

ISSUE BACKGROUND

Plasma Protein Therapeutics

Plasma Protein Therapies: Unique Biologicals · Rare Disease Patients

Set apart as a niche sector within the biotechnology and pharmaceutical industries, plasma protein therapies are biologics differentiated by:

- **Small, fragile patient populations;**
- **Therapies infused or injected by a patient often under medical supervision;**
- **Treatment of life-threatening, chronic, genetic diseases;**
- **Reliance on plasma as the essential starting material;**
- **Complex, lengthy manufacturing processes;**
- **Distinct sole source therapies with no generic equivalents and that cannot be substituted.**

Patients & Therapies

- Plasma protein therapies predominantly are indicated to treat chronic, genetic rare diseases and require access to physicians with specialized knowledge in the diagnosis and management of these diseases.
- Plasma protein therapies are derived from the protein rich portion of the blood called plasma. Blood clotting factors are either derived from plasma or manufactured using recombinant DNA technology.
 - Alpha-1-proteinase inhibitors treat alpha-1 antitrypsin deficiency, also known as genetic emphysema.
 - Immune globulins (IG) treat primary immune deficiencies and certain neurological disorders.
 - Blood clotting factors treat bleeding disorders such as hemophilia and von Willebrand disease.
 - Specialty immune globulin products are produced on a very small scale to treat or prevent specific and highly acute conditions such as rabies, tetanus, hepatitis B, cytomegalovirus, and hemolytic disease in newborns.
 - Albumin is used in critical care settings to treat shock, trauma and severe burns.
- Many patients require regular life-long infusions or therapy injections in a physician's office, a hospital outpatient setting, or at home, often under the supervision of a skilled medical professional.
 - There are no alternative treatments for these life-threatening, rare diseases.
- There are significant variations among brands of therapy due to complex manufacturing processes. Plasma-derived products are defined by the complex process by which they are refined into therapies, giving rise to significant therapeutic variation between brands and making them wholly non-interchangeable.

- Because each brand is unique, the industry has developed multiple brands within each therapeutic class. Providing patients with access to these options allows them to find a therapy best suited for their individual medical needs in consultation with their physician.

Safety & Quality

- Production requires complicated manufacturing processes involving numerous steps such as plasma collection, laboratory testing, fractionation, viral removal, quality control testing and final lot release, which may take seven to 12 months.
- Manufacturers invest substantial resources in manufacturing including the acquisition of the safe starting material source plasma. Manufacturers are continuously investing in new tests and viral inactivation and viral reduction processes to address threats of emerging pathogens.
- Production of plasma-derived therapies consists of two separate processes - the collection of human plasma and the production of safe and effective therapies from that donated plasma. Each of these processes is highly regulated and separately licensed by the U.S. Food and Drug Administration. By the time a plasma protein therapy is ready for infusion or injection by a patient, the product has been the subject of two rigorous and distinct sets of regulatory requirements including inspection, licensure and adherence to good manufacturing practices.
 - PPTA's members have developed and follow additional voluntary standards that complement existing regulations to help ensure a safe supply of source plasma and the therapies it yields. The International Quality Plasma Program (IQPP) and Quality Standards of Excellence, Assurance and Leadership (QSEAL) programs set benchmarks for quality and performance that help to protect the public interest.

Industry

- The plasma protein industry is a very small niche within the larger biotechnology industry, representing approximately \$7 billion in annual sales, or 2% of the overall industry.
- The distinct non-interchangeable nature of plasma protein therapies, the patient populations they serve, and the life-threatening, rare diseases they treat set plasma protein therapies apart as a niche sector within the biotechnology and pharmaceutical industries.
- Not all drug manufacturers are the same - the branded pharmaceuticals, the generics, the biologicals, the vaccines, and the plasma protein therapeutics industries not only offer different value to the patient, but also require considerably different business models and cost structures.
- Continuous innovation of therapies in terms of plasma protein yield, knowledge and understanding of transmissible diseases, and introduction of new testing requirements,

combined with the continuous monitoring for emerging pathogens, requires constant vigilance and investment by manufacturers.

- Unlike traditional pharmaceuticals, the viability of the plasma protein therapeutics industry depends on maintaining a healthy market for all plasma protein therapies, which generally treat small patient populations of individuals with genetic diseases. For example, immune globulin manufacturing decisions depend not only on the need for immune globulins but also for other plasma-derived products. Multiple therapies can be manufactured from human plasma; yet production costs and production time for plasma-derived therapies remain relatively constant regardless of whether one, two, or six different therapies are produced. *This is because the single largest manufacturing cost is the collecting and testing of human plasma.*