

Principles to Advance Patient Access to Care

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The Plasma Protein Therapeutics Association (PPTA) represents the private sector manufacturers of plasma-derived and recombinant analog therapies, collectively known as plasma protein therapies and the collectors of source plasma used for fractionation. Our global members are Bio Products Laboratory, Biotest, CSL Behring, Grifols, Kedrion Biopharma, and Shire. Plasma protein therapies treat individuals with conditions defined by certain plasma protein deficiencies. These conditions are genetic, chronic, and life-threatening rare diseases, including alpha-1 antitrypsin deficiency, bleeding disorders such as hemophilia and von Willebrand disease, hereditary angioedema, chronic inflammatory demyelinating polyneuropathy, and primary immunodeficiency diseases (PIDDs).¹ These therapies include alpha₁-proteinase inhibitor, antithrombin III, plasma-derived and recombinant blood clotting factor,² C1 esterase inhibitor, fibrin sealant, immune globulin, hyperimmune immune globulin, prothrombin complex concentrate and protein C concentrate.³

The manufacturing of most plasma protein therapies begins with the collection of donated human plasma from committed donors at more than 500 donation centers dispersed across the United States. The manufacturing of these therapies is a resource intensive process that requires a seven to twelve month process from the time of donation until the completion of the finished therapy. Notably, because each plasma donation only contains a fraction of the necessary proteins to produce a given therapy, there is an inherently finite supply of therapies. For example, it requires approximately 130 donations to provide enough Immunoglobulin G to treat one patient with a primary immunodeficiency diseases for one year, and 900 donations to provide enough alpha-1 proteinase inhibitor to treat one alpha-1 antitrypsin deficiency patient for one year.

The mission of the Plasma Protein Therapeutics Association (PPTA) is to promote the availability of and access to safe and effective plasma protein therapeutics for all patients in the world. We strive to achieve our mission by fostering the collection of high-quality plasma from healthy donors, establishing standards for the manufacturing of life-saving plasma protein therapies at the highest levels of safety and quality, and supporting payer policies that ensure patients' access to plasma protein therapies. In furthering our mission of supporting payer policies that ensure patients' access to plasma protein therapies, we share these principles with you.

¹ Diseases treated with plasma protein therapies also include chronic B-cell lymphocytic leukemia; hereditary antithrombin III deficiency; protein C deficiency; subtypes of PIDDs, such as common variable immunodeficiency, X-linked agammaglobulinemia (Bruton's disease), DiGeorge syndrome, Wiskott-Aldrich syndrome, Nezelof's syndrome, and severe combined immunodeficiency; graft-versus-host diseases; specific bleeding disorders, such as hemophilia A, hemophilia B, congenital fibrinogen deficiency, and factors VII, X, and XIII deficiencies. Cytomegalovirus disease associated with transplant patients; hepatitis B reinfection in liver transplant patients; idiopathic thrombocytopenic purpura (ITP); infant botulism; Kawasaki's disease; rabies; rhesus incompatible pregnancies; and tetanus are examples of acute rare conditions that are treated with plasma protein therapies.

² Recombinant blood clotting factor therapies are created using recombinant DNA technologies, which entail the integration of genes coded for the production of human blood clotting factor proteins into laboratory cell cultures. The cell cultures produce blood clotting factor proteins, which are subsequently collected, purified, and further refined into safe and effective biologic medicines.

³ Human plasma is the clear liquid portion of blood that remains after the red cells, white blood cells, and platelets are removed.

Due to its human origin, complexity, and richness in therapeutically useful proteins, human plasma is a unique biological material.

Summary of Principles:

Patients require medically appropriate access to all brands of plasma protein therapies

Due to the pharmacologic and manufacturing differences that exist across brands of plasma protein therapies, plasma protein therapies are non-interchangeable, sole source biologics that produce different therapeutic outcomes based on each patient's unique characteristics. Accordingly, patients depend on appropriate access to all brands within a therapeutic class to be assured that they, in close consultation with their physicians, are able to identify and become stabilized on the therapy that best fits their health status. Patients who rely on these therapies as part of their life-saving treatments often experience significant differences in outcomes on a brand-by-brand basis. Therefore, it is essential that patients have access to their medically appropriate therapy.

This position is supported by numerous studies^{4 5} and the recommendations of medical experts. The National Hemophilia Foundation's Medical and Scientific Advisory Council (MASAC) stated in MASAC recommendation 159 that, "The characteristics of each product and the resultant product choice for an individual patient require a complex decision making process with the ultimate product being agreed upon by the patient and their respective healthcare provider. It is critical that the bleeding disorders community has access to a diverse range of therapies and that prescriptions for specific clotting factor concentrates are respected and reimbursed."⁶ The Medical Advisory Committee of the Immune Deficiency Foundation "recommends with the strongest conviction that physicians be allowed flexibility to select appropriate products for patients."⁷ This recommendation is based on numerous factors, including the increase in the potential for adverse events when a patient changes therapies, and patient toleration of different therapies depends on their medical history and the therapies unique characteristics such as volume delivered, sugar content, IgA content, pH, route of administration and osmolality.

Patients need access to the appropriate providers

Individuals who rely on plasma protein therapies have extremely rare conditions, and because of this, not every provider has the training and experience necessary to provide quality care for such patients. For this reason, PPTA suggests payers consider policies that will allow these patients access to physicians, hemophilia treatment centers and specialty pharmacies with experience in treating their conditions. For example, individuals with bleeding disorders receive better care from pharmacies that have the experience of providing clotting factor and that meet the standards of service recommended in MASAC 188⁸. The standards for providing blood clotting factor for home infusion include these services:

- Maintain a product inventory to provide the full range of available therapies, including all available assays and vial sizes;
- Provide all necessary ancillary supplies for administration including needles, syringes, and sterile gloves;

⁴ Immune Deficiency Foundation Medical Advisory Committee. (2011). *IDF Medical Advisory Committee Resolution on Product Choice for Immunoglobulin Replacement Therapy*. Immune Deficiency Foundation.

⁵ Mannucci, P. M., Mancuso, M. E., Santagostino, E., Yang, Y., Zhang, L., Tian, M., & Yang, R. (2012). How we choose factor VIII to treat hemophilia. *Blood*, 119(18), 4108-14.

⁶ National Hemophilia Foundation Medical and Scientific Advisory Council. (2005). *MASAC Recommendation Regarding Factor Concentrate Prescriptions and Formulary Development and Restrictions*. New York: National Hemophilia Foundation.

⁷ Immune Deficiency Foundation Medical Advisory Committee. (2011). *IDF Medical Advisory Committee Resolution on Product Choice for Immunoglobulin Replacement Therapy*. Immune Deficiency Foundation.

⁸ National Hemophilia Foundation Medical and Scientific Advisory Committee. (2008). *MASAC Recommendations Regarding Standards of Service for Pharmacy Providers of Clotting Factor Concentrates for Home Use to Patients with Bleeding Disorders*. New York: National Hemophilia Foundation.

- Provide containers for the disposal of hazardous waste, and the collection of such containers shall be arranged pursuant to state and federal law;
- Fill all prescription orders within 48 hours and all emergency orders within 12 hours;
- 24 hour on-call support by nurses, pharmacists, multilingual interpreters and support staff trained in bleeding disorders;
- Case management services to evaluate and promote adherence to variable and, at times, complex dosing guidelines;
- Unique delivery requirements including temperature controlled shipments with proof of delivery;
- Provide medically necessary nursing services, including the administration of clotting factor therapies.

The rare and chronic diseases treated by plasma protein therapies are often difficult to diagnose, treat, and manage.⁹ Accordingly, to ensure the best possible health outcomes for patients, the individuals who rely on plasma protein therapies as part of their lifesaving treatment require medically appropriate access to the specialists who best understand the complexities of their diseases. A relatively select few specialists across the country have developed the enhanced knowledge and experience necessary to effectively treat the rare diseases treated by plasma protein therapies. Therefore, we recommend payer policies that allow individuals with plasma protein deficiencies access to those physicians who have experience treating these rare conditions.

Patients require transparent networks in order to access medically appropriate therapies and providers at the right site of care

When individuals with plasma protein deficiencies are selecting their health plan they need to know if they will have access to their physician, hemophilia treatment center, specialty pharmacy provider, and medically appropriate plasma protein therapy. Too often, this information is not available to these individuals during the selection process. This lack of transparency can lead to disruptions in necessary care as patients seek changes to their health coverage that will allow them access to the care they need. PPTA urges policymakers to implement standards that improve network transparency and quality, and safeguard robust patient access to the providers that are best suited to provide effective care for rare and chronic conditions.

Conclusion

In the preamble of a recent final rule, the Centers for Medicare & Medicaid Services states that “changes to the payment and service delivery systems should be aligned with better care quality and promote rather than reduce access to services¹⁰.” PPTA agrees with that goal and suggests that adherence to these principles will achieve better care quality for individuals with plasma protein deficiencies and promote rather than reduce access to services that they need to treat their rare, life-threatening conditions.

⁹ Immune Deficiency Foundation. (2009). *Primary Immune Deficiency Diseases in America: 2007*.

¹⁰ (2015). *Medicaid Program; Methods for Assuring Access to Covered Medicaid Services; Final Rule*. 80 Fed. Reg. 67578 Centers for Medicare & Medicaid Services, Department of Health and Human Services. U.S. Government Publishing Office.