VINTURA

EXECUTIVE SUMMARY

KEY ECONOMIC AND VALUE CONSIDERATIONS FOR PLASMA-DERIVED MEDICINAL PRODUCTS (PDMPS) IN EUROPE

ABOUT THIS PAPER

This paper aims to analyse and demonstrate the unique nature and value of PDMPs (Plasma-derived Medicinal Products) across clinical, economic, and societal dimensions, and focuses on improving Patient Access. Patient Access is viewed from two angles: formal access based on reimbursement coverage, and therapeutic access based on the availability of an optimal treatment paradigm. It also analyses key challenges that affect the full realisation of the value of PDMPs. Finally, it offers a comprehensive view of possible solutions to the identified challenges.

PDMPs are unique biological therapies derived from human plasma and are used to treat patients with rare, often genetic conditions with a high disease burden. Despite decades of effective therapeutic use in Europe, and demonstrable clinical and societal value, these treatments still face numerous Patient Access challenges pertaining to the plasma donation landscape, regulatory and reimbursement frameworks, and treatment paradigms. There is a growing clinical need of European patients for PDMPs, and considerably more plasma must be collected in Europe. As new indications arise more patients are diagnosed with diseases requiring PDMP treatment. Even when diagnosed and if therapy is available, patients often are denied adequate PDMP treatment because of therapeutic and formal Patient Access challenges. To overcome these challenges, it is necessary to form close and trust-based partnerships between industry and all healthcare stakeholders.

NATURE AND VALUE

PDMPs constitute several classes of biologic therapies, i.e. clotting factors, immunoglobulins (IgGs, including hyperimmune globulins), alpha-1 proteinase inhibitors, albumin and C1-esterase inhibitors. PDMPs share a unique nature: they are derived from human biologic material (plasma) and have a highly complex and regulated manufacturing process. Manufacturing takes 7-12 months, and constitutes the bulk of costs to companies (57 % for PDMPs compared to 14 % for small molecules pharma).[1] PDMPs treat rare, chronic, severe, often genetic in origin, and potentially life-threatening conditions, such as primary immunodeficiencies (PID) and certain secondary immunodeficiencies (SID), bleeding disorders such as haemophilia A and haemophilia B, alpha-1 antitrypsin deficiency (AATD), hereditary angioedema (HAE), neurological diseases (e.g. chronic inflammatory demyelinating polyneuropathy (CIDP), multifocal motor neuropathy (MMN), Guillain-Barré Syndrome (GBS), and other orphan diseases associated with absence or malfunction of specific proteins. Individually, these diseases affect small patient populations, and PMDPs address a severe subset which often require lifelong treatment. Taken together, the therapeutic and societal impact of PDMP treatments across these diseases is extensive.

PDMPs are often the only and/or most effective therapies for the beforementioned conditions, preventing premature death, minimizing disabilities, and promoting patients' quality of life. Since the introduction of IgGs, survival rates of patients with common variable immune deficiency (CVID) have increased from 30 % in 1979 to an almost normal life expectancy for patients without disease-related complications.[2] In turn, clotting factors have profoundly extended the life expectancy of patients with severe haemophilia A from 19 years before 1955 to 71 years in 2001.[3] These therapies have consistently achieved significant clinical results against primary endpoints (e.g. 80 % reduction in bleeds for haemophilia patients and over 65 % reduction in infections for patients with immune deficiencies).[4,5] These results positively impact patients' socio-economic activity and psychological

* Vintura analysis

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2. Bonilla FA et al: International Consensus Document (ICON): Common Variable Immunodeficiency Disorders. J Allergy Clin Immunol Pract. 2016 Jan-Feb;4(1):38-59.
3. Mejia-Carvajal C et al: Life expectancy in hemophilia outcome. J Thromb Haemost. 2006 Mar;4(3):507-9.
4. Manco-Johnson MJ et al: Prophylaxis versus Episodic Treatment to Prevent Joint Disease in Boys with Severe Hemophilia. N Engl J Med. 2007 Aug 9;357(6):535-44.
5. Routes J et al: Health-related quality of life and health resource utilization in patients with primary immunodeficiency disease prior to and following 12 months of immunoglobulin G treatment. J Clin Immunol. 2016 Jul;36(5):450-61.

well-being. They have also a much broader societal and economic benefit: comparing the time before and after the introduction of PDMPs for PIDs and haemophilia in Europe, treatments have yielded a combined health value gain (the magnitude of the socio-economic impact of PDMP treatments) of 2 Billion EUR/year. For PIDs this is approximately 1 Billion Eur/year (based on a PID population of 44,000). For severe haemophilia the figure is at least 1 Billion EUR/year (based on a severe haemophilia population of 47,000)*. In addition to the health value gains, these treatments can also prevent indirect healthcare costs in the range of 1.1 and 1.6 Billion EUR/year.* Limiting access to PDMPs often equates with denying Patient Access to the only effective therapy and reduces the concomitant socio-economic benefits.

CHALLENGES

FORMAL PATIENT ACCESS CHALLENGES:

In Europe, many PDMP treatments are not reimbursed, or are reimbursed only for narrowly defined eligible patient populations, resulting in unacceptable inequalities geographically among patients in Europe. IgGs for PIDs are consistently reimbursed, but this is not the case for the same therapeutic class in relation to SIDs. In many countries, PDMP treatments such as Factor X, Factor XIII and Protein C, are entirely omitted from reimbursement lists. When PDMPs are reimbursed, they often face additional economic challenges, including reimbursement issues, the consequences of external reference pricing (ERP model), and/or cost-containment measures such as clawback or payback taxes. Although several countries have lifted, deferred or reduced application of these taxes, in recognition of PDMPs' unique value and nature and unique risks to availability, there remain many others that continue to apply them. PDMP manufacturing costs are high and difficult to reduce. Thus, the continued cost-containment measures threaten the already fragile balance of the PDMP industry structure, ultimately limiting Formal Patient Access.

THERAPEUTIC PATIENT ACCESS CHALLENGES:

Access to optimal treatment is under pressure, particularly from procurement practices such as tendering where the decision is based on price alone. Tenders can be effective in controlling reimbursement budgets, but they are only appropriate if differences between medicines are negligible (when medicines are bioequivalent). However, this is not the case with PDMPs; they cannot be considered interchangeable because they are not required to prove bioequivalence (unlike generics or biosimilar medicines). Different brands within the same PDMP class have different tolerability profiles. Switching between them for economic reasons rather than clinical need can have adverse effects on patients. Availability of only a single PDMP brand of each class means not only that physicians will need to switch existing patients' therapies, but also that they will have no choice of customising naive patients' treatment regimens, e.g. choosing between differentiated brand properties and routes of administration. When a procurement system contravenes the clinical guidelines and therapeutic need, this system may require adjustments to better serve the patients.

PRODUCT AVAILABILITY:

Plasma is a gift from healthy donors. Plasma collection policies and collection volumes directly impact the amount of PDMPs produced. In Europe, availability of source plasma is extremely uneven: just four countries contribute more than 55 % of the total amount of plasma collected in Europe for manufacturing. Additionally, the plasma volume collected in Europe fulfils only around 63 % of the European PDMP clinical need; the rest is imported from the United States (see Figure 12). It is difficult to attract enough plasma donors in Europe to meet the clinical need for patients. Source plasma donors face greater inconveniences and expenses than whole blood donors, so it is difficult to maintain the necessary donation volumes. Also, in Europe, there are fewer plasmapheresis centres than blood collection centres, and the plasmapheresis process takes significantly longer and is more burdensome. In recognition of these factors, the four countries collecting the most plasma per capita have allowed a system of monetary compensation for the donors' inconvenience and expenses, which has proven to be singularly effective. Since the growing clinical need for PDMPs is a global phenomenon, without an increased European contribution in plasma collection, there is a high risk of falling short of meeting patients' clinical needs.

RECOMMENDATIONS

The PDMP Ecosystem is in a fragile balance as it depends on a large number of variables: often uncertain volumes of donations, complex regulations, strict safety procedures and lengthy manufacturing processes. Additionally, heterogenous reimbursement across Europe and varied economic measures may further impact its current stability. These challenges negatively impact the end-goal of optimal Patient Access and require multi-stakeholder solutions. There are four actions that need the most urgent attention from all stakeholders:

1.

Apply effective measures, in collaboration with the private industry, to promote and grow plasma donations across Europe to fulfil the clinical need for PDMPs.

- Establish dedicated plasma collection (plasmapheresis) programs and outreach campaigns directed towards plasma donors in all EU Member States.
- Allow co-existence of public and private sector owned plasma collection centres.
- Stimulate plasma donations by allowing compensation for donors' expenses and inconvenience related to donation.

These items should be implemented and also addressed in the most appropriate policy frameworks at the EU Member States level or at the EU level.

2.

Ensure the broadest possible reimbursement coverage for all eligible patients to maximise clinical and socio-economic benefits.

3.

Optimise reimbursement policies, considering Value Based Pricing such as value informed affordable pricing (VIA) models, and revise cost-containment measures in order to maintain the PDMP industry's sustainability and improve equitable access to treatment for patients in Europe.

4.

Revise and align procurement practices with clinical needs to ensure the right treatment for the right patient.

With a strong partnership and open trust-based dialogue between industry, policymakers, patients and other healthcare stakeholders, these solutions can be achieved.

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