CSL

The Economics of Plasma-Derived Medicinal Products

1. *Plasma-Derived Medicinal Products are critical to European health*

Plasma-Derived Medicinal Products (PDMPs), extracted from human plasma[1], are lifesaving treatments for rare and complex diseases. Many people rely on them as the only effective treatment option for their condition[2], and there are often few or no alternatives.

A category of PDMPs is immunoglobulins (IGs), which can treat diseases such as primary and secondary immunodeficiency, as well as blood clotting factor therapies and anticoagulant proteins for people living with haemophilia or other rare haematological disorders[3]. They are also an essential product in wider healthcare settings – for example, they can be used to treat emergency-related injuries for patients suffering from trauma[4].

Their critical role in improving the health of European citizens has led to many PDMPs being listed as critical medicines by the European Medicines Agency,[5] with over 300,000 people depending on them across Europe.[6]

In recent decades, there have been major advancements to scale up global plasma collection capacity, improve safety and quality standards, and advance knowledge in new innovative technologies. This has resulted in significantly decreased morbidity, and improved quality of life and life expectancy in rare disease patients[7]. Since the introduction of IGs, ten-year survival rates for people living with common variable immunodeficiency (CVID) have increased from 37% in 1971 to more than 90% by 2008.[8,9] IGs, when compared to non-IG treatments, also have the potential to reduce the number and severity of infections in people living with secondary immunodeficiency (SID).[10,11] This could, therefore, result in reduced antibiotic use among people treated with IGs,[12,13,14]

2. *These drugs are unique for several reasons*

PDMPs are made in very different ways from other medicines. First, there is a systemic imbalance between their origin as human plasma (scarce by definition) and the constant growth in demand, particularly for IGs. Second, paradoxically, and unlike chemical drugs, the costs of manufacturing of certain PDMPs increase with more volumes being processed. These issues present unique challenges in manufacturing and supplying these products to patients.

i. *The imbalance between raw materials and demand*

Challenges exist from the composition of plasma itself. It is made up mostly of water and contains different proteins (e.g. IG, Albumin, Coagulation factors), so it needs to be broken down into its various parts. This process is known as “fractionation” and has very strict quality constraints[15].

One of the most representative examples is that of IGs, which make up less than 12% of plasma proteins[16] but 54% of global protein demand.[17] There is no synthetic version of plasma, and so meeting this demand requires many people to donate their plasma. Thanks to millions of plasma donations per year, patients can have access to these essential medicines.

To produce these therapies, human plasma is collected from individual healthy donors. It can take hundreds to thousands of individual donations to treat one patient for one year. For example, it takes 1000 donations per year to treat a person with hereditary angioedema.[18]

The demand for PDMPs is expected to increase due to improved diagnosis, new indications, and ageing populations[19]. Across the European Union, patient need for PDMPs, such as IGs, is increasing, with the gap widening between demand and supply. As such, over one-third of plasma needed to meet demand for PDMPs in Europe is currently collected and imported from the US, making European PDMP supply highly dependent on non-EU plasma[20]. With worldwide demand set to grow further, Europe is struggling to meet growing patient demand.

3. The 'last litre' problem or absence of economies of scale

This mismatch between demand for and prevalence of each kind of protein presents another issue for PDMP development. Not all the proteins in every donation will be needed or used, but plasma manufacturers must fractionate them all to access in-demand proteins.

Unlike other industries, plasma manufacturers do not benefit from economies of scale (costs increase, not decrease, with larger production volumes). Due to the least-prevalent proteins (IGs) being in the highest demand, the opposite is true. At a certain point in the process of breaking down plasma, the demand for other proteins has been met, and the only ones needed are IGs. However, to get hold of IGs, the entire plasma litre still needs to be broken down into its components. At the start of the process, all the proteins in a litre can be sold to meet demand. By the end of the process - *the last litre* – only IGs can be sold, as the demand is already met for other components.

Therefore, increasing the volume of PDMPs produced increases the relative costs per litre. Even as the same effort is needed to manufacture, the return on that investment drops. With the cost per litre increasing as production volume grows, there is an ever-greater financial challenge in a high-demand environment.

ii. Complexity, length and increased costs of manufacturing

PDMPs also take far longer to make than most other medicines, accompanied by costs stemming from the specific manufacturing requirements involved. Developing and producing PDMPs requires distinct investment and industrial capacities from small-molecule medicines (e.g. chemically synthesised drugs or biologicals).

There are no shortcuts to reducing the time needed to produce PDMPs. The lead time for delivering PDMPs is around 7-12 months for the entire process of collecting plasma, conducting extensive mandatory safety testing, breaking it down into proteins, and developing the final treatment, compared to 1-3 months for small-molecule medicines.[21]

Plasma also differs from most active substances in that it can only be obtained through donations. Collection centres and the high costs associated with them, , are an inherent part of the manufacturing process[22,23,24,25]. As demand rises for PDMPs, more collection centres are needed to handle the extra donations required, as well as additional investment in state-of-the-art quality and safety techniques. Continuous investment in innovation to increase manufacturing yield is key. In addition to the fixed costs of manufacturing PDMPs, the overall costs certainly exceed those of small-molecule medicines.

4. *Recognising their uniqueness to create an environment making their development sustainable and accessible*

As patient need for PDMPs increases in the EU and around the world, the gap between supply and demand grows ever wider.

Current pricing and fiscal policies typically do not reflect the specific economic aspects of PDMPs and IGs, and that results in sustained erosion of the economic viability of these products and related competitiveness of EU countries

The distinctive nature of PDMPs—derived from donated human plasma—necessitates a thoughtful, tailored, and multipronged approach. As EU institutions and Member States seek to enhance strategic autonomy and competitiveness in key biotechnology sectors, it is essential to reinforce supply chain resilience and diversification, while fostering an ecosystem that supports a robust and high-performing industrial base.

About CSL

CSL is a global biotechnology leader with a dynamic portfolio of lifesaving medicines, operating in highly specialised areas that require advanced, complex technologies, broad scientific expertise, and sustained long-term investment.

Focused on addressing unmet medical needs and helping patients lead full lives, we discover, develop, and deliver innovative biotech therapies in the immunology, haematology, cardiovascular and metabolic, respiratory, and transplant therapeutic areas.

CSL expertise lies in the biopharmaceutical and the biotechnology sector and encompasses plasma protein technology, recombinant protein technology, cell and gene therapy, and vaccines technology. CSL is proud of our critical biotech infrastructure located in Europe. CSL has four manufacturing sites in Europe and our products are commercialised in 36 European countries.

---

[1] Laursen IA, Blou L, Sullivan JS, Bang P, Balstrup F, Houen G. Development, manufacturing and characterization of a highly purified, liquid immunoglobulin g preparation from human plasma. Transfus Med Hemother 2014; 41(3): 205-12.
[2] Plasma Protein Therapeutics Association (PPTA). Rare Diseases. Available at: https://www.pptaglobal.org/material/rare-diseases Accessed: July 2025
[3] World Health Organization. WHO model list of essential medicines - 23rd list, 2023. https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2023.02
[4] Baskaran, J, Lopez, R, Cassagnol, M. Prothrombin Complex Concentrate. In: StatPearls [Internet]. StatPearls Publishing; 2023. Accessed July 2025. https://www.ncbi.nlm.nih.gov/books/NBK539716/
[5] European Medicines Agency. Union list of critical medicines. 2024. Available at: https://www.ema.europa.eu/en/human-regulatory-overview/post-authorisation/medicine-shortages-availability-issues/availability-medicines-during-crises/union-list-critical-medicines. Accessed: July 2025.
[6] Bonacker L. Open Strategic Autonomy for plasma therapies in the EU [Sponsored Content from CSL Behring]. Politico, 2024. Available at: https://www.politico.eu/sponsored-content/open-strategic-autonomy-for-plasma-therapies-in-the-eu/. Accessed: July 2025.
[7] Ibid.
[8] Chapel H, Lucas M, Lee M, et al. Common variable immunodeficiency disorders: division into distinct clinical phenotypes. Blood 2008; 112(2): 277-86.
[9] Grabowski H, Manning R. Key economic and value considerations in the U.S. Market for Plasma protein therapies. Bates White Economic Consulting (white paper) 2018.
[10] Spadaro G, Pecoraro A, De Renzo A, Della Pepa R, Genovese A. Intravenous versus subcutaneous immunoglobulin replacement in secondary hypogammaglobulinemia. Clin Immunol 2016; 166-167: 103-4.

[11] Mallick R, Divino V, Smith BD, Jolles S, DeKoven M, Vinh DC. Infections in secondary immunodeficiency patients treated with Privigen((R)) or Hizentra((R)): a retrospective US administrative claims study in patients with hematological malignancies. Leuk Lymphoma 2021; 62(14): 3463-73.
[12] Vacca A, Melaccio A, Sportelli A, Solimando AG, Dammacco F, Ria R. Subcutaneous immunoglobulins in patients with multiple myeloma and secondary hypogammaglobulinemia: a randomized trial. Clin Immunol 2018; 191: 110-5.
[13] Compagno N, Cinetto F, Semenzato G, Agostini C. Subcutaneous immunoglobulin in lymphoproliferative disorders and rituximab-related secondary hypogammaglobulinemia: a single-center experience in 61 patients. Haematologica 2014; 99(6): 1101-6.
[14] Streu E BV, Dhaliwal DH,. The efficacy and cost effectiveness of Subcutaneous Immunoglobulin (SCIG) replacement in patients with immune deficiency secondary to chronic lymphocytic leukemia. Am Soc Hematology. 2016.
[15] Kluszczynski T, Rohr S, Ernst R. Key economic and value considerations for plasma-derived medicinal products (PDMPs) in Europe Vintura (white paper) 2020.
[16] Laub R, Baurin S, Timmerman D, Branckaert T, Strengers P. Specific protein content of pools of plasma for fractionation from different sources: impact of frequency of donations. Vox Sang 2010; 99(3): 220-31
[17] Markets and Markets. Plasma Fractionation Market – Global Forecast to 2025, MarketsandMarkets, 2020
[18] CSL Plasma. Plasma Donation: Essential and Safe. Available at: https://www.cslplasma.com/plasma-safe-donation-information.pdf. Accessed: July 2025.
[19] Markets and Markets. Plasma Fractionation Market – Global Forecast to 2025, MarketsandMarkets, 2020
[20] Farrugia A. International challenges for all stakeholders of the plasma therapeutics industry - PPTA Congress Amsterdam, 19 March 2019.
[21] Kluszczynski T, Rohr S, Ernst R. Key economic and value considerations for plasma-derived medicinal products (PDMPs) in Europe Vintura (white paper) 2020.
[22] Ibid.
[23] Morgan Stanley Research. Plasma Primer. 2019.
[24] Copenhagen Economics. The impact of plasma-derived therapies in Europe. The health and economic case for ensuring sustainable supply. 2021.
[25]CSL Behring. Data on file. Plasma collection costs (2017-2023). 2025.