AIFA)

Region	2023		2024		% Var 2023-2024
	IU	IU per 1,000 pop	IU	IU per 1,000 pop	
Abruzzo	52,500	41.3	47,500	37.4	-9.3
Aosta Valley	-	-	-	-	NA
AP Bolzano	-	-	-	-	NA
AP Trento	-	-	-	-	NA
Apulia	-	-	-	-	NA
Basilicata	30,000	55.8	35,000	65.6	17.6
Calabria	170,000	92.1	162,500	88.4	-4.0
Campania	37,500,0	6.7	37,500,0	6.7	0.3
E.-Romagna	15,000,0	3.4	15,000,0	3.4	-0.3
Friuli V. Giulia	15,000,0	12.6	-	-	-100.0
Latium	-	-	-	-	NA
Liguria	65,000	43.1	92,500	61.3	42.2
Lombardy	87,500	8.8	102,500	10.2	16.7
Marche	-	-	-	-	NA
Molise	-	-	-	-	NA
Piedmont	30,000	7.1	62,500	14.7	108.3
Sardinia	-	-	-	-	NA
Sicily	-	-	-	-	NA
Tuscany	-	-	-	-	NA
Umbria	-	-	-	-	NA
Veneto	20,000	4.1	20,000	4.1	-0.1
Italy	522,500	8.9	575,000	9.8	10.1

PROTEIN C (ATC B01AD12)

Protein C is one of the most important factors of the anticoagulant system togheter with AT and protein S. It is a vitamin K-dependent serine-protease produced by the liver, which is indicated in purpura fulminans and in patients with severe congenital deficiencies. The mean concentration of protein C in plasma is approximately 3-5 µg / mL (47).

Table 71 shows the brand names of medicinal products containing protein C currently available on the Italian market and the amount of the active ingredients they contain, expressed in IUs.

Table 71. Products containing protein C currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	IU	Manufacturer	NHS class
035389016	CEPROTIN*IV 500IU	500	BAXTER SpA	H
035389028	CEPROTIN*IV 1000IU	1000	BAXTER SpA	H

Quantification of the demand

In 2024, the national demand for protein C stood at a volume of 787,000 IUs (13.3 IUs per 1,000 population) with an increase of 9.6% compared to 2023 (Table 72).

Table 72. Total demand (public and private) and total standardised demand for protein C, expressed in International Units and International Units per 1,000 population, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	IU	IU per 1,000 pop	IU	IU per 1,000 pop	
Abruzzo	5,000	3.9	4,500	3.5	-9.8
Aosta Valley	-	-	-	-	NA
AP Bolzano	-	-	-	-	NA
AP Trento	-	-	-	-	NA
Apulia	8,000	2.0	-	-	-100.0
Basilicata	1,000	1.9	-	-	-100.0
Calabria	181,000	98.0	202,500	110.1	12.4
Campania	211,500	37.7	264,000	47.2	25.2
E.-Romagna	5,000	1.1	3,000	0.7	-40.2
Friuli V. Giulia	-	-	-	-	NA
Latium	135,500	23.7	154,500	27.0	14.1
Liguria	45,000	29.8	3,000	2.0	-93.3
Lombardy	80,000	8.0	48,500	4.8	-39.6
Marche	12,000	8.1	22,000	14.8	83.5
Molise	-	-	-	-	NA
Piedmont	-	-	8,000	1.9	NA
Sardinia	-	0.0	7,500	4.8	NA
Sicily	6,500	1.4	33,500	7.0	417.2
Tuscany	13,000	3.5	20,000	5.5	53.9
Umbria	-	0.0	6,000	7.0	NA
Veneto	15,000	3.1	10,000	2.1	-33.4
Italy	718,500	12.2	787,000	13.3	9.6

The highest regional demand was recorded in Calabria and Campania, with 110 and 47 IUs per 1,000 population respectively.

The lowest regional demand was in Emilia-Romagna, Piedmont, Liguria and Veneto with volumes between 0.7 and 2.1 IUs per 1,000 population.

OTHER PLASMA PROTEIN FRACTIONS (ATC B05AA02)

Other plasma protein fractions include products with different compositions and therapeutic indications and include solvent/detergent-treated plasma (Plasmasafe™, Plasmagrade™ and Octaplas™) and products with an albumin content between 85 and 90% (Umanserum™).

Solvent/detergent-treated plasma is a product obtained from a pool by hundreds of donors of the same blood group and has the following characteristics:

– high batch-to-batch standardisation;
– declaration of the concentration/activity of biologically active proteins;
– reduction of the immunological risks due to the presence of antibodies, cells (or their fragments);
– inactivation of potentially transmissible pathogens.

Solvent/detergent-treated plasma has the same therapeutic indications as fresh frozen plasma.

Table 73 shows the brand names of the drugs containing other plasma protein fractions currently available on the Italian market and the amount of the active ingredients they contain, expressed in millilitres (mL).

Table 73. Products containing other plasma protein fractions currently available on the Italian market (adapted by the CNS on data from Farmadati, 31/12/2024)

AIC code	Brand name	mL	Manufacturer	NHS class
033369012	PLASMASAFE*INFUS SACCA 200mL	200	KEDRION SpA	H
034540017	OCTAPLAS*INFUS SACCA 200mL	200	OCTAPHARMA PHARM.	H
041868011	PLASMAGRADE*INFUS SACCA 200mL	200	KEDRION SpA	H
021112040	UMANSERUM*INFUS 250mL 5%	250	KEDRION SpA	C

Quantification of the demand

As regards the different composition and different clinical use, the demands of these two sub-groups of medicinal products have been quantified distinctly.

Table 74 shows the utilisation of Plasmasafe™ and Octaplas™, while Table 75 illustrates the data related to Umanserum™, the demand for which, in 2024, recorded an increase of +5%, and a total volume of 6,884,000 mL.

The national demand for solvent/detergent-treated plasma in 2024 decreased by -8.3% compared to 2023, with large regional differences; its value stood at 22,009,800 mL (373.2 mL/1,000 pop.). The most noticeable decrease was recorded in Marche (-33%) and in Apulia (-20%). In contrast, a significant increase in demand was recorded in Sardinia (+845%), in the AP of Trento and Friuli V. Giulia (+100%), in Molise (+64%) and in Tuscany (+40%) (Table 74).

Table 74. Total demand (public and private) and total standardised demand for solvent/detergent-treated plasma (excluding Umanserum™), expressed in millilitres and millilitres per 1,000 population, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	mL	mL per 1,000 pop	mL	mL per 1,000 pop	
Abruzzo	-	-	-	-	NA
Aosta Valley	-	-	-	-	NA
AP Bolzano	-	-	-	-	NA
AP Trento	-	-	10,000	18.3	100.0
Apulia	3,104,000	794.3	2,482,000	637.9	-19.7
Basilicata	448,000	833.4	402,000	753.9	-9.5
Calabria	1,038,000	562.1	898,000	488.4	-13.1
Campania	4,056,200	723.1	3,814,400	681.9	-5.7
E.-Romagna	346,000	78.0	282,000	63.3	-18.8
Friuli V. Giulia	-	-	12,000	10.0	100.0
Latium	3,104,200	542.6	2,742,600	479.9	-11.6
Liguria	126,000	83.6	140,000	92.8	11.0
Lombardy	476,000	47.7	478,000	47.7	0.1
Marche	1,774,000	1195.2	1,184,000	798.5	-33.2
Molise	228,000	784.5	372,000	1286.2	64.0
Piedmont	3,782,000	889.6	3,672,000	863.7	-2.9
Sardinia	6,400	4.1	60,200	38.3	845.2
Sicily	3,235,200	672.0	2,763,000	575.9	-14.3
Tuscany	1,156,000	315.7	1,613,600	440.8	39.6
Umbria	146,000	170.5	148,000	173.5	1.8
Veneto	984,000	202.9	936,000	192.9	-4.9
Italy	24,010,000	407.0	22,009,800	373.2	-8.3

Table 75. Total demand (public and private) and total standardised demand for Umanserum™ expressed in millilitres and millilitres per 1,000 population, and variations in percentage between 2023 and 2024 (adapted by the CNS on data from the Traceability information flow)

Region	2023		2024		% Var 2023-2024
	mL	mL per 1,000 pop	mL	mL per 1,000 pop	
Abruzzo	-	-	-	-	NA
Aosta Valley	-	-	-	-	NA
AP Bolzano	-	-	-	-	NA
AP Trento	-	-	-	-	NA
Apulia	2,990,000	765.2	3,006,250	772.7	1.0
Basilicata	3,750	7	2,500	4.7	-32.8
Calabria	300,000	162	487,500	265.2	63.2
Campania	250	0	-	-	-100.0
E.-Romagna	-	-	-	-	NA
Friuli V. Giulia	-	-	-	-	NA
Latium	550,000	96	850,000	148.7	54.7
Liguria	-	-	-	-	NA
Lombardy	500	0.1	750	0.1	49.5
Marche	-	-	-	-	NA
Molise	-	-	-	-	NA
Piedmont	-	-	-	-	NA
Sardinia	-	-	-	-	NA
Sicily	2,617,750	543.8	2,463,250	513.5	-5.6
Tuscany	-	-	-	-	NA
Umbria	77,750	90.8	73,750	86.5	-4.8
Veneto	-	-	-	-	NA
Italy	6,540,000	110.9	6,884,000	116.7	5.3

PART C
National self-sufficiency in toll-fractionated plasma derived medicinal products

SELF-SUFFICIENCY

According to the Italian legislation, the term PDMP self-sufficiency refers to the capacity of regional health systems (through agreements signed by several or by single Regions) to meet their needs for PDMPs. This is achieved by using products obtained from the processing of the plasma collected by BEs and dispatched to companies to be toll fractionated, which also reduces the quantity of PDMPs supplied via the pharmaceutical market. However, PDMP self-sufficiency must take into account the levels of appropriateness of clinical use and the management of available resources.

Self-sufficiency in PDMPs and blood components is one of the objectives of the 219/2005 Law, which aimes at guaranteeing the same standards of quality and safety in the transfusion therapy to all citizens. It is a non-divisible national and supraregional interest, for which the Regions and the Health Authorities have to contribute to its final accomplishment.
To this end, the law establishes some principles of regional health planning (Art. 11) and entrusts all coordination activities to the CNS (Art. 12). It also acknowledges the annual programme of national self-sufficiency (Art. 14) as the instrument to determine every aspect of national self-sufficiency, such as historical consumptions, real needs, production levels required, resources, prospective financing criteria, compensation methods among the Regions and import/export levels whenever necessary.

Furthermore, Article 26 of the 20th of December 2007 Legislative Decree, n. 261 (48) provides for the definition of a programme by the MoH focusing on developing the collection of plasma in BEs and BCUs, promoting the rational and appropriate use of PDMPs; while with the DM of 2 December 2016, the first national plasma and PDMP programme for the five-year period 2016-2020 was published (49).

Toll fractionation system

The plasma collected in Italy comes from voluntary, periodic, responsible, anonymous and non-remunerated donations. The Regions, individually or in association, send the plasma collected by the BEs, from their local territory, to the authorised and affiliated company for it to be industrially transformed into PDMPs. The contract with the companies, which operate as service providers, is considered a "toll fractionation process" and constitutes a contract agreement for the production of PDMPs. The acquisition of the toll fractionation processes is carried out through a tender procedure in compliance with the current legislation. For this purpose, during 2015 and 2016, in addition to the Lombardy-Piedmont-Sardinia Agreement (LPS) by then already implemented, three new inter-regional agreements were signed:

- the New Interregional Agreement for Plasma-Derived Medicinal Products (Nuovo Accordo Interregionale per la Plasmaderivazione - NAIP), which includes Abruzzo, Basilicata, Friuli V. Giulia, Liguria, the AP of Bolzano, the AP of Trento, Umbria, Veneto (Leading Region), and Aosta Valley;
- the Plasma/Plasma-Derived Interregional Grouping (Raggruppamento Interregionale Plasma e Plasmaderivati - RIPP) of which Calabria, Emilia-Romagna (Leading Region), Apulia and Sicily are part;
- the Plasma Network (PlaNet) which includes Campania, Latium (including the General Inspectorate of Military Health), Marche, Molise and Tuscany (Leading Region).

Under the terms of this type of agreement, as set forth in the DM of 12 April 2012 (50), and later in the DM of 19 December 2022 (51), the production of PDMPs is defined by a quali-quantitative production plan. The company in question agrees to produce the quantity and to guarantee the quality of the PDMPs requested by the Regions complying with the schedules and the established procedures.

The contracting Regions, in turn, undertake to make available the necessary plasma according to agreed quantities and quality specifications. The Regions have the right to full ownership of the plasma sent for industrial processing, of all the pharmaceutical specialties derived from it, as well as of the residual material. Consequently, the supplier of the industrial processing service cannot use the plasma, the intermediate fractions, nor the finished products, nor the residual raw material for purposes other than those provided for under the agreement, without a prior agreement with the Regions. For the purpose of the call for tender, DM of 12 April 2012 ruled d that at least human albumin, FVIII and IG-IV had to be guaranteed to be produced, while the subsequent DM of 19 December 2022 considers only albumin and immunoglobulins, both intravenous and subcutaneous administration, as production driver products. All other PDMPs are to be considered as optional.

Pursuant to the Ministerial Decree of July 22, 2024, and the DM of November 6, 2024 (which repeal the DM of December 5, 2014), the only companies authorized to fractionate national plasma are Baxter Manufacturing, Csl Behring S.p.A., Grifols Italia, Kedrion, Octapharma Italy (52).

In 2016, the tender for the supply of toll fractionation services for the NAIP Regions was won by CSL Behring S.p.A. The contract provided for the supply of albumin, IV IGs, SC/IM IGs, pdFVIII, FVIII / vWF in combination and fibrinogen.

In December 2016, the call for tenders was published for the provision of contract fractionation services for the RIPP Regions, and won by the companies Kedrion and Grifols, with the first plasma collection taking place in November 2020. On the other hand, regarding the PlaNet Agreement Regions, Takeda company, winner of the tender launched in November 2017, started plasma collection in September 2020. Until then, therefore, for all Regions, excluding those of the NAIP, the agreements with the contract fractionation company Kedrion, whose contracts covered the production of albumin, IVIG, pdFVIII, pdFIX, 3F-PCCs, AT and solvent/detergent virus-inactivated plasma, remained in force.

Plasma for fractionation

Since the year 2000, the amount of plasma collected nationwide (Figure 42) has steadily increased, going from a total of 462,805 kilograms sent for fractionation in the year 2000 to 906,938 kilograms in 2024, with a percentage increase over the entire period considered, by 96%.

The mean annual rate of variation over the period considered was 2.9%.

In 2024, a sharp increase was observed compared to the previous year (+3%)(Figure 43). However, the delivery of plasma to industrial fractionation by individual Regions shows extreme variability in terms of quantity and quality.

In 2024, the Regions participating in the LPS agreement collected about one third of the plasma sent for fractionation for a share equal to 260,411 kilograms (28.7%), those adhering to the RIPP 249,590 kilograms (27.5%), those of the NAIP 207,786 kilograms (22.9%) and those of the PlaNet 189,151 kilograms (20.9%) (Figure 44).

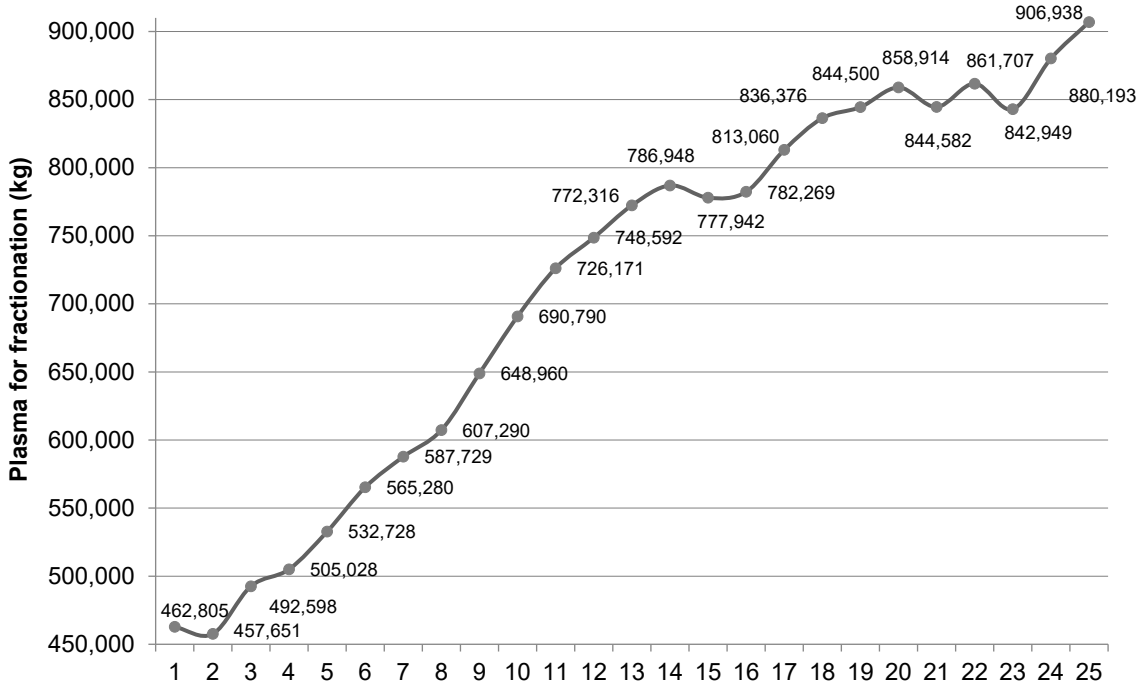

Figure 42. Plasma sent for fractionation 2000-2024
(adapted by the CNS on fractionation companies data, January 2024)

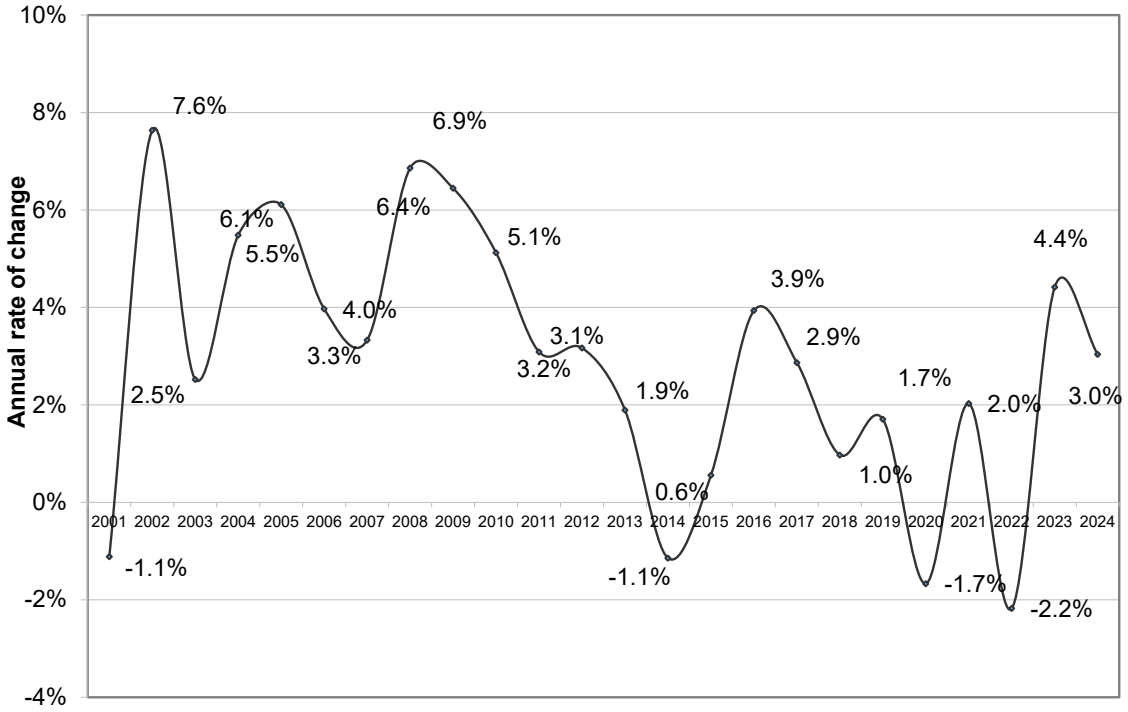

Figure 43. Annual rate of variation in the amount of plasma for fractionation, from 2001 to 2023
(adapted by the CNS on fractionation companies data, January 2024)

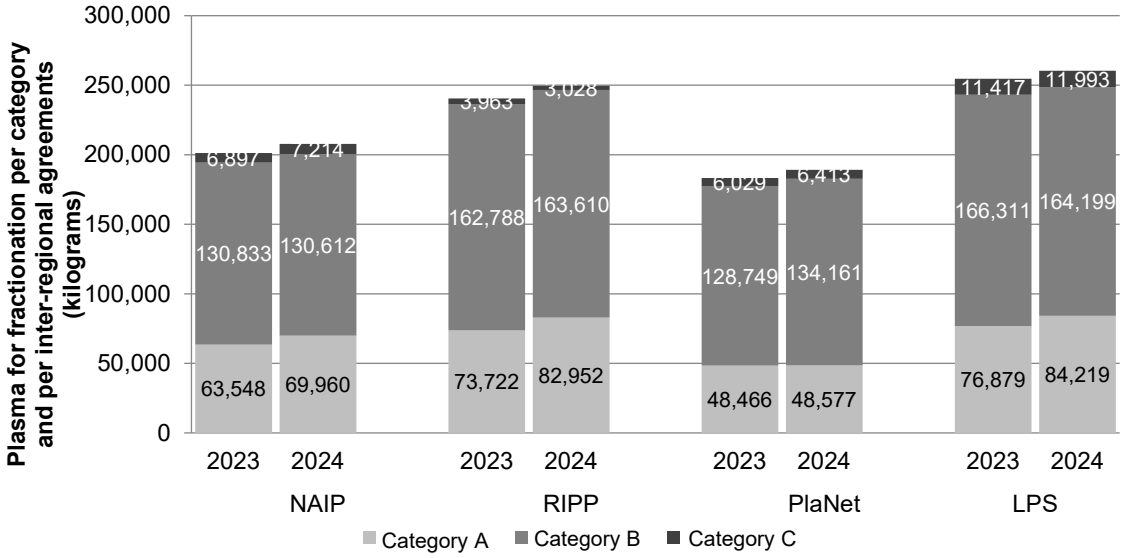

Figure 44. Total amount of plasma for fractionation by category under interregional agreements (kilograms), 2023-2024 (adapted by the CNS on fractionation companies data, January 2025)

As regards the amount of plasma sent for fractionation in 2024, for the resident population, the NAIP sent 18.2 kilograms of plasma per thousand population units for processing (17.6 in 2023, with the same number of Regions and PAs participating), LPS 16.4 kilograms (16.1 kilograms of plasma per thousand population units in 2023), RIPP 16.7 (16.0 kilograms of plasma per thousand population units in 2023), and finally PlaNet contributed 11.3 kilograms of plasma per thousand population units (11.0 kilograms of plasma per thousand population units the previous year) (Figure 45).

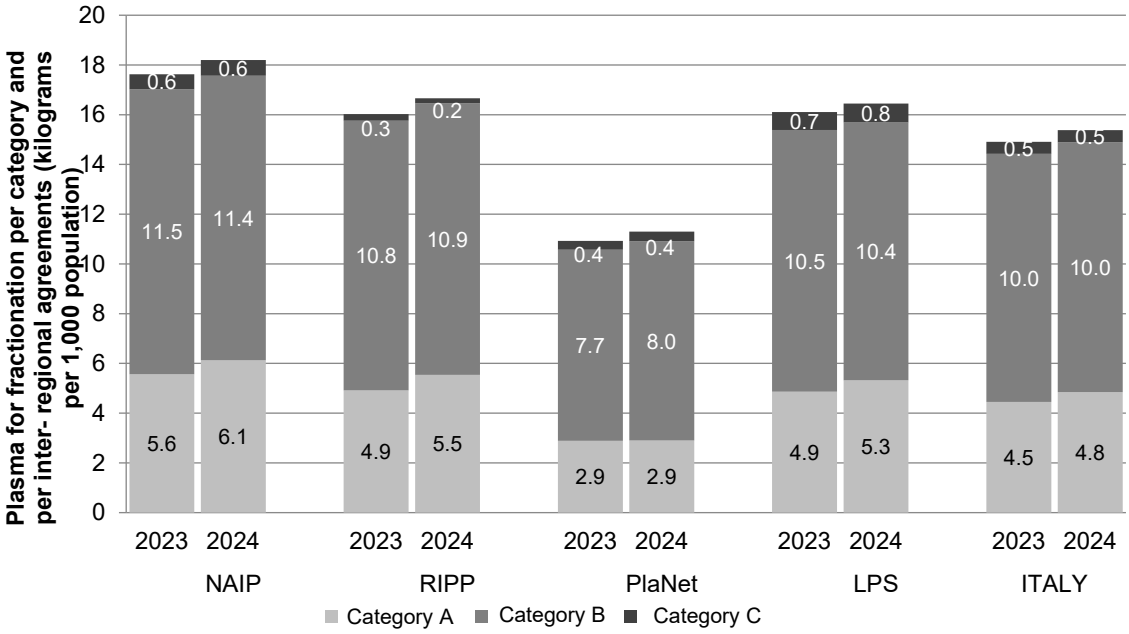

Figure 45. Total amount of plasma for fractionation by category under interregional agreements (kilograms per 1,000 population), 2023-2024 (adapted by the CNS on fractionation companies data, January 2025)

In 2024, although the national volume of plasma for fractionation stood at 15.4 kilograms per 1,000 population (14.9 in 2023), with regional contributions in volumes differing greatly one from another. In point of fact, the best performance was achieded by Friuli V. Giulia with 24.8 kilograms per 1,000 population, followed by Marche with 24.0 and Emilia-Romagna with 23.7, while the lowest volumes were recorded in Calabria, Latium and Campania with 10.9, 8.5 and 6.0 kilograms per 1,000 population, respectively (Figure 46).

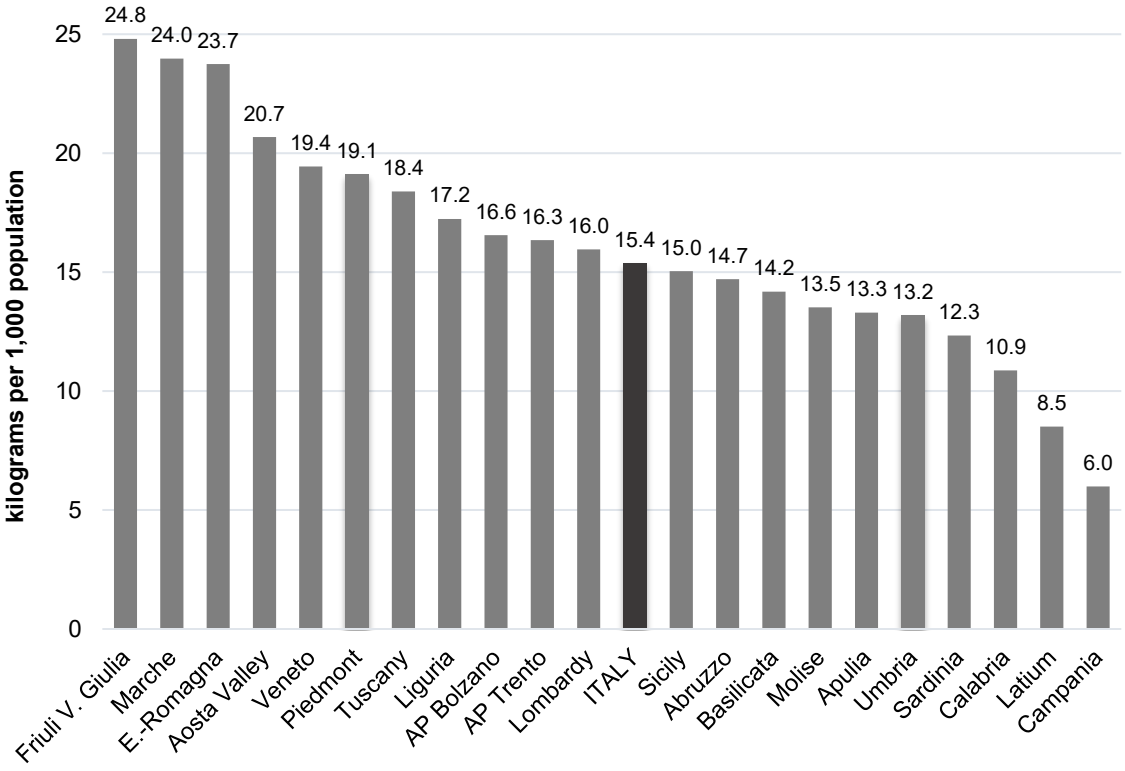

Figure 46.Total amount of plasma (kilograms per 1,000 population) for fractionation by Region, year 2024 (adapted by the CNS on fractionation companies data, January 2025)

Supply of PDMPs from toll fractionation

In 2024, the total quantity of plasma sent for fractionation by the Italian Regions was 906,938 kilograms (Table 76); of these, 32% (285,707 kilograms) was apheresis plasma (category A), 65% (592,583 kilograms) recovered plasma (category B) and the remaining 3% (28,648 kilograms) plasma intended solely for the recovery of non-labile proteins (category C).

The percentages of all three categories of plasma sent for fractionation varied from one regional area to another and from one consortium to another. In particular, the percentages of apheresis plasma (category A) for fractionation varied from 25.7% sent by PlaNet to 33.7% sent by NAIP, while the percentage of plasma intended solely for the recovery of non-labile proteins (category C) varied from 1.2% sent by RIPP to 4.6% sent by the LPS consortium.

Table 76. Total quantity, expressed in kilograms, quantity per 1,000 population and variation in percentage for the years 2023-2024 classified by Region and plasma category (adapted by the CNS on fractionation companies data, January 2024)

Region	A	%	B	%	C	%	Tot. Fract.	Total per 1,000 pop
Abruzzo	4,987	2.7	13,578	5.5	106	-9.3	18,671	14.7
Aosta Valley	1,196	8.5	1,345	1.1	-	NA	2,541	20.7
AP Bolzano	3,039	18.9	5,859	3.7	-	NA	8,897	16.6
AP Trento	2,061	53.5	6,851	0.8	-	NA	8,911	16.3
Basilicata	2,179	12.3	4,034	21.0	1,350	-21.2	7,562	14.2
Friuli V. Giulia	14,554	4.1	14,953	1.3	120	0.9	29,626	24.8
Liguria	8,397	23.8	17,611	-3.6	-	NA	26,008	17.2
Umbria	2,238	16.8	9,015	0.8	-	NA	11,252	13.2
Veneto	31,309	7.7	57,369	-2.5	5,638	13.9	94,317	19.4
NAIP	**69,960**	**10.1**	**130,612**	**-0.2**	**7,214**	**4.6**	**207,786**	**18.2**
Apulia	9,263	9.0	41,572	-0.7	904	-12.5	51,740	13.3
Calabria	2,911	20.4	17,060	-1.7	12	127.0	19,983	10.9
Emilia-Romagna	51,007	16.8	52,615	0.3	2,096	-27.9	105,717	23.7
Sicily	19,771	3.4	52,363	2.5	16	-6.2	72,150	15.0
RIPP	**82,952**	**12.5**	**163,610**	**0.5**	**3,028**	**-23.6**	**249,590**	**16.7**
Campania	713	14.7	32,185	6.8	605	-30.8	33,503	6.0
Latium	5,754	6.1	37,143	0.5	5,728	14.5	48,625	8.5
Marche	16,219	-1.7	19,330	1.7	-	NA	35,549	24.0
Molise	947	8.2	2,963	2.2	-	NA	3,910	13.5
Tuscany	24,943	-0.4	42,369	6.9	-	NA	67,312	18.4
Ministry of Defence	-	NA	171	57.5	80	-47.8	251	NA
PlaNet	**48,577**	**0.2**	**134,161**	**4.2**	**6,413**	**6.4**	**189,151**	**11.3**
Lombardy	52,668	2.7	98,269	-1.1	8,800	-2.8	159,738	16.0
Piedmont	30,987	23.6	48,268	-0.3	2,049	-0.5	81,304	19.1
Sardinia	563	9.0	17,662	-4.7	1,144	281.9	19,369	12.3
LPS	**84,219**	**9.5**	**164,199**	**-1.3**	**11,993**	**5.0**	**260,411**	**16.4**
Italy	**285,707**	**8.8**	**592,583**	**0.7**	**28,648**	**1.2**	**906,938**	**15.4**

Tables 77 and 78 shows the amount of PDMPs potentially obtainable from the industrial manufacturing of the total amount of plasma sent for fractionation in 2024 (from July 2023 to June 2024). These figures show the quantities, expressed in grams and IUs, of medicinal products that the fractionators have potentially guaranteed the consortia (potential supply or production capacity) estimated from the industrial yields and contractual agreements. Further quantities of plasma, around 16,600 kilograms, as shown in Table 79, were sent to Kedrion for the production of plasma solvent/detergent-treated, beyond the provisions of the aforementioned regional agreements.

Tables 80 and 81 provide the quantities of PDMPs distributed to the individual Regions in 2024 in accordance with the specified production and distribution programmes (effective supply or toll fractionation).

Table 77. Potential supply of toll fractionated PDMPs (driver) based on the amount of plasma sent for fractionation from July 2023 to June 2024 and the yields provided by the fractionation industry – year 2024 (adapted by the CNS on fractionation companies data, March 2025)

Region	2nd semester 2023	1st semester 2024	TOTAL	Albumin	SCIG*	IVIG**
	kg	kg	kg	g	g	g
Abruzzo	8,862	9,595	18,457	468,806	92,285	92,285
Aosta Valley	1,040	1,363	2,403	61,040	12,016	12,016
AP Bolzano	4,376	4,252	8,628	219,160	43,142	43,142
AP Trento	4,105	4,213	8,318	211,273	41,589	41,589
Basilicata	3,440	3,724	7,164	181,953	35,818	35,818
FVG	14,352	15,044	29,396	746,658	146,980	146,980
Liguria	12,624	12,802	25,426	645,827	127,131	127,131
Umbria	5,362	5,653	11,015	279,791	55,077	55,077
Veneto	46,819	46,527	93,346	2,370,995	466,731	466,731
NAIP	**100,981**	**103,172**	**204,154**	**5,185,504**	**1,020,769**	**1,020,769**
Apulia	26,400	25,833	52,233	1,346,567	189,083	213,633
Calabria	10,107	10,738	20,845	537,384	75,459	85,256
E.-Romagna	50,057	52,802	102,859	2,651,701	101,917	420,693
Sicily	35,856	36,017	71,873	1,852,886	260,180	293,961
RIPP	**122,420**	**125,390**	**247,810**	**6,388,538**	**626,640**	**1,013,542**
Campania	17,531	17,326	34,857	881,887	156,857	174,286
Latium	23,334	23,523	46,858	1,185,499	210,859	234,288
Marche	17,582	18,249	35,831	906,526	161,240	179,155
Molise	1,971	1,924	3,895	98,534	17,526	19,473
Tuscany	31,927	34,052	65,980	1,669,290	296,909	329,899
Ministry of Defence	139	60	200	5,048	898	998
PlaNet	**92,485**	**95,135**	**187,620**	**4,746,784**	**844,290**	**938,100**
Lombardy	76,545	79,689	156,234	4,027,713	565,567	638,997
Piedmont	37,795	41,809	79,604	2,052,191	288,166	325,580
Sardinia	8,343	10,378	18,721	482,627	67,770	76,569
LPS	**122,683**	**131,876**	**254,559**	**6,562,531**	**921,504**	**1,041,146**
Italy	**438,569**	**455,573**	**894,142**	**22,883,357**	**3,413,202**	**4,013,557**

* potential supply deriving from the processing of 100% of the plasma delivered for the production of Immunoglobulins for subcutaneous administration
** potential supply deriving from the processing of 100% of the plasma delivered for the production of Immunoglobulins for intravenous administration

Table 78. Potential supply of toll fractionated PDMPs based on the amount of plasma sent for fractionation from July 2023 to June 2024 and the yields provided by the fractionation industry – year 2024 (adapted by the CNS on fractionation companies data, March 2025)

Region	2nd semester 2023	1st semester 2024	TOTAL	FVIII	FVIII/vWF	FIX/3F-PCCs	AT	Fibrinogen	Alpha-1	aPCCs	4F-PCCs	FVII	Protein C
	kg	kg	kg	UI	UI	UI	UI	g	g	UF	UI	UI	UI
Abruzzo	8,862	9,595	18,457	703,209	207,936	-	-	2,193	-	-	-	-	-
Aosta Valley	1,040	1,363	2,403	91,561	27,074	-	-	285	-	-	-	-	-
AP Bolzano	4,376	4,252	8,628	328,740	97,207	-	-	1,025	-	-	-	-	-
AP Trento	4,105	4,213	8,318	316,910	93,709	-	-	988	-	-	-	-	-
Basilicata	3,440	3,724	7,164	272,930	80,704	-	-	851	-	-	-	-	-
FVG	14,352	15,044	29,396	1,119,987	331,176	-	-	3,492	-	-	-	-	-
Liguria	12,624	12,802	25,426	968,741	286,453	-	-	3,021	-	-	-	-	-
Umbria	5,362	5,653	11,015	419,686	124,100	-	-	1,309	-	-	-	-	-
Veneto	46,819	46,527	93,346	3,556,493	1,051,641	-	-	11,090	-	-	-	-	-
NAIP	**100,981**	**103,172**	**204,154**	**7,778,256**	**2,300,000**	**-**	**-**	**24,253**	**-**	**-**	**-**	**-**	**-**
Apulia	26,400	25,833	52,233	7,161,700	-	17,556,034	9,960,000	-	-	-	-	-	-
Calabria	10,107	10,738	20,845	2,918,300	-	7,006,213	3,320,000	-	-	-	-	-	-
E.-Romagna	50,057	52,802	102,859	3,768,520	7,470,485	9,462,841	19,920,972	-	4,000	-	-	-	-
Sicily	35,856	36,017	71,873	10,058,720	-	24,157,234	13,280,000	-	-	-	-	-	-
RIPP	**122,420**	**125,390**	**247,810**	**23,907,240**	**7,470,485**	**58,182,322**	**46,480,972**	**-**	**4,000**	**-**	**-**	**-**	**-**
Campania	17,531	17,326	34,857	-	4,880,007	20,042,884	-	-	-	20,914,314	18,021,167	6,971,438	4,252,577
Latium	23,334	23,523	46,858	-	6,560,071	26,943,149	-	-	-	28,114,590	24,225,405	9,371,530	5,716,633
Marche	17,582	18,249	35,831	-	5,016,348	20,602,860	-	-	-	21,498,636	18,524,658	7,166,212	4,371,389
Molise	1,971	1,924	3,895	-	545,250	2,239,418	-	-	-	2,336,784	2,013,529	778,928	475,146
Tuscany	31,927	34,052	65,980	-	9,237,180	37,938,420	-	-	-	39,587,916	34,111,588	13,195,972	8,049,543
Min. Def.	139	60	200	-	27,931	114,718	-	-	-	119,706	103,147	39,902	24,340
PlaNet	**92,485**	**95,135**	**187,620**	**-**	**26,266,787**	**107,881,448**	**-**	**-**	**-**	**112,571,946**	**96,999,493**	**37,523,982**	**22,889,629**
Lombardy	76,545	79,689	156,234	20,610,800	-	52,511,810	28,220,000	-	-	-	-	-	-
Piedmont	37,795	41,809	79,604	10,830,680	-	26,755,700	14,940,000	-	-	-	-	-	-
Sardinia	8,343	10,378	18,721	2,454,340	-	6,292,315	3,320,000	-	-	-	-	-	-
LPS	**122,683**	**131,876**	**254,559**	**33,895,820**	**-**	**85,559,825**	**46,480,000**	**-**	**-**	**-**	**-**	**-**	**-**
Italy	**438,569**	**455,573**	**894,142**	**65,581,316**	**36,037,272**	**251,623,595**	**92,960,972**	**24,253**	**4,000**	**112,571,946**	**96,999,493**	**37,523,982**	**22,889,629**

Table 79. Potential supply of solvent/detergent-treated plasma based on the amount of plasma sent for fractionation from July 2023 to June 2024 and the yields provided by the fractionation industry – year 2024 (adapted by the CNS on data provided by Kedrion)

Region	2nd semester 2023	1st semester 2024	Total	Solvent/ detergent-treated plasma
	kg	kg	kg	mL
Abruzzo	-	-	-	-
Aosta Valley	-	-	-	-
AP Bolzano	-	-	-	-
AP Trento	-	-	-	-
Apulia	-	-	-	-
Basilicata	2,679	2,045	4,724	4,369,700
Calabria	-	-	-	-
Campania	-	-	-	-
E.-Romagna	1,463	1,518	2,981	2,757,425
Friuli V. Giulia	-	-	-	-
Latium	-	-	-	-
Liguria	178	1,221	1,399	1,294,075
Lombardy	114	137	251	232,175
Marche	-	-	-	-
Molise	-	-	-	-
Piedmont	1,581	871	2,452	2,268,100
Sardinia	-	-	-	-
Sicily	639	792	1,431	1,323,675
Tuscany	1,520	1,658	3,178	2,939,650
Umbria	-	-	-	-
Veneto	159		159	147,075
Ministry of Defence	-	-	-	-
Italy	**8,333**	**8,242**	**16,575**	**15,331,875**

Table 80. Effective supply (expressed in grams and International Units) of toll fractionated PDMPs (driver) classified by Region for the year 2024 (adapted by the CNS on fractionation companies data, March 2025)

Region	Albumin	IVIG	SCIG
	g	g	g
Abruzzo	772,170	114,600	9,440
AostaValley	76,330	19,550	360
APBolzano	248,980	27,900	880
APTrento	545,880	121,600	2,520
Basilicata	526,800	144,950	1,016
FriuliV.Giulia	156,360	48,700	1,120
Liguria	279,130	42,550	1,680
Umbria	506,420	74,200	8,120
Veneto	2,019,490	337,400	20,880
NAIP	**5,131,560**	**931,450**	**46,016**
Apulia	1,164,420	194,290	25,764
Calabria	544,830	71,075	8
E.-Romagna	2,633,040	402,625	4,776
Sicily	2,050,910	274,525	3,552
RIPP	**6,393,200**	**942,515**	**34,100**
Campania	1,079,338	118,290	-
Latium	1,174,075	220,730	20,115
Marche	655,250	156,255	21,353
Molise	69,725	10,050	512
Tuscany	1,587,548	285,095	106,160
Ministry of Defence	5,000	350	-
PlaNet	**4,570,935**	**790,770**	**148,140**
Lombardy	3,392,410	568,523	-
Piedmont	1,556,050	367,680	-
Sardinia	1,047,090	90,558	-
LPS	**5,995,550**	**1,026,760**	**-**
Italy	**22,091,245**	**3,691,495**	**228,256**

Table 81. Effective supply (expressed in grams and International Units) of toll fractionated PDMPs classified by Region for the year 2024 (adapted by the CNS on fractionation companies data, March 2025)

Region	Factor VIII	Factor VIII/ vW Factor	Factor IX	3F-PCCs	AT	Fibrinogen	S/D - treated plasma	Protein C	Alpha-1	aPCCs	4F-PCCs
	UI	UI	UI	UI	UI	g	mL	UI	g	UF	UI
Abruzzo	60,000	1,010,000	-	262,500	-	1,800	-	-	-	-	-
Aosta Valley	-	-	-	-	-	70	-	-	-	-	-
AP Bolzano	20,000	-	-	-	-	330	-	-	-	-	-
AP Trento	590,000	190,000	-	500,000	-	1,940	-	-	-	-	-
Basilicata	200,000	130,000	-	400,000	-	980	-	-	-	-	-
Friuli V. Giulia	340,000	30,000	-	175,000	-	920	-	-	-	-	-
Liguria	-	80,000	12,000	187,500	-	760	-	-	-	-	-
Umbria	100,000	190,000	-	381,000	-	1,460	-	-	-	-	-
Veneto	3,390,000	840,000	-	2,528,000	-	10,290	856,000	-	-	-	-
NAIP	**4,700,000**	**2,470,000**	**12,000**	**4,434,000**	**-**	**18,550**	**856,000**	**-**	**-**	**-**	**-**
Apulia	6,756,000	2,111,000	184,000	1,832,000	5,936,000	-	-	-	1,234	-	-
Calabria	380,000	106,000	59,000	685,500	5,998,000	-	-	-	222	-	-
E.-Romagna	403,000	5,397,000	91,000	2,792,500	2,817,000	-	-	-	2,603	-	-
Sicily	1,187,000	411,000	336,000	3,007,000	12,267,000	-	1,085,400	-	1,383	-	-
RIPP	**8,726,000**	**8,025,000**	**670,000**	**8,317,000**	**27,018,000**	**-**	**1,085,400**	**-**	**5,442**	**-**	**-**
Campania	-	156,000	7,200	462,000	755,000	-	3,680,400	113,000	-	42,000	485,400
Latium	121,000	3,333,000	455,600	1,310,800	1,470,000	-	2,111,600	152,000	-	402,000	1,012,200
Marche	-	2,190,000	322,800	354,000	2,345,000	-	1,184,000	22,000	-	70,000	894,000
Molise	-	84,000	50,000	203,000	625,000	-	372,000	-	-	-	-
Tuscany	743,000	688,000	37,200	1,812,500	1,811,000	4,500	1,006,600	20,000	-	-	1,965,000
Min.of Defence	-	-	-	6,000	60,000	-	-	-	-	-	-
PlaNet	**864,000**	**6,451,000**	**872,800**	**4,148,300**	**7,066,000**	**4,500**	**8,354,600**	**307,000**	**-**	**514,000**	**4,356,600**
Lombardy	5,556,000	-	1,757,000	5,899,000	5,997,000	-	468,000	-	-	-	-
Piedmont	4,309,000	-	130,000	2,866,000	5,994,000	-	3,672,000	-	-	-	-
Sardinia	458,000	-	-	838,500	2,059,000	-	48,000	-	-	-	-
LPS	**10,323,000**	**-**	**1,887,000**	**9,603,500**	**14,050,000**	**-**	**4,188,000**	**-**	**-**	**-**	**-**
Italy	**24,613,000**	**16,946,000**	**3,441,800**	**26,502,800**	**48,134,000**	**23,050**	**14,484,000**	**307,000**	**5,442**	**514,000**	**4,356,600**

ANALYSIS OF SELF-SUFFICIENCY

Albumin

In 2024, the Italian NHS demand for albumin accounted for 87.5% of the total. The national potential self-sufficiency, estimated on the basis of the relationship between potential supply and NHS demand, was 79% (+4% compared to 2023) while the effective self-sufficiency, considered as the ratio between the actual supply of toll fractionation and the NHS demand, was 76% (73% in 2023).

The Regions that in 2024 achieved effective self-sufficiency - more than 90% - were Friuli V. Giulia, the AP of Bolzano, the AP of Trento, Umbria, Aosta Valley, Veneto, Piedmont, Tuscany and Marche.

Table 82. Estimates of regional and national self-sufficiency in albumin, 2024

Region	Total demand	NHS demand	Potential supply	Effective supply	Potential self-sufficiency	Effective self-sufficiency
	g	g	g	g	%	%
Abruzzo	920,715	875,373	468,806	772,170	54	88
Aosta Valley	76,780	76,570	61,040	76,330	80	100
AP Bolzano	168,915	168,805	219,160	156,360	130	93
AP Trento	290,840	285,390	211,273	279,130	74	98
Basilicata	356,698	349,705	181,953	248,980	52	71
Friuli V. Giulia	563,050	547,200	746,658	545,880	136	100
Liguria	778,553	665,840	645,827	526,800	97	79
Umbria	522,370	520,335	279,791	506,420	54	97
Veneto	2,106,590	2,058,948	2,370,995	2,019,490	115	98
NAIP	**5,784,510**	**5,548,165**	**5,185,504**	**5,131,560**	**93**	**92**
Apulia	1,957,875	1,669,080	1,346,567	1,164,420	81	70
Calabria	912,988	816,510	537,384	544,830	66	67
E.-Romagna	3,373,635	3,149,435	2,651,701	2,633,040	84	84
Sicily	2,701,860	2,321,888	1,852,886	2,050,910	80	88
RIPP	**8,946,358**	**7,956,913**	**6,388,538**	**6,393,200**	**80**	**80**
Campania	4,074,410	3,701,498	881,887	1,079,338	24	29
Latium	3,399,305	2,098,880	1,185,499	1,174,075	56	56
Marche	791,570	695,050	906,526	655,250	130	94
Molise	107,250	96,458	98,534	69,725	102	72
Tuscany	1,629,718	1,592,685	1,669,290	1,587,548	105	100
Min. of Def.	-	-	5,048	5,000	-	-
PlaNet	**10,002,253**	**8,184,570**	**4,746,784**	**4,570,935**	**58**	**56**
Lombardy	5,198,585	4,201,980	4,027,713	3,392,410	96	81
Piedmont	1,712,795	1,650,630	2,052,191	1,556,050	124	94
Sardinia	1,592,850	1,544,915	482,627	1,047,090	31	68
LPS	**8,504,230**	**7,397,525**	**6,562,531**	**5,995,550**	**89**	**81**
Italy	**33,237,350**	**29,087,173**	**22,883,357**	**22,091,245**	**79**	**76**

The Regions that mostly benefitted from interregional compensation in 2024 were: Umbria (97% effective self-sufficiency compared to the potential 54%) and Abruzzo (88% compared to 54%) for NAIP, Sardinia (68% compared to 31%) for LPS, Sicily (effective self-sufficiency 88% compared to the potential 80%) for the RIPP consortium and Campania for the PlaNet consortium (effective self-sufficiency 29% compared to the potential 24%).

The Regions that remained farthest from the goal of effective self-sufficiency were Campania, Latium, Calabria and Sardinia, with percentages ranging between 29% and 68% of the NHS demand met by the toll fractionation supply.

Normal human immunoglobulins

In 2024, the NHS demand for normal IGs accounted for 95% of the total demand (Table 83).

Table 83. Estimates of regional and national self-sufficiency in human immunoglobulins, 2024

Region	Total demand	NHS demand	Potential supply	Effective supply	Potential self-sufficiency	Effective self-sufficiency
	g	g	g	g	%	%
Abruzzo	158,615	158,400	92,285	124,040	58	78
Aosta Valley	21,290	21,290	12,016	19,910	56	94
AP Bolzano	62,255	62,255	43,142	49,820	69	80
AP Trento	60,428	60,428	41,589	44,230	69	73
Basilicata	42,789	42,789	35,818	28,780	84	67
Friuli V. Giulia	136,620	136,245	146,980	124,120	108	91
Liguria	199,669	198,814	127,131	145,966	64	73
Umbria	129,721	129,721	55,077	82,320	42	63
Veneto	558,347	555,116	466,731	358,280	84	64
NAIP	**1,369,734**	**1,365,058**	**1,020,769**	**977,466**	**75**	**71**
Apulia	452,309	432,819	205,330	220,054	45	49
Calabria	127,967	127,967	81,772	71,083	64	56
E.-Romagna	677,955	648,365	354,684	407,401	52	60
Sicily	389,853	380,578	285,295	278,077	73	71
RIPP	**1,648,083**	**1,589,728**	**927,081**	**976,615**	**56**	**59**
Campania	450,945	450,206	168,732	118,290	37	26
Latium	584,224	525,773	225,667	240,845	39	41
Marche	233,647	228,077	175,651	177,608	75	76
Molise	18,873	13,873	19,122	10,562	101	56
Tuscany	564,629	547,109	318,078	391,255	56	69
Min. of Def.	-	-	-	-	-	-
PlaNet	**1,852,318**	**1,765,037**	**907,250**	**938,560**	**49**	**51**
Lombardy	1,124,964	948,194	627,809	568,523	56	51
Piedmont	533,634	532,129	318,713	367,680	60	69
Sardinia	153,180	152,840	76,185	90,558	50	59
LPS	**1,811,778**	**1,633,163**	**1,022,707**	**1,026,760**	**56**	**57**
Italy	**6,681,914**	**6,352,986**	**3,877,806**	**3,919,401**	**58**	**59**

* The value does not include high-title IG

The national potential self-sufficiency, espressed by the ratio of the potential supply to the total demand, in 2024 was 58%, where effective self-sufficiency, understood as the ratio of the actual supply of toll fractionation to total demand, was 59%.

Some Regions managed to achieve actual self-sufficiency in IG in 2024 above 90%, such as Friuli V. Giulia and Aosta Valley, while the Regions that achieved the lowest actual self-sufficiency were Latium (41%) and Campania (26%).

Normal human immunoglobulins for subcutaneous use

In 2024, the NHS demand for immunoglobulins for subcutaneous/intramuscular use represented approximately 97.5% of the total demand (Table 84). The effective self-sufficiency, regarded as the ratio between the actual supply of the processing account and the total demand, was 14% (17% in 2023). No Region in 2024 achieved effective self-sufficiency > 90%; the highest levels of self-sufficiency were recorded in Tuscany and Valle d'Aosta, with percentages of 52% and 48% respectively, followed by the Autonomous Province of Bolzano and the Marche Region with 47%.

Table 84. Estimates of regional and national self-sufficiency in human immunoglobulin for subcutaneous use, 2024

Region	Total demand	NHS demand	Potential supply	Effective supply	Potential self-sufficiency	Effective self-sufficiency
	g	g	g	g	%	%
Abruzzo	40,155	40,055	92,285	9,440	230	24
Aosta Valley	749	749	12,016	360	1604	48
AP Bolzano	2,365	2,365	43,142	1,120	1824	47
AP Trento	7,928	7,928	41,589	1,680	525	21
Basilicata	13,622	13,622	35,818	880	263	6
Friuli V. Giulia	10,695	10,695	146,980	2,520	1374	24
Liguria	21,889	21,889	127,131	1,016	581	5
Umbria	53,586	53,586	55,077	8,120	103	15
Veneto	154,112	153,936	466,731	20,880	303	14
NAIP	**305,102**	**304,826**	**1,020,769**	**46,016**	**335**	**15**
Apulia	152,983	152,533	189,083	25,764	124	17
Calabria	45,511	45,511	75,459	8	166	0
E.-Romagna	140,385	140,385	101,917	4,776	73	3
Sicily	100,003	100,003	260,180	3,552	260	4
RIPP	**438,882**	**438,432**	**626,640**	**34,100**	**143**	**8**
Campania	143,700	143,696	156,857	-	109	0
Latium	214,974	214,343	210,859	20,115	98	9
Marche	45,707	45,707	161,240	21,353	353	47
Molise	3,403	3,403	17,526	512	515	15
Tuscany	202,326	202,326	296,909	106,160	147	52
Min. of Def.	-	-	898	-	-	-
PlaNet	**610,110**	**609,474**	**844,290**	**148,140**	**138**	**24**
Lombardy	171,401	132,792	565,567	-	330	0
Piedmont	97,949	97,949	288,166	-	294	0
Sardinia	6,683	6,683	67,770	-	1014	0
LPS	**276,032**	**237,423**	**921,504**	**-**	**334**	**0**
Italy	**1,630,126**	**1,590,155**	**3,413,202**	**228,256**	**209**	**14**

* potential offer deriving from the processing of 100% of the plasma delivered for the production of Immunoglobulins for subcutaneous administration

Normal human immunoglobulins for intravenous use

In 2024, the NHS demand for IV IGs accounted for 94% of the total demand (Table 85).

Table 85. Estimates of regional and national self-sufficiency in human immunoglobulin for intravenous use, 2024

Region	Total demand	NHS demand	Potential supply	Effective supply	Potential self-sufficiency	Effective self-sufficiency
	g	g	g	g	%	%
Abruzzo	118,460	118,345	92,285	114,600	78	97
Aosta Valley	20,541	20,541	12,016	19,550	58	95
AP Bolzano	59,890	59,890	43,142	48,700	72	81
AP Trento	52,500	52,500	41,589	42,550	79	81
Basilicata	29,167	29,167	35,818	27,900	123	96
Friuli V. Giulia	125,925	125,550	146,980	121,600	117	97
Liguria	177,780	176,925	127,131	144,950	72	82
Umbria	76,135	76,135	55,077	74,200	72	97
Veneto	404,235	401,180	466,731	337,400	115	83
NAIP	**1,064,633**	**1,060,233**	**1,020,769**	**931,450**	**96**	**87**
Apulia	299,326	280,286	213,633	194,290	71	65
Calabria	82,455	82,455	85,256	71,075	103	86
E.-Romagna	537,570	507,980	420,693	402,625	78	75
Sicily	289,850	280,575	293,961	274,525	101	95
RIPP	**1,209,202**	**1,151,297**	**1,013,542**	**942,515**	**84**	**78**
Campania	307,245	306,510	174,286	118,290	57	39
Latium	369,250	311,430	234,288	220,730	63	60
Marche	187,940	182,370	179,155	156,255	95	83
Molise	15,470	10,470	19,473	10,050	126	65
Tuscany	362,303	344,783	329,899	285,095	91	79
Min. of Def.	-	-	998	-	-	-
PlaNet	**1,242,208**	**1,155,563**	**938,100**	**790,420**	**76**	**64**
Lombardy	953,563	815,402	638,997	568,523	67	60
Piedmont	435,685	434,180	325,580	367,680	75	84
Sardinia	146,498	146,158	76,569	90,558	52	62
LPS	**1,535,746**	**1,395,739**	**1,041,146**	**1,026,760**	**68**	**67**
Italy	**5,051,788**	**4,762,832**	**4,013,557**	**3,691,145**	**79**	**73**

*potential offer deriving from the processing of 100% of the plasma delivered for the production of Immunoglobulins for intravenous administration
** The value does not include high-title IG.

The national potential self-sufficiency, espressed by the ratio of the potential supply to total demand, in 2024 was 79%. Effective self-sufficiency, assumed as the ratio of the actual supply of toll fractionation to total demand, was 73%.

The Regions that achieved effective self-sufficiency >90% in 2024 were Abruzzo, Basilicata, Friuli V. Giulia, Umbria, and Aosta Valley for NAIP, together with Sicily for RIPP.

Campania is the Region with the lowest effective self-sufficiency value, equal to 39%.

Antithrombin

In 2024 NHS demand for AT accounted for about 90% of total demand. Effective self-sufficiency recorded a value of 60% in 2024 (77% in 2023), less than the potential self-sufficiency (116%) (Table 86).

Table 86. Estimates of regional and national self-sufficiency in antithrombin, 2024

Region	Total demand	NHS demand	Potential supply	Effective supply	Potential self-sufficiency	Effective self-sufficiency
	IU	IU	IU	IU	%	%
Abruzzo	1,443,500	1,285,000	-	-	-	-
Aosta Valley	105,000	105,000	-	-	-	-
AP Bolzano	200,000	200,000	-	-	-	-
AP Trento	1,000	-	-	-	-	-
Basilicata	409,000	409,000	-	-	-	-
Friuli V. Giulia	2,344,000	2,340,000	-	-	-	-
Liguria	2,568,500	2,353,000	-	-	-	-
Umbria	90,000	90,000	-	-	-	-
Veneto	1,043,500	986,000	-	-	-	-
NAIP	**8,204,500**	**7,768,000**	**-**	**-**	**-**	**-**
Apulia	6,610,000	5,981,000	9,960,000	5,936,000	167	99
Calabria	6,054,500	5,998,000	3,320,000	5,998,000	55	100
E.-Romagna	4,622,000	4,316,000	19,920,972	2,817,000	462	65
Sicily	13,928,000	12,772,000	13,280,000	12,267,000	104	96
RIPP	**31,214,500**	**29,067,000**	**46,480,972**	**27,018,000**	**160**	**93**
Campania	10,817,000	10,039,000	-	755,000	-	8
Latium	11,134,500	9,001,500	-	1,470,000	-	16
Marche	2,350,000	2,345,000	-	2,345,000	-	100
Molise	697,000	625,000	-	625,000	-	100
Tuscany	6,055,500	6,055,500	-	1,811,000	-	30
Min. of Def.	-	-	-	-	-	-
PlaNet	**31,054,000**	**28,066,000**	**-**	**7,006,000**	**-**	**25**
Lombardy	9,785,500	7,170,500	28,220,000	5,997,000	394	84
Piedmont	6,423,500	5,994,000	14,940,000	5,994,000	249	100
Sardinia	2,157,500	2,154,000	3,320,000	2,059,000	154	96
LPS	**18,366,500**	**15,318,500**	**46,480,000**	**14,050,000**	**303**	**92**
Italy	**88,839,500**	**80,219,500**	**92,960,972**	**48,074,000**	**116**	**60**

Since AT is not included among the PDMPs provided under the CSL Behring toll fractionation contract, its potential supply for NAIP Regions was equal to zero. Neverthless, their NHS demand could be met by the existing stock of products provided within the scope of the previous contract with Kedrion and by interregional compensation. Some Regions have achieved actual self-sufficiency of more than 90% of NHS demand by 2024, with the exception of almost all NAIP Regions and Emilia-Romagna, Campania, Latium, Tuscany and Lombardy.

The Regions that benefited most from interregional compensation or product stocks related to the previous convention in 2024 were Marche and Molise (100% effective *vs.* 0% potential), and Calabria (100% effective *vs.* 55% potential).

Coagulation Factor VIII

In the analysis of demand and supply for pdFVIII, it should be taken into account that the choice of the pharmaceutical specialty for the treatment of haemophilia A is based on considerations stemming from the therapeutic alliance between doctor and patient, which has to be safeguarded and may not even allow for the prescribed medicine to be replaced with a medicine from the same class or ATC group. Therefore, in this Report self-sufficiency is described by distinguishing pdFVIII from pdFVIII in combination with vWF.

In 2024, PlaNet Regions could benefit from the still existing stock of plasma-derived coagulation Factor VIII provided for in the previous agreement with Kedrion (Klott™).

Plasma-derived coagulation Factor VIII

In 2024, all the Regions largely achieved effective self-sufficiency in pdFVIII (Table 87).

Table 87. Estimates of regional and national self-sufficiency in plasma-derived Factor VIII, 2024

Region	Total demand	NHS demand	Potential supply	Effective supply	Potential self-sufficiency	Effective self-sufficiency
	IU	IU	IU	IU	%	%
Abruzzo	60,000	60,000	703,209	60,000	1172	100
Aosta Valley	-	-	91,561	-	NA	NA
AP Bolzano	340,000	340,000	328,740	340,000	97	100
AP Trento	-	-	316,910	-	NA	NA
Basilicata	20,000	20,000	272,930	20,000	1365	100
Friuli V. Giulia	590,000	590,000	1,119,987	590,000	190	100
Liguria	200,000	200,000	968,741	200,000	484	100
Umbria	130,000	130,000	419,686	100,000	323	77
Veneto	3,390,000	3,390,000	3,556,493	3,390,000	105	100
NAIP	**4,730,000**	**4,730,000**	**7,778,256**	**4,700,000**	**164**	**99**
Apulia	6,756,000	6,756,000	7,161,700	6,756,000	106	100
Calabria	380,000	380,000	2,918,300	380,000	768	100
E.-Romagna	403,000	403,000	3,768,520	403,000	935	100
Sicily	1,187,000	1,187,000	10,058,720	1,187,000	847	100
RIPP	**8,726,000**	**8,726,000**	**23,907,240**	**8,726,000**	**274**	**100**
Campania	-	-	-	-	-	-
Latium	183,000	167,000	-	121,000	-	72
Marche	-	-	-	-	-	-
Molise	1,000	-	-	-	-	-
Tuscany	1,917,000	1,774,000	-	743,000	-	42
Min. of Def.	-	-	-	-	NA	NA
PlaNet	**2,101,000**	**1,941,000**	**-**	**864,000**	**-**	**45**
Lombardy	6,102,000	6,100,000	20,610,800	5,556,000	338	91
Piedmont	4,309,000	4,309,000	10,830,680	4,309,000	251	100
Sardinia	458,000	458,000	2,454,340	458,000	536	100
LPS	**10,869,000**	**10,867,000**	**33,895,820**	**10,323,000**	**312**	**95**
Italy	**26,426,000**	**26,264,000**	**65,581,316**	**24,613,000**	**250**	**94**

Plasma-derived coagulation Factor VIII and von Willebrand Factor in combination

Table 88 shows the regional and national self-sufficiency in plasma-derived Factor VIII and von Willebrand Factor in combination. For this active ingredient, the effective self-sufficiency recorded in 2024 was 33%.

Table 88. Estimates of regional and national self-sufficiencyin plasma-derived Factor VIII and von Willebrand Factor in combination, 2024

Region	Total demand	NHS demand	Potential supply	Effective supply	Potential self-sufficiency	Effective self-sufficiency
	IU	IU	IU	IU	%	%
Abruzzo	2,131,000	2,057,000	207,936	1,010,000	10	49
Aosta Valley	29,000	5,000	27,074	-	541	0
AP Bolzano	30,000	30,000	97,207	30,000	324	100
AP Trento	120,000	120,000	93,709	80,000	78	67
Basilicata	26,000	26,000	80,704	-	310	0
Friuli V. Giulia	284,000	272,000	331,176	190,000	122	70
Liguria	316,000	316,000	286,453	130,000	91	41
Umbria	715,000	715,000	124,100	190,000	17	27
Veneto	2,148,000	2,132,500	1,051,641	840,000	49	39
NAIP	**5,799,000**	**5,673,500**	**2,300,000**	**2,470,000**	**41**	**44**
Apulia	6,060,000	6,020,000	-	2,111,000	-	35
Calabria	1,365,500	1,184,500	-	106,000	-	9
E.-Romagna	9,948,500	8,518,500	7,470,485	5,397,000	88	63
Sicily	1,889,000	1,875,000	-	411,000	-	22
RIPP	**19,263,000**	**17,598,000**	**7,470,485**	**8,025,000**	**42**	**46**
Campania	3,797,000	3,782,000	4,880,007	156,000	129	4
Latium	9,771,500	8,951,500	6,560,071	3,333,000	73	37
Marche	2,679,500	2,679,500	5,016,348	2,190,000	187	82
Molise	272,000	272,000	545,250	84,000	200	31
Tuscany	3,409,000	3,409,000	9,237,180	688,000	271	20
Min. of Def.	-	-	27,931	-	-	-
PlaNet	**19,929,000**	**19,094,000**	**26,266,787**	**6,451,000**	**138**	**34**
Lombardy	4,279,000	4,196,000	-	-	-	-
Piedmont	2,225,500	2,223,000	-	-	-	-
Sardinia	2,464,000	2,370,000	-	-	-	-
LPS	**8,968,500**	**8,789,000**	**-**	**-**	**-**	**-**
Italy	**53,959,500**	**51,154,500**	**36,037,272**	**16,946,000**	**70**	**33**

* The value does not include *Wilfactin*.

Factor IX and 3-Factor Prothrombin Complex Concentrates

The industrial production of pdFIX and 3F-PCCs is strictly alternative and therefore self-sufficiency in these two PDMPs have been analysed together.

While national self-sufficiency in pdFIX and 3F-PCCs was substantially reached (higher than 90% of the NHS demand), the regional self-sufficiency still bore significant differences with a range, varying from 0 to 100% confirming the need of improvement in the inter-regional exchange and compensation mechanisms (Table 89).

Table 89. Estimates of regional and national self- sufficiency in plasma-derived Factor IX and 3-factor prothrombin complex concentrates, 2024

Region	Total demand	NHS demand	Potential supply	Effective supply	Potential self-sufficiency	Effective self-sufficiency
	IU	IU	IU	IU	%	%
Abruzzo	268,500	262,500	-	262,500	-	100
Aosta Valley	-	-	-	-	-	-
AP Bolzano	187,000	187,000	-	187,000	-	100
AP Trento	187,500	187,500	-	187,500	-	100
Basilicata	82,500	80,000	-	-	-	-
Friuli V. Giulia	500,000	500,000	-	500,000	-	100
Liguria	623,000	429,000	-	400,000	-	93
Umbria	477,000	477,000	-	381,000	-	80
Veneto	3,369,500	3,368,000	-	2,528,000	-	75
NAIP	**5,695,000**	**5,491,000**	**-**	**4,446,000**	**-**	**81**
Apulia	2,716,000	2,016,000	17,556,034	2,016,000	871	100
Calabria	748,000	744,500	7,006,213	744,500	941	100
E.-Romagna	3,322,500	2,885,000	9,462,841	2,883,500	328	100
Sicily	3,556,000	3,383,000	24,157,234	3,343,000	714	99
RIPP	**10,342,500**	**9,028,500**	**58,182,322**	**8,987,000**	**644**	**100**
Campania	1,821,200	1,330,200	20,042,884	469,200	1,507	35
Latium	1,848,600	1,803,900	26,943,149	1,766,400	1,494	98
Marche	841,300	816,800	20,602,860	676,800	2,522	83
Molise	285,500	253,000	2,239,418	253,000	885	100
Tuscany	1,855,700	1,852,700	37,938,420	1,849,700	2,048	100
Min. of Def.	-	-	114,718	-	NA	-
PlaNet	**6,652,300**	**6,056,600**	**107,881,448**	**5,015,100**	**1781**	**83**
Lombardy	7,963,500	7,742,500	52,511,810	7,656,000	678	99
Piedmont	3,337,500	2,996,000	26,755,700	2,996,000	893	100
Sardinia	838,500	838,500	6,292,315	838,500	750	100
LPS	**12,139,500**	**11,577,000**	**85,559,825**	**11,490,500**	**739**	**99**
Italy	**34,829,300**	**32,153,100**	**251,623,595**	**29,938,600**	**783**	**93**

Fibrinogen

RiaSTAP™ is a product containing fibrinogen concentrate currently made available by CSL Behring under the toll fractionation contract with NAIP Regions. RiaSTAP is indicated for the treatment of congenital fibrinogen deficiency, which comprises congenital afibrinogenemia and hypofibrinogenemia. In 2024, the potential self-sufficiency in RiaSTAP was equal to 56% (54% in 2023) (Table 90). However, effective self-sufficiency of 53% was achieved (44% in 2023), also given the marked increase of demand also in 2024 (+10%), demonstrating a continuing upward trend for this product. Most of NAIP Regions, except for Aosta Valley, achieved effective self-sufficiency higher than 90%. It is clear that Tuscany, despite belonging to an agreement that does not provide for the return of fibrinogen by Toll fractionation system, has achieved 100% self-sufficiency by taking advantage of inter-agreement compensation mechanisms.

Table 90. Estimates of regional and national self-sufficiency in fibrinogen by toll manufacturing system, 2024

Region	Total demand	NHS demand	Potential supply	Effective supply	Potential self-sufficiency	Effective self-sufficiency
	g	g	g	g	%	%
Abruzzo	1,842	1,840	2,193	1,800	119	98
Aosta Valley	89	89	285	70	321	79
AP Bolzano	920	920	1,025	920	111	100
AP Trento	760	760	988	760	130	100
Basilicata	330	330	851	330	258	100
Friuli V. Giulia	1,948	1,940	3,492	1,940	180	100
Liguria	1,140	1,140	3,021	980	265	86
Umbria	1,460	1,460	1,309	1,460	90	100
Veneto	11,227	11,227	11,090	10,290	99	92
NAIP	**19,716**	**19,706**	**24,253**	**18,550**	**123**	**94**
Apulia	163	-	-	-	-	-
Calabria	16	-	-	-	-	-
E.-Romagna	63	63	-	-	-	-
Sicily	3,482	3,264	-	-	-	-
RIPP	**3,724**	**3,327**	**-**	**-**	**-**	-
Campania	4,625	4,383	-	-	-	-
Latium	3,026	1,680	-	-	-	-
Marche	1,476	1,476	-	-	-	-
Molise	14	14		-	-	-
Tuscany	4,500	4,500	-	4,500	-	100
Min. of Def.	-	-	-	-	-	-
PlaNet	**13,641**	**12,053**	**-**	**4,500**	**-**	**37**
Lombardy	7,012	4,543	-	-	-	-
Piedmont	1,438	1,409	-	-	-	-
Sardinia	2,202	2,202	-	-	-	-
LPS	**10,652**	**8,154**	**-**	**-**	**-**	**-**
Italy	**47,733**	**43,240**	**24,253**	**23,050**	**56**	**53**

Solvent/detergent virus-inactivated plasma

Differently from the main PDMPs that were included in the agreements between the Regions and the fractionation company, the production of solvent/detergent virus-inactivated plasma (S/D plasma) from national plasma was determined by the production planning of the individual Regions (and in some cases of Local Health Centers). Therefore, not all the Regions contributed to the achievement of national self-sufficiency.

For S/D plasma, the therapeutic indications are the same as those for fresh-frozen plasma. There is not sufficient evidence to justify the priority or preferential use of S/D plasma rather than fresh frozen plasma (52).

In 2024, the NHS demand for S/D plasma was almost equal to the total demand. For the same year, effective national self-sufficiency was 68% (62% in 2023) (Table 91).

Table 91. Estimates of regional and national self-sufficiency in solvent/detergent virus-inactivated plasma, 2024

Region	Total demand	NHS demand	Potential supply	Effective supply	Potential self-sufficiency	Effective self-sufficiency
	mL	mL	mL	mL	%	%
Abruzzo	-	-		-	-	-
Aosta Valley	-	-		-	-	-
AP Bolzano	-	-		-	-	-
AP Trento	10,000	10,000		-	-	-
Basilicata	402,000	402,000		-	-	-
Friuli V. Giulia	12,000	12,000		-	-	-
Liguria	140,000	130,000		-	-	-
Umbria	148,000	106,000		-	-	-
Veneto	936,000	856,000	147,075	856,000	17	100
NAIP	**1,648,000**	**1,516,000**	**147,075**	**856,000**	**10**	**56**
Apulia	2,482,000	2,222,000		-	-	-
Calabria	898,000	874,000		-	-	-
E.-Romagna	282,000	242,000		-	-	-
Sicily	2,763,000	2,763,000	1,323,675	1,085,400	48	39
RIPP	**6,425,000**	**6,101,000**	**1,323,675**	**1,085,400**	**22**	**18**
Campania	3,814,400	3,786,400	4,369,700	3,680,400	115	97
Latium	2,742,600	2,606,600	2,757,425	2,111,600	106	81
Marche	1,184,000	1,184,000	1,294,075	1,184,000	109	100
Molise	372,000	372,000	232,175	372,000	62	100
Tuscany	1,613,600	1,613,600	2,939,650	1,006,600	182	62
Min. of Def.	-	-		-	-	-
PlaNet	**9,726,600**	**9,562,600**	**11,593,025**	**8,354,600**	**121**	**87**
Lombardy	478,000	478,000		468,000	-	98
Piedmont	3,672,000	3,672,000	2,268,100	3,672,000	62	100
Sardinia	60,200	60,200		48,000	-	80
LPS	**4,210,200**	**4,210,200**	**2,268,100**	**4,188,000**	**54**	**99**
Italy	**22,009,800**	**21,389,800**	**15,331,875**	**14,484,000**	**72**	**68**

Some of the Regions that used S/D plasma produced by toll fractionation, have achieved effective regional self-sufficiency of 100%, such as Veneto, Marche, Molise and Piedmont.

Protein C

In 2021, for the first time in Italy, the distribution by toll fractionation of protein C from Takeda company began, which includes this active ingredient as an ancillary product in its agreement with the Regions. In the 2024, 307,000 IU of protein C were distributed among Campania, Latium, Marche and Tuscany, enabling these Regions to reach a self-sufficiency percentage of 43% for the first and 100% for the other three. At the national level, the self-sufficiency percentage stood at 40% (Table 92).

Table 92. Estimates of regional and national self-sufficiency in Protein C, 2024

Region	Total demand	NHS demand	Potential supply	Effective supply	Potential self-sufficiency	Effective self-sufficiency
	IU	IU	IU	IU	%	%
Abruzzo	4,500	4,500	-	-	-	-
Aosta Valley	-	-	-	-	-	-
AP Bolzano	-	-	-	-	-	-
AP Trento	-	-	-	-	-	-
Basilicata	-	-	-	-	-	-
Friuli V. Giulia	-	-	-	-	-	-
Liguria	3,000	3,000	-	-	-	-
Umbria	6,000	6,000	-	-	-	-
Veneto	10,000	10,000	-	-	-	-
NAIP	**23,500**	**23,500**	**-**	**-**	**-**	**-**
Apulia	-	-	-	-	-	-
Calabria	202,500	191,000	-	-	-	-
E.-Romagna	3,000	3,000	-	-	-	-
Sicily	33,500	33,500	-	-	-	-
RIPP	**239,000**	**227,500**	**-**	**-**	**-**	**-**
Campania	264,000	264,000	4,252,577	113,000	1,611	43
Latium	154,500	152,000	5,716,633	152,000	3,761	100
Marche	22,000	22,000	4,371,389	22,000	19,870	100
Molise	-	-	475,146	-	NA	-
Tuscany	20,000	20,000	8,049,543	20,000	40,248	100
Min. of Def.			24,340	-	NA	NA
PlaNet	**460,500**	**458,000**	**22,889,629**	**307,000**	**4,998**	**67**
Lombardy	48,500	48,500	-	-	-	-
Piedmont	8,000	8,000	-	-	-	-
Sardinia	7,500	7,500	-	-	-	-
LPS	**64,000**	**64,000**	**-**	**-**	**-**	**-**
Italy	**787,000**	**773,000**	**22,889,629**	**307,000**	**2,961**	**40**

Activated Prothrombin Complex Concentrates

In 2022, for the first time in Italy, the distribution of activated Prothrombin Complex Concentrates on consignment began by the Takeda Company, which included this active ingredient as an ancillary product in its agreement with the Regions. In 2024, 514,000 FU of aPCCs were distributed among Campania, Latium and Marche enabling these Regions to reach a

self-sufficiency percentage of 50%, 54% and 57%, respectively. At the national level, the percentage of self-sufficiency stood at 11% (Table 93).

Table 93. Estimates of regional and national self-sufficiency in Activated Prothrombin Complex Concentrates, 2024

Region	Total demand	NHS demand	Potential supply	Effective supply	Potential self-sufficiency	Effective self-sufficiency
	FU	FU	FU	FU	%	%
Abruzzo	198,000	198,000	-	-	-	-
Aosta Valley	-	-	-	-	-	-
AP Bolzano	-	-	-	-	-	-
AP Trento	-	-	-	-	-	-
Basilicata	-	-	-	-	-	-
Friuli V. Giulia	-	-	-	-	-	-
Liguria	10,000	10,000	-	-	-	-
Umbria	-	-	-	-	-	-
Veneto	212,000	212,000	-	-	-	-
NAIP	**420,000**	**420,000**	**-**	**-**	**-**	**-**
Apulia	161,000	161,000	-	-	-	-
Calabria	37,000	37,000	-	-	-	-
E.-Romagna	830,000	830,000	-	-	-	-
Sicily	107,000	107,000	-	-	-	-
RIPP	**1,135,000**	**1,135,000**	**-**	**-**	**-**	**-**
Campania	84,000	84,000	20,914,314	42,000	24,898	50
Latium	819,000	744,000	28,114,590	402,000	3,779	54
Marche	122,000	122,000	21,498,636	70,000	17,622	57
Molise	-	-	2,336,784	-	-	-
Tuscany	-	-	39,587,916	-	-	-
Min. of Def.	-	-	119,706	-	-	-
PlaNet	**1,025,000**	**950,000**	**112,571,946**	**514,000**	**11,850**	**54**
Lombardy	1,354,000	1,354,000	-	-	-	-
Piedmont	202,000	202,000	-	-	-	-
Sardinia	571,000	571,000	-	-	-	-
LPS	**2,127,000**	**2,127,000**	**-**	**-**	**-**	**-**
Italy	**4,707,000**	**4,632,000**	**112,571,946**	**514,000**	**2,430**	**11**

Alpha-1-proteinase inhibitor

Plitalfa is a product containing the human alpha1-proteinase inhibitor currently made available by Grifols under the RIPP Agreement fractionation contract with Regions. Plitalfa is indicated for chronic replacement therapy in individuals with documented severe alpha1-proteinase inhibitor deficiency. Because it is the only drug containing this active ingredient to be returned by toll fractionation contracts, specific product self-sufficiency was considered. In 2024, actual self-sufficiency recorded only within the same RIPP Regions was 100% of NHS demand.

Table 94. Estimates of regional and national self-sufficiency in Alpha-1 by toll manufacturing system, 2024

Region	Total demand	NHS demand	Potential supply	Effective supply	Potential self-sufficiency	Effective self-sufficiency
	g	g	g	g	%	%
Abruzzo	-	-	-	-	-	-
Aosta Valley	-	-	-	-	-	-
AP Bolzano	-	-	-	-	-	-
AP Trento	-	-	-	-	-	-
Basilicata	-	-	-	-	-	-
Friuli V. Giulia	-	-	-	-	-	-
Liguria	-	-	-	-	-	-
Umbria	-	-	-	-	-	-
Veneto	-	-	-	-	-	-
NAIP	**-**	**-**	**-**	**-**	**-**	**-**
Apulia	1,234	1,234	-	1,234	-	100
Calabria	222	222	-	222	-	100
E.-Romagna	2,603	2,603	4,000	2,603	154	100
Sicily	1,383	1,383	-	1,383	-	100
RIPP	**5,442**	**5,442**	**4,000**	**5,442**	**74**	**100**
Campania	-	-	-	-	-	-
Latium	-	-	-	-	-	-
Marche	-	-	-	-	-	-
Molise	-	-	-	-	-	-
Tuscany	-	-	-	-	-	-
Min. of Def.	-	-	-	-	-	-
PlaNet	**-**	**-**	**-**	**-**	**-**	**-**
Lombardy	-	-	-	-	-	-
Piedmont	-	-	-	-	-	-
Sardinia	-	-	-	-	-	-
LPS	-	-	-	-	-	-
Italy	**5,442**	**5,442**	**4,000**	**5,442**	**74**	**100**

4-Factor Prothrombin Complex Concentrates

Proplex is a preparation obtained from human plasma containing blood coagulation factors II, VII, IX and X and also protein C, which play an important role in blood coagulation. Proplex is therefore used in cases of acquired or congenital deficiency of coagulation factors for the prevention and treatment of bleeding.

On subcontracting this product was made available by the Takeda Company for the first time in 2023, as part of the current agreement with the PlaNet Agreement. Being the only medicine containing this active ingredient to be returned on account, specific product self-sufficiency was considered. In 2024, The self-sufficiency recorded only within the same PlaNet Regions was equal to 100% of the NHS demand (Table 95).

Table 95. Estimates of regional and national self-sufficiency in 4-Factor Prothrombin Complex Concentrates by toll manufacturing system (*Proplex*), 2024

Region	Total demand	NHS demand	Potential supply	Effective supply	Potential self-sufficiency	Effective self-sufficiency
	IU	IU	IU	IU	%	%
Abruzzo	-	-	-	-	-	-
Aosta Valley	-	-	-	-	-	-
AP Bolzano	-	-	-	-	-	-
AP Trento	-	-	-	-	-	-
Basilicata	-	-	-	-	-	-
Friuli V. Giulia		-	-	-	-	-
Liguria	33,000	-	-	-	-	-
Umbria	3,000	3,000	-	-	-	-
Veneto	-	-	-	-	-	-
NAIP	**36,000**	**3,000**	**-**	**-**	**-**	**-**
Apulia	39,000	-	-	-	-	-
Calabria	-	-	-	-	-	-
E.-Romagna	112,200	-	-	-	-	-
Sicily	56,400	-	-	-	-	-
RIPP	**207,600**	**-**	**-**	**-**	**-**	**-**
Campania	519,000	485,400	18,021,167	485,400	3,713	100
Latium	1,554,600	1,024,200	24,225,405	1,012,200	2,365	99
Marche	894,000	894,000	18,524,658	894,000	2,072	100
Molise	85,800	-	2,013,529	-	-	-
Tuscany	1,965,000	1,965,000	34,111,588	1,965,000	1,736	100
Min. of Def.	-	-	103,147	-	-	-
PlaNet	**5,018,400**	**4,368,600**	**96,999,493**	**4,356,600**	**2,220**	**100**
Lombardy	930,600	-	-	-	-	-
Piedmont	-	-	-	-	-	-
Sardinia	-	-	-	-	-	-
LPS	**930,600**	**-**	**-**	**-**	**-**	**-**
Italy	**6,192,600**	**4,371,600**	**96,999,493**	**4,356,600**	**2,219**	**100**

INTERREGIONAL AND INTER-AGREEMENT EXCHANGE OF PLASMA-DERIVATIVE MEDICINAL PRODUCTS

Exchanges of plasmaderived products are an important strategy for optimizing the use of available resources in the country's healthcare system, ensuring that patients receive the therapies they need, reducing the vulnerability associated with dependence on external providers, and equipping the System with greater autonomy. The exchange mechanism also offers a significant economic benefit to the Health System; thanks to what was established by the *State Regions Agreement* of June 17, 2021, it is possible to access plasmaderivatives produced by toll fractionation system at significantly reduced costs. This reduction in costs not only lightens the budgets of individual health facilities but also allows for more efficient use of public resources, enabling funds to be invested in the Blood Transfusion System itself, as well as other critical areas of public health.

In addition, the practice of exchanges makes it possible to optimize stock management by avoiding the accumulation of surplus products, while also preventing their expiration. Finally, careful planning efforts can help feed the system of product exchanges, while also increasing the self-sufficiency of the System. In the year 2024, exchanges or purchases at the *State Regions Agreement* rate of the products made available by the various agreement mainly involved seven active ingredients: antithrombin (about 2 million IU exchanged), 3-Factor prothrombin complex concentrates (7.2 million IU), albumin (944 kg), Von Willebrand Factor and coagulation Factor VIII in combination (about 1,1 milion IU exchanged), fibrinogen (3,500 g), Immunoglobulins (516 grams) and Factor IX (550,000 IU) with an economic valuation at average unit cost recorded in the market in the year 2024 of approximately 7 million (Table 96).

Table 96. Active ingredients subject to exchange or acquisition at ASR rate of June 17, 2021 - year 2024

From	To	Active ingredient	Unit of measure	g/IU	Economic valuation at average unit cost 2023 (€)
PlaNet	NAIP	Albumin	g	656,270	1,883,495
Marche	RIPP	Albumin	g	9,620	27,609
Marche	RIPP	Albumin	g	60,000	172,200
Latium	Calabria	Albumin	g	3,950	11,337
Latium	E.-Romagna	Albumin	g	21,200	60,844
Latium	Apulia	Albumin	g	9,520	27,322
Latium	Sicily	Albumin	g	14,060	40,352
Marche	RIPP	Albumin	g	60,000	172,200
PlaNet	NAIP	Albumin	g	109,380	313,921
RIPP	Marche	Antithrombin	UI	196,000	19,600
RIPP	Marche	Antithrombin	UI	618,000	61,800
RIPP	Molise	Antithrombin	UI	1,200,000	120,000
E.-Romagna	NAIP	3F-PCCs	UI	6,483,500	1,620,875
Molise	RIPP	3F-PCCs	UI	100,000	25,000
Molise	RIPP	3F-PCCs	UI	568,500	142,125
NAIP	PlaNet	Fibrinogen	g	3,000	1,207,172
NAIP	PlaNet	Fibrinogen	g	500	201,195
RIPP	Marche	FIX	UI	200,000	100,234
RIPP	Latium	FIX	UI	200,000	100,234
RIPP	Molise	FIX	UI	50,000	25,058
RIPP	Marche	FIX	UI	100,000	50,117
E.-Romagna	NAIP	FVIII/vWF	UI	1,124,000	562,000
RIPP	Marche	IVIg	g	500	30,024
E.-Romagna	Liguria	SCIg	g	16	1,075
Total					**6,975,790**

Over the past few years, the different regional levels of plasma collection for industrial processing, combined with the expansion and diversification of products available under the new agreements, have generated situations of regional and interregional surpluses, encouraging the intensification of interregional and inter-agreement exchanges of PDMPs and production intermediates and limiting the use, by hospital companies, of the market, with significant savings for the National Health Service.

Figure 47 shows in economic terms the value of products exchanged from 2016 to 2024, with a total trade value of about 74 million euros over the period.

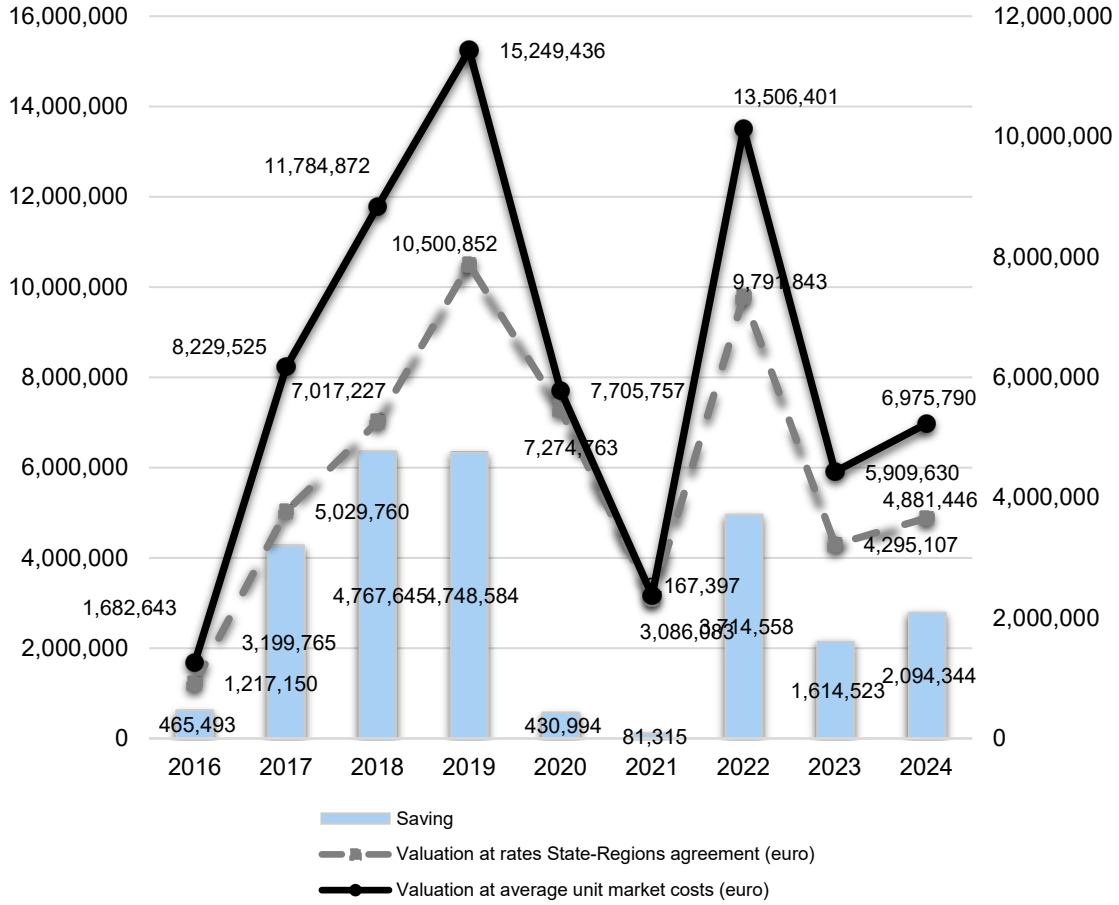

Figure 47. Economic valuation of active ingredients from toll manufacturing system exchanged in the years 2016-2024 (adapted by the CNS on data from the Traceability information flow)

PART D
Expenditure for the purchase of plasma-derived and recombinant medicinal products

EXPENDITURE FOR PLASMA-DERIVED AND RECOMBINANT MEDICINAL PRODUCTS

This chapter describes the pharmaceutical expenditure incurred by the NHS for the purchase of the following medicinal products on the market:

1. PDMPs included in the agreements between the Regions and the toll fractionation companies for the quota of the demand not covered by toll fractionation (albumin, IV IGs, SC/IM IGs, pdFVIII, pdFVIII/vWF, pdFIX, 3F-PCC, AT, Protein C, aPCCs, alpha-1 antitrypsin and fibrinogen);
2. recombinant medicinal products, including extended half-life products, used in the treatment of coagulation disorders (rFVIIa, rFVIII, rFIX and rFXIII)[i];
3. Emicizumab;
4. specific immunoglobulins and all other PDMPs, for which the distribution of the products by toll fractionation is not foreseen or in any case that has not taken place, including the production of solvent/detergent-treated plasma from national plasma.

With regard to the medicinal products distributed through public health facilities, the aggregate purchase cost was quantified based on information taken from the drug Traceability system. For the distribution through accredited pharmacies, on the other hand, the quantities of PDMPs provided by AIFA were valued based on the price in force on the 31st of December 2024, applying the discounts envisaged by law for pharmaceutical expenditure.

Tables 97 and 98 show the NHS total expenditure and the NHS total *per capita* expenditure incurred by the Regions for the purchase of the medicinal products specified in point one. In 2024, the expenditure for purchasing the aforementioned PDMPs was approximately 270 million euros (4.6 euro *per capita*). Table 99 shows the total and total *per capita* expenditure relative to supply of recombinant medicinal products (rFVIIa, rFVIII, rFVIII/vWF, rFIX and rFXIII), including extended-half life ones.

For these drugs, the total expenditure was 402 million euros (6.8 euros *per capita*). The Regions with the highest *per capita* expenditure were Abruzzo, with 9.6 euros *per capita*, Latium, Emilia-Romagna and Apulia, with 9.0 euros *per capita* for the first Region and 8.6 euros *per capita* for the other two Regions. The expenditure for recombinant factors increased compared to 2023 (+2.0%). Table 100 shows the expenditure incurred in 2024 for the purchase of Emicizumab which has experienced an increase of +14%, from 1.90 to 2.17 euros *per capita*, reflecting how much the use of this drug is progressively increasing.

In 2024, as regards all the other PDMPs (Tables 101-104), the total expenditure was approximately 98.3 million euros, equal to around 1.67 euros *per capita* of which approximately 36 million for the purchase of specific immunoglobulins, a slightly higher cost compared to year 2023 (+1%) (Table 101), with a *per capita* expenditure of 0.61, slightly higher than the previous year (Table 102).

The other PDMPs (Tables 103 and 104), recorded a considerable increase in expenditure compared to the previous year (+11%), in particular as regards local haemostatics (+10%), C1-inhibitor (+21%), FX (+209%), FXIII (+27%), FVII (+4%). On the other hand, a decrease in expenditure was recorded for the other plasma protein fractions (-20%), and FXI (-8%).

Table 97. Estimate of total expenditure and total *per capita* expenditure incurred by the National Health Service for the purchase on the market of main plasma-derived medicinal products included in toll fractionation contracts in 2024

Region	Albumin		Human Immunoglobulin intravenous use*		Human Immunoglobulin subcutaneous use		Total	
	€	€ *per capita*	€	€ *per capita*	€	€ *per capita*	€	€ *per capita*
Abruzzo	340,109	0.27	374,547	0.30	2,190,045	1.73	2,904,701	2.29
Aosta Valley	944	0.01	82,519	0.67	27,496	0.22	110,958	0.90
AP Bolzano	32,495	0.06	786,651	1.46	89,018	0.17	908,163	1.69
AP Trento	24,336	0.04	703,217	1.29	446,732	0.82	1,174,285	2.15
Basilicata	311,255	0.58	257,407	0.48	890,720	1.67	1,459,382	2.74
Friuli V. G.	5,238	0.00	511,284	0.43	584,513	0.49	1,101,035	0.92
Liguria	366,452	0.24	2,550,391	1.69	1,490,985	0.99	4,407,829	2.92
Umbria	51,303	0.06	151,577	0.18	3,250,449	3.81	3,453,329	4.05
Veneto	144,019	0.03	4,957,730	1.02	9,512,388	1.96	14,614,137	3.01
NAIP	**1,276,152**	**0.11**	**10,375,323**	**0.91**	**18,482,344**	**1.62**	**30,133,819**	**2.64**
Calabria	1,725,127	0.44	6,797,026	1.75	9,059,058	2.33	17,581,211	4.52
E.-Romagna	1,036,313	0.56	846,748	0.46	3,250,454	1.77	5,133,515	2.79
Puglia	800,194	0.18	4,800,878	1.08	9,696,341	2.18	15,297,413	3.44
Sicilia	1,006,239	0.21	1,614,398	0.34	6,895,260	1.44	9,515,897	1.98
RIPP	**4,567,873**	**0.30**	**14,059,051**	**0.94**	**28,901,112**	**1.93**	**47,528,036**	**3.17**
Campania	8,239,643	1.47	14,385,118	2.57	10,273,041	1.84	32,897,802	5.88
Lazio	2,967,223	0.52	6,101,784	1.07	13,885,836	2.43	22,954,843	4.02
Marche	108,737	0.07	2,002,296	1.35	1,741,531	1.17	3,852,564	2.60
Molise	105,620	0.37	29,380	0.10	206,707	0.71	341,706	1.18
Toscana	15,550	0.00	4,301,143	1.18	6,868,719	1.88	11,185,412	3.06
M. Difesa	-	-	-	-	-	-	-	NA
PlaNet	**11,436,772**	**0.68**	**26,819,720**	**1.60**	**32,975,834**	**1.97**	**71,232,326**	**4.25**
Lombardy	2,532,104	0.25	17,825,482	1.78	9,485,656	0.95	29,843,241	2.98
Piedmont	227,671	0.05	4,857,431	1.14	6,987,476	1.64	12,072,579	2.84
Sardinia	1,348,278	0.86	3,930,868	2.50	477,675	0.30	5,756,821	3.67
LPS	**4,108,053**	**0.26**	**26,613,781**	**1.68**	**16,950,807**	**1.07**	**47,672,641**	**3.01**
Italy	**21,388,850**	**0.36**	**77,867,876**	**1.32**	**97,310,097**	**1.65**	**196,566,822**	**3.33**

* Includes high-title IG

Table 98. Estimate of total expenditure and total per capita expenditure incurred by the National Health Service for the purchase on the market of ancillary plasma-derived medicinal products included in toll fractionation contracts in 2024

Region	FVIII		FVIII/vWF*		FIX		3F-PCC		4F-PCC		AT		Fibrinogen		Protein C		aPCCs		Alpha-1 antitrypsin		Total	
	€	€ p.c.	€	€ p.c.	€	€ p.c.	€	€ p.c.	€	€ p.c.	€	€ p.c.	€	€ p.c.	€	€ p.c.	€	€ p.c.	€	€ p.c.	€	€ p.c.
Abruzzo	-	-	746,394	0.59	-	-	-	-	161,713	0.13	132,977	0.10	32,120	0.03	9,851	0.01	242,414	0.19	629,397	0.50	1,954,865	1.54
A. Valley	-	-	1,469	0.01	-	-	-	-	22,070	0.18	10,649	0.09	7,135	0.06	-	-	-	-	155,099	1.26	196,422	1.60
AP Bolzano	-	-	-	-	-	-	-	-	202,232	0.38	20,295	0.04	-	-	-	-	-	-	1,013,426	1.89	1,235,953	2.30
AP Trento	-	-	22,440	0.04	-	-	-	-	34,188	0.06	-	-	-	-	-	-	-	-	290,174	0.53	346,802	0.64
Basilicata	-	-	12,481	0.02	-	-	22,880	0.04	104,617	0.20	40,082	0.08	108,240	0.20	-	-	-	-	-	-	288,300	0.54
FVG	-	-	45,100	0.04	-	-	-	-	262,807	0.22	223,938	0.19	-	-	-	-	-	-	809,540	0.68	1,341,385	1.12
Liguria	-	-	126,274	0.08	1,188	0.001	7,013	0.00	293,084	0.19	236,056	0.16	300,284	0.20	-35,024	-	12,243	0.01	986,520	0.65	1,927,638	1.28
Umbria	10,890	0.01	291,085	0.34	42,240	0.05	-	-	97,159	0.11	9,504	0.01	-	-	13,134	0.02	-	-	578,351	0.68	1,042,362	1.22
Veneto	-	-	1,422,934	0.29	41,863	0.01	193,177	0.04	542,698	0.11	101,598	0.02	456,632	0.09	14,355	0.00	259,552	0.05	1,050,656	0.22	4,083,463	0.84
NAIP	**10,890**	**0.00**	**2,668,176**	**0.23**	**85,291**	**0.01**	**223,069**	**0.02**	**1,720,567**	**0.15**	**775,099**	**0.07**	**904,411**	**0.08**	**2,316**	**0.00**	**514,208**	**0.05**	**5,513,162**	**0.48**	**12,417,189**	**1.09**
Apulia	-	-	2,021,014	0.52	-	-	-	-	54,624	0.01	4,455	0.00	1,119,217	0.29	-	0.00	195,146	0.05	672,308	0.17	4,066,763	1.05
Calabria	-	-	1,109,306	0.60	-	-	-	-	70,699	0.04	-	-	756,028	0.41	412,819	0.22	45,300	0.02	499,041	0.27	2,893,192	1.57
ER	-	-	1,583,464	0.36	-	-	347	0.00	672,832	0.15	330	0.00	1,846,181	0.41	6,567	0.00	1,016,178	0.23	820,756	0.18	5,946,654	1.34
Sicily	-	-	1,601,609	0.33	-	-	10,486	0.00	58,197	0.01	51,581	0.01	1,530,235	0.32	69,069	0.01	115,275	0.02	1,469,688	0.31	4,906,140	1.02
RIPP	**-**	**-**	**6,315,393**	**0.42**	**-**	**-**	**10,832**	**0.00**	**856,352**	**0.06**	**56,366**	**0.00**	**5,251,660**	**0.35**	**488,455**	**0.03**	**1,371,900**	**0.09**	**3,461,793**	**0.23**	**17,812,750**	**1.19**
Campania	-	-	2,092,566	0.37	-	-	189,420	0.03	448,102	0.08	917,572	0.16	2,056,473	0.37	330,539	0.06	51,421	0.01	2,639,414	0.47	8,725,507	1.56
Latium	17,357	0.00	2,903,026	0.51	1,925	0.00	9,473	0.00	180,448	0.03	777,615	0.14	1,430,621	0.25	-	-	418,711	0.07	1,799,086	0.31	7,538,261	1.32
Marche	-	-	289,105	0.19	-	-	37,422	0.03	12,601	0.01	-	-	660,785	0.45	-	-	63,378	0.04	177,513	0.12	1,240,805	0.84
Molise	-	-	103,400	0.36	-	-	-	-	-	-	-	-	13,904	0.05	-	-	-	-	19,422	0.07	136,726	0.47
Tuscany	385,660	0.11	1,673,421	0.46	-	-	779	0.00	-	-	413,302	0.11	-	-	-	-	-	-	1,064,553	0.29	3,537,715	0.97
Min. Def.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PlaNet	**403,017**	**0.02**	**7,061,519**	**0.42**	**1,925**	**0.00**	**237,094**	**0.01**	**641,151**	**0.04**	**2,108,489**	**0.13**	**4,161,783**	**0.25**	**330,539**	**0.02**	**533,510**	**0.03**	**5,699,987**	**0.34**	**21,179,014**	**1.27**
Lombardy	283,188	0.03	2,816,147	0.28	45,949	0.00	-	-	254,050	0.03	112,278	0.01	2,595,762	0.26	106,167	0.01	1,657,717	0.17	2,969,445	0.30	10,840,702	1.08
Piedmont	-	-	1,158,654	0.27	-	-	-	-	608,860	0.14	-	-	1,349,373	0.32	17,512	0.00	247,309	0.06	2,115,063	0.50	5,496,770	1.29
Sardinia	-	-	1,018,159	0.65	-	-	-	-	442,087	0.28	9,823	0.01	968,880	0.62	16,417	0.01	699,082	0.45	2,098,888	1.34	5,253,336	3.35
LPS	**283,188**	**0.02**	**4,992,960**	**0.32**	**45,949**	**0.00**	**-**	**-**	**1,304,997**	**0.08**	**122,101**	**0.01**	**4,914,015**	**0.31**	**140,096**	**0.01**	**2,604,107**	**0.16**	**7,183,395**	**0.45**	**21,590,808**	**1.36**
Italy	**697,095**	**0.01**	**21,038,048**	**0.36**	**133,164**	**0.00**	**470,995**	**0.01**	**4,523,067**	**0.08**	**3,062,055**	**0.05**	**15,231,869**	**0.26**	**961,406**	**0.02**	**5,023,725**	**0.09**	**21,858,337**	**0.37**	**72,999,761**	**1.24**

* Including Wilfactin and importation

Table 99. Estimate of the total expenditure and the total *per capita* expenditure for recombinant Factors VII, VIII, FVIII/vWF, IX and XIII in 2024

Region	rFVIIa		rFVIII		rFVIII/vWF		rFIX		rFXIII		Total	
	€	€ *pc*	€	€ *pc*	€	€ *pc*	€	€ *pc*	€	€ *pc*	€	€ *pc*
Abruzzo	308,631	0.24	7,428,160	5.85	-	-	4,122,404	3.25	294,960	0.23	12,154,154	9.6
A. Valley	12,083	0.10	336,773	2.74	-	-	-	-	-	-	348,856	2.8
AP Bolzano	-28,611	-0.05	1,826,937	3.40	-	-	366,937	0.68	-	-	2,165,263	4.0
AP Trento	19,505	0.04	2,459,871	4.51	-	-	757,391	1.39	-	-	3,236,767	5.9
Basilicata	231,767	0.43	1,782,201	3.34	-	-	292,221	0.55	217,339	0.41	2,523,528	4.7
FVG	537,653	0.45	2,319,137	1.94	-	-	1,765,930	1.48	0	0.00	4,622,720	3.9
Liguria	797,683	0.53	7,013,844	4.65	-	-	3,226,847	2.14	574,395	0.38	11,612,769	7.7
Umbria	157,689	0.18	3,218,612	3.77	-	-	1,302,684	1.53	-	-	4,678,985	5.5
Veneto	921,109	0.19	17,402,268	3.59	-	-	7,248,900	1.49	124,194	0.03	25,696,470	5.3
NAIP	**2,957,508**	**0.26**	**43,787,803**	**3.84**	**-**	**-**	**19,083,313**	**1.67**	**1,210,888**	**0.11**	**67,039,511**	**5.9**
Apulia	2,329,576	0.60	22,472,504	5.78	-	-	8,684,210	2.23	-	-	33,486,290	8.6
Calabria	721,904	0.39	9,950,877	5.41	-	-	2,277,656	1.24	1,009,073	0.55	13,959,509	7.6
E.-Romagna	2,311,705	0.52	27,062,722	6.08	-	-	8,805,611	1.98	93,145	0.02	38,273,183	8.6
Sicily	954,116	0.20	26,002,628	5.42	-	-	6,232,730	1.30	-	-	33,189,474	6.9
RIPP	**6,317,302**	**0.42**	**85,488,730**	**5.71**	**-**	**-**	**26,000,207**	**1.74**	**1,102,218**	**0.07**	**118,908,456**	**7.9**
Campania	1,400,811	0.25	33,529,896	5.99	-	-	11,355,152	2.03	232,863	0.04	46,518,722	8.3
Latium	1,722,821	0.30	42,495,308	7.44	-	-	7,257,133	1.27	-	-	51,475,261	9.0
Marche	291,574	0.20	5,301,972	3.58	-	-	2,336,770	1.58	-	-	7,930,316	5.3
Molise	23,109	0.08	1,451,174	5.02	-	-	0	0.00	-	-	1,474,283	5.1
Tuscany	2,894,422	0.79	9,803,569	2.68	145,002	0.04	8,207,811	2.24	-	-	21,050,803	5.8
Min. of Def.	-	-	-	-	-	-	-	-	-	-	-	-
PlaNet	**6,332,736**	**0.38**	**92,581,918**	**5.53**	**145,002**	**0.01**	**29,156,865**	**1.74**	**232,863**	**0.01**	**128,449,385**	**7.7**
Lombardy	1,532,620	0.15	38,916,022	3.89	-	-	15,663,203	1.56	636,492	0.06	56,748,337	5.7
Piedmont	2,596,257	0.61	13,826,916	3.25	-	-	6,620,228	1.56	388,105	0.09	23,431,506	5.5
Sardinia	754,994	0.48	6,850,842	4.36	-	-	13,652	0.01	-	-	7,619,487	4.9
LPS	**4,883,870**	**0.31**	**59,593,780**	**3.76**	**-**	**-**	**22,297,083**	**1.41**	**1,024,597**	**0.06**	**87,799,331**	**5.5**
Italy	**20,491,416**	**0.35**	**281,452,232**	**4.77**	**145,002**	**0.00**	**96,537,468**	**1.64**	**3,570,566**	**0.06**	**402,196,684**	**6.8**

Table 100. Estimate of the total expenditure and the total *per capita* expenditure for Emicizumab in 2024

Region	€	€ *pc*
Abruzzo	3,020,491	2.38
Aosta Valley	476,184	3.88
AP Bolzano	1,354,151	2.52
AP Trento	71,006	0.13
Basilicata	497,380	0.93
Friuli V. Giulia.	1,964,047	1.64
Liguria	2,044,986	1.36
Umbria	1,909,949	2.24
Veneto	10,838,703	2.23
NAIP	**22,176,897**	**1.94**
Apulia	4,250,283	1.09
Calabria	5,283,664	2.87
E.-Romagna	6,218,900	1.40
Sicily	8,474,276	1.77
RIPP	**24,227,122**	**1.62**
Campania	14,575,865	2.61
Latium	8,765,898	1.53
Marche	3,429,983	2.31
Molise	841,148	2.91
Tuscany	12,803,133	3.50
Min. of Def.	-	-
PlaNet	**40,416,027**	**2.41**
Lombardy	26,299,217	2.63
Piedmont	14,376,919	3.38
Sardinia	439,321	0.28
LPS	**41,115,457**	**2.60**
Italy	**127,935,503**	**2.17**

Table 101. Estimate of total expenditure incurred by the National Health Service for the purchase on the market of specific immunoglobulins in 2024

Region	Hepatitis B IGs	Hepatitis B IGs for IV use	Tetanus IGs	Anti-D IGs	CMV IGs	Varicella IGs	Rabies IGs	Total
Abruzzo	251,925	-	265,288	66,975	22,445	-	-	606,634
Aosta Valley	61,615	-	14,595	5,625	-	-	1,078	82,913
AP Bolzano	39,262	-	22,225	50,784	6,384	1,773	12,074	132,501
AP Trento	72,148	-	21,650	32,920	1,236	-	-	127,954
Basilicata	158,380	-	82,993	20,094	-	-	-	261,467
Friuli V. Giulia	171,136	-	1,792	259	131,240	2,508	27,166	334,100
Liguria	209,952	12,763	198,652	65,884	18,121	-	-	505,372
Umbria	112,690	810	119,943	37,672	40,105	-	2,372	313,592
Veneto	1,051,784	148,582	173,559	199,810	628,538	3,641	40,317	2,246,232
NAIP	**2,128,892**	**162,154**	**900,697**	**480,023**	**848,069**	**7,922**	**83,006**	**4,610,764**
Apulia	2,455,257	74,311	518,925	124,854	103,975	-	1,725	3,279,047
Calabria	639,873	22,896	467,978	81,236	69,759	-	-	1,281,743
E.-Romagna	875,305	196,628	413,295	203,769	285,628	-	27,381	2,002,006
Sicily	1,508,859	-	1,061,559	178,177	116,139	-	1,509	2,866,243
RIPP	**5,479,294**	**293,835**	**2,461,757**	**588,037**	**575,501**	**-**	**30,615**	**9,429,038**
Campania	4,691,543	170,737	2,056,058	143,458	289,952	-	-	7,351,749
Latium	939,681	83,257	688,292	150,551	74,914	190	3,018	1,939,904
Marche	298,581	30,318	254,388	77,118	37,481	8,509	6,037	712,432
Molise	70,846	0	57,829	10,663	-	-	-	139,337
Tuscany	436,178	66,805	575,751	171,433	286,284	571	31,909	1,568,930
Min. of Def.	-	-	-	-	-	-	-	-
PlaNet	**6,436,829**	**351,117**	**3,632,318**	**553,223**	**688,631**	**9,270**	**40,964**	**11,712,353**
Lombardy	3,826,583	178,663	676,597	514,497	137,627	5,154	81,712	5,420,834
Piedmont	1,996,220	25,707	264,776	207,959	482,373	6,832	23,932	3,007,800
Sardinia	1,489,545	104,135	240,033	25,281	16,107	190	-	1,875,291
LPS	**7,312,348**	**308,505**	**1,181,406**	**747,738**	**636,108**	**12,176**	**105,644**	**10,303,925**
Italy	**21,357,364**	**1,115,611**	**8,176,178**	**2,369,021**	**2,748,309**	**29,368**	**260,229**	**36,056,080**

Table 102. Estimate of standardised expenditure (euro *per capita* and euro per 1,000 population) incurred by the National Health Service for the purchase on the market of specific immunoglobulins in 2024

Region	Hepatitis B IGs	Hepatitis B IGs for IV use	Tetanus IGs	Anti-D IGs	CMV IGs	Varicella IGs*	Rabies IGs*	Total
Abruzzo	0.20	-	0.21	0.05	0.02	-	-	0.48
Aosta Valley	0.50	-	0.12	0.05	-	-	8.77	0.67
AP Bolzano	0.07	-	0.04	0.09	0.01	3.30	22.46	0.25
AP Trento	0.13	-	0.04	0.06	0.00	-	-	0.23
Basilicata	0.30	-	0.16	0.04	0.00	-	-	0.49
Friuli V. Giulia	0.14	-	0.00	0.00	0.11	2.10	22.74	0.28
Liguria	0.14	0.01	0.13	0.04	0.012	-	-	0.33
Umbria	0.13	0.00	0.14	0.04	0.05	-	2.78	0.37
Veneto	0.22	0.03	0.04	0.04	0.13	0.75	8.31	0.46
NAIP	**0.19**	**0.01**	**0.08**	**0.04**	**0.07**	**0.69**	**7.27**	**0.40**
Apulia	0.63	0.02	0.13	0.03	0.03	-	0.44	0.84
Calabria	0.35	0.01	0.25	0.04	0.04	-	-	0.70
E.-Romagna	0.20	0.04	0.09	0.05	0.06	-	6.15	0.45
Sicily	0.31	0.00	0.22	0.04	0.02	-	0.31	0.60
RIPP	**0.37**	**0.02**	**0.16**	**0.04**	**0.04**	**-**	**2.04**	**0.63**
Campania	0.84	0.03	0.37	0.03	0.05	-	-	1.31
Latium	0.16	0.01	0.12	0.03	0.01	0.03	0.53	0.34
Marche	0.20	0.02	0.17	0.05	0.03	5.74	4.07	0.48
Molise	0.24	-	0.20	0.04	-	-	-	0.48
Tuscany	0.12	0.02	0.16	0.05	0.08	0.16	8.72	0.43
Min. of Def.	-	-	-	-	-	-	-	-
PlaNet	**0.38**	**0.02**	**0.22**	**0.03**	**0.04**	**0.55**	**2.45**	**0.70**
Lombardy	0.38	0.02	0.07	0.05	0.01	0.51	8.16	0.54
Piedmont	0.47	0.01	0.06	0.05	0.11	1.61	5.63	0.71
Sardinia	0.95	0.07	0.15	0.02	0.01	0.12	-	1.19
LPS	**0.46**	**0.02**	**0.07**	**0.05**	**0.04**	**0.77**	**6.67**	**0.65**
Italy	**0.36**	**0.02**	**0.14**	**0.04**	**0.05**	**0.00**	**0.00**	**0.61**

*values per 1,000 population

Table 103. Estimate of total expenditure incurred by the National Health Service for the purchase on the market of all other PDMPs in 2024

Region	FVII	Local Haemostatic agents-combinations	Other plasma Proteins fractions	Human C1 esterase inhibitor	Factor X	Factor XI	Factor XIII	Total
Abruzzo	687,477	1,262,630	-	364,315	-	-	-	2,314,422
Aosta Valley	-	94,778	-	21,418	-	-	-	116,196
AP Bolzano	-	397,654	-	96,780	-	-	32,352	526,786
AP Trento	-	179,956	3,905	27,598	-	-	110,848	322,306
Basilicata	20,536	482,026	158,068	1,691	-	-	-	662,320
Friuli V. Giulia	-	472,864	4,699	24,172	5,390	91,080	-	598,205
Liguria	35,471	528,072	52,424	225,576	-	-	72,466	914,008
Umbria	-	641,600	50,760	212,692	-	-	-	905,052
Veneto	-	2,085,399	-	863,589	-	-	185,376	3,134,363
NAIP	**743,483**	**6,144,978**	**269,855**	**1,837,831**	**5,390**	**91,080**	**401,041**	**9,493,659**
Apulia	298,233	1,754,768	1,223,549	921,871	-	-	4,689	4,203,111
Calabria	12,601	1,211,114	437,861	496,003	438,515	-	-	2,596,095
E.-Romagna	357,040	2,205,751	95,167	745,668	-	-	276,239	3,679,865
Sicily	258,096	2,377,058	957,724	2,733,369	-	-	-	6,326,247
RIPP	**925,971**	**7,548,692**	**2,714,300**	**4,896,911**	**438,515**	**-**	**280,928**	**16,805,317**
Campania	506,390	6,386,046	40,752	2,158,362	-	-	-	9,091,550
Latium	1,003,647	2,143,615	193,936	4,081,924	-	-	65,641	7,488,762
Marche	12,135	740,123	-	720,960	-	-	78,535	1,551,753
Molise	233,360	197,601	-	7,891	-	-	-	438,852
Tuscany	62,994	2,080,526	232,006	611,182	-	-	50,286	3,036,994
Min. of Def.	-	-	-	-	-	-	-	-
PlaNet	**1,818,525**	**11,547,911**	**466,694**	**7,580,319**	**-**	**-**	**194,462**	**21,607,910**
Lombardy	1,007,390	4,589,461	4,017	2,678,683	325,820	-	40,635	8,646,006
Piedmont	192,288	2,182,628	-	1,864,050	22,770	20,240	37,900	4,319,876
Sardinia	7,934	824,616	4,965	561,200	-	-	-	1,398,716
LPS	**1,207,612**	**7,596,705**	**8,983**	**5,103,933**	**348,590**	**20,240**	**78,535**	**14,364,597**
Italy	**4,695,591**	**32,838,286**	**3,459,832**	**19,418,994**	**792,495**	**111,320**	**954,966**	**62,271,484**

Table 104. Estimate of standardised expenditure (*per capita* and euro per 1,000 population) incurred by the National Health Service for the purchase on the market of all other PDMPs in 2024

Region	FVII	Local Haemostatic agents-combinations	Other plasma Proteins fractions	Human C1 esterase inhibitor	Factor X *	Factor XI*	Factor XIII *	Total
Abruzzo	0.54	0.99	-	0.29	-	-	-	1.82
Aosta Valley	-	0.77	-	0.17	-	-	-	0.95
AP Bolzano	-	0.74	-	0.18	-	-	60.19	0.98
AP Trento	-	0.33	0.01	0.05	-	-	203.33	0.59
Basilicata	0.04	0.90	0.30	0.00	-	-	-	1.24
Friuli V. Giulia	-	0.40	0.00	0.02	4.51	76.24	-	0.50
Liguria	0.02	0.35	0.03	0.15	-	-	48.02	0.61
Umbria	-	0.75	0.06	0.25	-	-	-	1.06
Veneto	-	0.43	-	0.18	-	-	38.20	0.65
NAIP	**0.07**	**0.54**	**0.02**	**0.16**	**0.47**	**7.98**	**35.13**	**0.83**
Apulia	0.08	0.45	0.31	0.24	-	-	1.21	1.08
Calabria	0.01	0.66	0.24	0.27	238.51	-	-	1.41
E.-Romagna	0.08	0.50	0.02	0.17	-	-	62.05	0.83
Sicily	0.05	0.50	0.20	0.57	-	-	-	1.32
RIPP	**0.06**	**0.50**	**0.18**	**0.33**	**29.28**	**-**	**18.76**	**1.12**
Campania	0.09	1.14	0.01	0.39	-	-	-	1.63
Latium	0.18	0.38	0.03	0.71	-	-	11.49	1.31
Marche	0.01	0.50	-	0.49	-	-	52.97	1.05
Molise	0.81	0.68	-	0.03	-	-	-	1.52
Tuscany	0.02	0.57	0.06	0.17	-	-	13.74	0.83
Min. of Def.	-	-	-	-	-	-	-	-
PlaNet	**0.11**	**0.69**	**0.03**	**0.45**	**-**	**-**	**11.62**	**1.29**
Lombardy	0.10	0.46	0.000	0.27	32.5	-	4.06	0.86
Piedmont	0.05	0.51	-	0.44	5.36	4.76	8.91	1.02
Sardinia	0.01	0.53	0.003	0.36	-	-	0.00	0.89
LPS	**0.08**	**0.48**	**0.001**	**0.32**	**22.0**	**1.28**	**4.96**	**0.91**
Italy	**0.08**	**0.56**	**0.06**	**0.33**	**13.4**	**1.89**	**16.19**	**1.06**

* values per 1,000 population

National and Regional mean price per gram or International Unit

Tables 105-107 show the mean price per unit paid by the Regions to purchase albumin, IVIGs and pdFVIII/vWF in combination (ATC B02BD06). The price varied depending on the distribution channel (NHS facilities and pharmacies open to the public).

For each PDMP, the percentage of product by distribution channel and the costs recorded in both distribution channels were reported. All the aforementioned prices include VAT.

However, it should be noted that in some Regions the mean price per unit exceeded the maximum sale price to the NHS public structures as defined in the annex to the 5th of August 2006 AIFA (54).

Regarding albumin (Table 105), the national mean price per gram was 3.15 euros (2.87 in the year 2023). The variability observed among Regions (range: 2.41-3.97 euro per gram) was affected by the different contribution of each distribution channel to the definition of costs, as well as volumes.

In particular, the mean price paid by NHS facilities was subject to variability that could be linked to the different contracts awarded following a tender procedure, while the cost recorded through the public pharmacies was substantially similar in all Regions.

In actual fact, the prices of the packages and the discounts applied are the same nationwide and the slight differences are probably due to the different composition of the "basket" compared to the dosages and relative prices.

Liguria, the AP of Bolzano, Emilia-Romagna, Marche and Piedmont were the Regions where more than 90% of the commercial demand was dispensed by NHS facilities, and where the use of the pharmacy channel was modest.

In other Regions, such as Friuli V. Giulia, the AP of Trento, Aosta Valley, Molise and Calabria, the commercial demand (although not significant) was mainly dispensed through the accredited pharmacies channel, showing significantly higher mean prices per gram.

The overall expenditure of pdFVIII/vWF (without Wilfactin) on the market was 15,211,317 euros (0.51 euros per IU), and almost entirely accounted for the distribution through NHS facilities (96%) (Table 106).

The market demand for IVIGs (excluding the specific demand for products containing IVIGs with high titers of IGM – see Table 7) recorded an expenditure equal to 71,366,901 million euros with an increase of +44% compared to 2023. The mean unit price per gram at national level was 68.95 euros (range: 60.71-71.50 euros) (Table 107).

Table 105. National and Regional mean price per gram for the purchase of albumin by distribution channel. Absolute and percentage values for associated utilisation and expenditure in 2024

Region	Mean price			Demand				Total expenditure			
	NHS facilities	Pharmacies	Total	NHS facilities		Pharmacies		NHS facilities		Pharmacies	
	€/g	€/g	€/g	g	%	g	%	€	%	€	%
Abruzzo	2.49	3.94	3.30	46,025	45%	57,178	55%	114,696	34%	225,413	66%
Aosta Valley	-	3.93	3.93	-	0%	240,00	100%	-	0%	943,60	100%
AP Bolzano	2.59	3.97	2.61	12,265	99%	180	1%	31,780	98%	714	2%
AP Trento	-	3.89	3.89	-	0%	6,260	100%	-	0%	24,336	100%
Basilicata	2.25	3.95	3.09	50,875	51%	49,850	49%	114,591	37%	196,664	63%
Friuli V. Giulia	-	3.97	3.97	-	0%	1,320	100%	-	0%	5,238	100%
Liguria	2.52	3.94	2.64	128,088	92%	10,953	8%	323,260	88%	43,192	12%
Umbria	2.55	3.94	3.69	2,563	18%	11,353	82%	6,525	13%	44,778	87%
Veneto	2.61	3.94	3.65	8,625	22%	30,833	78%	22,542	16%	121,477	84%
NAIP	**2.47**	**3.94**	**3.06**	**248,440**	**60%**	**168,165**	**40%**	**613,395**	**48%**	**662,756**	**52%**
Apulia	2.41	3.93	3.42	170,660	34%	334,000	66%	411,413	24%	1,313,714	76%
Calabria	2.62	3.91	3.81	20,950	8%	250,730	92%	54,791	5%	981,522	95%
E.-Romagna	2.51	3.93	2.53	310,875	98%	4,830	2%	781,232	98%	18,962	2%
Sicily	2.62	3.93	3.71	44,255	16%	226,723	84%	116,039	12%	890,200	88%
RIPP	**2.49**	**3.93**	**3.35**	**546,740**	**40%**	**816,283**	**60%**	**1,363,475**	**30%**	**3,204,398**	**70%**
Campania	2.49	3.91	3.14	1,420,610	54%	1,201,550	46%	3,538,254	43%	4,701,389	57%
Latium	2.58	3.94	3.21	494,250	53%	430,555	47%	1,272,751	43%	1,694,472	57%
Marche	2.73	-	2.73	39,800	100%	-	0%	108,737	100%	-	0%
Molise	-	3.95	3.95	-	0%	26,733	100%	-	0%	105,620	100%
Tuscany	1.94	3.90	3.03	2,290	45%	2,848	55%	4,451	29%	11,098	71%
Min. of Def.	-	-	-	-	-	-	-	-	-	-	-
PlaNet	**2.52**	**3.92**	**3.16**	**1,956,950**	**54%**	**1,661,685**	**46%**	**4,924,194**	**43%**	**6,512,579**	**57%**
Lombardy	2.47	3.93	3.13	446,533	55%	363,038	45%	1,103,928	44%	1,428,176	56%
Piedmont	2.33	3.93	2.41	89,875	95%	4,705	5%	209,159	92%	18,513	8%
Sardinia	2.30	3.94	2.71	374,720	75%	123,105	25%	862,713	64%	485,565	36%
LPS	**2.39**	**3.94**	**2.93**	**911,128**	**65%**	**490,848**	**35%**	**2,175,800**	**53%**	**1,932,253**	**47%**
Italy	**2.48**	**3.92**	**3.15**	**3,663,258**	**54%**	**3,136,980**	**46%**	**9,076,863**	**42%**	**12,311,987**	**58%**

Table 106. National and Regional mean price per IU for the purchase of Factor VIII/ von Willebrand Factor in combination by distribution channel. Absolute and percentage values for associated utilisation and expenditure in 2024

Region	Mean price *			Demand*				Total expenditure*			
	NHS facilities	Pharmacies	Total	NHS facilities		Pharmacies		NHS facilities		Pharmacies	
	€/IU	€/IU	€/IU	IU	%	IU	%	€	%	€	%
Abruzzo	0.51	-	0.51	857,000	100%	-	0%	438,156	100%	-	0%
Aosta Valley	0.24	-	0.24	2,000	100%	-	0%	484	100%	-	0%
AP Bolzano	-	-	-	-	-	-	-	-	-	-	-
AP Trento	0.56	-	0.56	40,000	100%	-	0%	22,440	100%	-	0%
Basilicata	0.50	-	0.50	20,000	100%	-	0%	9,900	100%	-	0%
Friuli V. Giulia	0.55	-	0.55	82,000	100%	-	0%	45,100	100%	-	0%
Liguria	0.55	-	0.55	186,000	100%	-	0%	102,300	100%	-	0%
Umbria	0.54	-	0.54	477,000	100%	-	0%	259,816	100%	-	0%
Veneto	0.54	-	0.54	1,041,500	100%	-	0%	564,450	100%	-	0%
NAIP	**0.53**	**-**	**0.53**	**2,705,500**	**100%**	**-**	**0%**	**1,442,646**	**100%**	**-**	**0%**
Apulia	0.52	-	0.52	3,558,000	100%	-	0%	1,850,591	100%	-	0%
Calabria	0.55	-	0.55	820,500	100%	-	0%	451,045	100%	-	0%
E.-Romagna	0.55	-	0.55	2,731,500	100%	-	0%	1,501,951	100%	-	0%
Sicily	0.53	0.54	0.53	1,436,000	99%	18,000	1%	764,049	99%	9,633	1%
RIPP	**0.53**	**0.54**	**0.53**	**8,546,000**	**99.8%**	**18,000**	**0.2%**	**4,567,635**	**99.8%**	**9,633**	**0.2%**
Campania	0.50	-	0.50	3,488,000	100%	-	0%	1,734,212	100%	-	0%
Latium	0.52	0.57	0.52	4,268,000	99%	38,500	1%	2,214,953	99%	22,051	1%
Marche	0.54	-	0.54	489,500	100%	-	0%	265,131	100%	-	0%
Molise	0.55	-	0.55	188,000	100%	-	0%	103,400	100%	-	0%
Tuscany	0.45	-	0.45	2,721,000	100%	-	0%	1,211,917	100%	-	0%
Min. of Def.	-	-	-	-	-	-	-	-	-	-	-
PlaNet	**0.50**	**0.57**	**0.50**	**11,154,500**	**99.7%**	**38,500**	**0.3%**	**5,529,612**	**99.6%**	**22,051**	**0.4%**
Lombardy	0.55	0.60	0.56	2,951,000	77%	880,000	23%	1,621,070	75%	529,688	25%
Piedmont	0.37	-	0.37	1,511,000	100%	-	0%	564,367	100%	-	0%
Sardinia	0.43	-	0.43	2,152,000	100%	-	0%	924,615	100%	-	0%
LPS	**0.47**	**0.60**	**0.49**	**6,614,000**	**88%**	**880,000**	**12%**	**3,110,052**	**85%**	**529,688**	**15%**
Italy	**0.50**	**0.60**	**0.51**	**29,020,000**	**97%**	**936,500**	**3%**	**14,649,945**	**96%**	**561,371**	**4%**

*The value does not include Wilfactin (vWF) and imported products

Table 107. National and Regional mean price per gram for the purchase of intravenous immunoglobulins by distribution channel (year 2024).

Region	Mean price per gram (€) NHS facilities* (€/g)	Total demand NHS facilities* (g)	Total expenditure NHS facilities* (€)
Abruzzo	71.06	3,745	266,127
Aosta Valley	70.82	991	70,193
AP Bolzano	70.14	11,190	784,823
AP Trento	70.23	9,950	698,817
Basilicata	68.08	1,267	86,246
Friuli V. Giulia	71.50	3,950	282,425
Liguria	69.88	31,975	2,234,446
Umbria	71.01	1,935	137,404
Veneto	71.00	63,780	4,528,208
NAIP	**70.57**	**128,783**	**9,088,689**
Apulia	69.27	85,996	5,957,306
Calabria	71.32	11,380	811,586
E.-Romagna	65.32	68,695	4,487,298
Sicily	60.71	6,050	367,290
RIPP	**67.53**	**172,122**	**11,623,481**
Campania	68.86	188,220	12,960,398
Latium	66.49	90,700	6,030,316
Marche	64.74	26,115	1,690,560
Molise	69.95	420	29,380
Tuscany	68.40	59,688	4,082,388
Min. of Def.	-	-	-
PlaNet	**67.90**	**365,143**	**24,793,042**
Lombardy	70.46	246,879	17,394,367
Piedmont	68.22	66,500	4,536,456
Sardinia	70.70	55,600	3,930,868
LPS	**70.09**	**368,979**	**25,861,690**
Italy	**68.95**	**1,035,027**	**71,366,901**

* The value does not include high-title IG

FINAL CONSIDERATIONS

The national demand for albumin, although slightly lower than that recorded in 2023, was still quite high at about 564 grams per 1,000 population.

An increased demand was observed in the AP of Trento (+9%), Latium (+23%), Sardinia (+8%) and Friuli V. Giulia (+15%). The Regions with the highest standardised demand per 1,000 population were Sardinia, Emilia-Romagna and Campania, with standardised volumes of 1,014, 758 and 728 grams, respectively.

About 9% of the national demand was distributed through public pharmacies, reaching a quantity of approximately 3,137 kilograms, The pharmacy channel was particularly used in Campania, Calabria and Molise where it accounts respectively for 29%, 27% and 25% of the regional demands.

In the two-year period 2023-2024 the total demand of IG registered a +4.3%; in particular, there was +13% in demand for SC/IM-IG and +2% in demand for IVIG.

There were noticeable differences from one Region to another. The three Regions with the highest standardised demand per 1,000 population were Aosta Valley, Marche and Tuscany, with about 174 grams/1000 pop. for the first, 159 grams/1000 pop. for the second and 155 grams/1000 pop.for the third.

The demand for AT recorded a sharp decrease (-25%) in 2024, as well as the demand for 3F-PCCs (-7.3%); on the contrary, the demand for 4F-PCCs is confirmed to be continuously rising (+6.4%).

As regards the haemophilia A treatment the demand for FVIIIpd (alone and in combination with vWF) decreased slightly (-5%), in contrast to demand for FVIIIr, which increased slightly (+1%), mainly due to the increased use of FVIII medicines with a prolonged half-life (+13%).

The consumption of Emicizumab also increased significantly (+17%); the demand for activated prothrombin complex concentrates, on the other hand, fell sharply (-46%).

As regards the treatment of hemophilia B, the clinical use of recombinant FIX (+3% compared to 2023), especially that with a prolonged half-life (+12%), is gradually replacing the demand for FIXpd, whose demand in 2024 remained substantially in line with that of the previous year (+1.1%).

The demand for Fibrinogen continues to rise, recording an increase of +10% compared to the previous year, reaching 73,693 grams (1.2 g/1,000 pop.).

The total volume of plasma sent by Regions for fractionation increased by 3% compared to the previous year. There were still great differences in the volumes from one Region to another, ranging from 6.0 kilograms per 1,000 population sent by Campania to 24.8 sent by Friuli V. Giulia, with an average volume of 15.4 kilograms per 1,000 population.

The level of albumin self-sufficiency is 76% of the NHS demand (73% in 2023). As regards IGs, on the other hand, self-sufficiency in human immunoglobulin for intravenous and subcutaneous/intramuscolar use (excluding high titre IG) achieved at national level was 59% of the total demand, while self-sufficiency in IVIG reached 73% (excluding high titre IG); self-sufficiency for SC / IM IG was 14%.

AT self-sufficiency was found to be equal to 60% of NHS demand and above 90% in the two agreements that currently return it by toll fractionation system.

National self-sufficiency was substantially reached in pdFVIII, pdFIX and 3F-PCCs.

In general, through improved cross-Agreement planning, the System could benefit more from interregional compensation, in order to enhance the opportunities offered by the toll fractionation system.

The expenditure sustained by the Regions for PDMPs produced by toll fractionation, excluding the expenditure associated with the production of plasma (collection, processing, biological qualification, storage and transport), was estimated to be about 104.4 million euros, in line with the costs estimated by the contracts in force in 2024, while approximately 2.5 million euros had to be taken into account for the treatment of plasma virus-inactivated by solvent / detergent, for a total of approximately 106.9 million euros.

The estimated expenditure incurred by the NHS in 2024 for the market supply of the PDMPs included in the toll fractionation agreements between Regions and companies, for the quantity not produced under the agreements, was approximately 269.6 million euros. An additional 98.3 million euros were used for the purchase of all the other PDMPs. The cost of purchasing Emicizumab was 127.9 million euros. The expenditure associated to recombinant products was about 402.2 million euros. The total expenditure for medicinal products described in this Report was around 3.4% of the total NHS pharmaceutical expenditure recorded in 2024 (55).

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