

January 31, 2012

Via Electronic Delivery

Secretary Kathleen Sebelius
U.S. Department of Health and Human Services
c/o Center for Consumer Information and Insurance Oversight
Office of Oversight, MLS Division, Room 737F
200 Independence Avenue S.W.
Washington, DC 20201

Re: Essential Health Benefits Pre-Rule Bulletin

Dear Secretary Sebelius:

The Plasma Protein Therapeutics Association (“PPTA”) appreciates the opportunity to comment on the Department of Health and Human Services’ (“HHS”), December 16, 2011, pre-regulatory guidance, “Essential Health Benefits Bulletin.” PPTA recognizes that the implementation of the essential health benefits (“EHB”) provisions of the Patient Protection and Affordable Care Act (“ACA”) is integral to achieving the ACA’s overall goals and objectives of increasing the number of American citizens with access to comprehensive and affordable health coverage. Accordingly, we appreciate the significance of the bulletin’s proposals, and wish to provide insight into its potential affect on the plasma protein therapeutics industry.

While we understand HHS’s desire is to provide states with flexibility to meet the needs of its population when developing Health Insurance Exchanges, PPTA is concerned that the tremendous discretion afforded to the states in selecting a benchmark plan will result in substantial differences in patient benefits. These differences will result from the lack of specificity in the ten benefit categories outlined in the EHB provisions and the multiple variations in the benchmark plans that states may ultimately select.

Because plasma protein therapies almost exclusively treat patients with rare diseases, disorders, and conditions, PPTA is particularly sensitive to policies that may hinder or help patient access to the therapeutic intervention best suited for their individual needs. Thus, PPTA respectfully recommends that HHS consider State Health Insurance Exchange Principles developed by PPTA and its members, (attached) and that EHB regulations and guidance include the following:

- A prohibition on utilization controls that place plasma protein patients at risk for adverse events that may result from switching therapies and delays in treatment;
- The establishment of standards for a transparent and expedited process to appeal denials;
- A mechanism that ensures clearly stated medical necessity standards that recognize the need for access to specialty services and physicians;

- Explicit and binding nondiscrimination requirements;
- Means to protect against cost-sharing mechanisms that burden chronically ill patients.

PPTA Background

PPTA represents human plasma collection centers and the manufacturers of lifesaving medicinal therapies, including albumin, alpha-1 proteinase inhibitor, antithrombin III, blood clotting factors, C1 esterase inhibitor, fibrin sealant, immune globulin, hyperimmune immune globulins, and protein C concentrate, from this human plasma. Some of our members also use recombinant DNA technology to produce blood clotting factors. Collectively, these therapies – both plasma-derived and recombinant – are known as “plasma protein therapies.” The manufacturer membership of PPTA in the United States (“U.S.”) currently includes Baxter, Biotest, Cangene, CSL Behring, Grifols and Kedrion.

Many plasma protein therapies are solely approved for marketing in the U.S. by the Food and Drug Administration (“FDA”) for the treatment of rare diseases, disorders, and conditions. Plasma protein therapies are unique, non-interchangeable therapies that are infused or injected by patients who require them, often for the duration of their lives. In the U.S., a “rare disease or condition” is generally defined as a disease or condition that affects less than 200,000 people.¹ The majority of the rare conditions that require treatment with plasma protein therapies are genetic, chronic, and life threatening, including alpha-1 antitrypsin deficiency, chronic B-cell lymphocytic leukemia, chronic inflammatory demyelinating polyneuropathy, hereditary angioedema, hereditary antithrombin III deficiency, protein C deficiency, primary immune deficiency diseases, such as common variable immunodeficiency, X-linked agammaglobulinemia (Bruton’s disease), DiGeorge syndrome, Wiskott-Aldrich syndrome, severe combined immunodeficiency, and graft-versus-host diseases, and bleeding disorders, such as hemophilia A, hemophilia B, congenital fibrinogen deficiency, Von Willebrand’s disease, and factor XIII deficiency, cytomegalovirus disease associated with transplant patients, hepatitis B reinfection in liver transplant patients, idiopathic thrombocytopenic purpura, infant botulism, Kawasaki’s disease, rabies, rhesus incompatible pregnancies, and tetanus.

As representatives of a niche segment of the biologics industry with considerable experience in treating rare diseases, disorders, and conditions, PPTA emphasizes that the diverse clinical characteristics of these diseases translate to unique policy needs that demand special consideration.

Utilization Controls May Risk Plasma Protein Patient Health

The Essential Health Benefits pre-rule Bulletin states that if a benchmark plan offers a drug in a certain category or class, all plans must offer at least one drug in that same category or class. There are multiple brands in each therapeutic class of plasma protein therapies, including alpha-1 proteinase inhibitor, blood clotting factors and immune globulin. Plasma protein therapies are

¹ See 21 U.S.C. § 360bb(a)(2) (2006).

non-interchangeable biologics, yielding unique pharmacokinetics and pharmacodynamics on a per patient basis.² Due to the unique nature of these therapies, the safe and effective treatment of patients who use them demands comprehensive prescription drug coverage, routine access to medical providers, and access to physicians with specialized knowledge of rare diseases and the therapies used to treat them. Therefore, patients suffering from the rare disorders that require these therapies must have access to the full range of brands in the respective therapeutic class to ensure they receive the treatment best suited for their individual needs. We urge HHS to ensure adequate prescription drug coverage within the design of Essential Health Benefits that provides patients with access to the therapy that works best for them, as determined in consultation with their physician. Utilization controls that do not consider the non-interchangeable nature of plasma protein therapies such as fail first, prior authorization, and step therapy policies limit patient access to the therapeutic intervention best suited for their individual needs and threaten their safe and effective treatment.³

Future HHS EHB regulations and guidance should establish utilization standards that protect plasma protein patients from control mechanisms that limit access and will threaten their health. PPTA urges HHS to include the following utilization standards:

- Prohibitions against utilization controls that have the effect of limiting patient access to the specific therapy best suited to the patient's individual needs;
- Explicit recognition that certain therapies are clinically non-interchangeable, and that the safe and effective treatment of patients that require those therapies demands they be made available without the hindrances of fail first, prior authorization, or step therapy control policies, or any similar utilization controls;
- Specific prohibitions against utilization controls that have the effect of discriminating against patients with rare diseases or disorders; and
- Transparency requirements stipulating minimum timeframes for advance notice of implementation of utilization controls.

² See, e.g., Laurence Feldmeyer et al., *Not All Intravenous Immunoglobulin Preparations Are Equally Well Tolerated*, 90 *Acta Derm Venereol* 494-497 (2010); M.H. Tsai et al., *Clinical Responses of Patients with Kawasaki Disease to Different Brands of Intravenous Immunoglobulin*, 148 *J. PEDIATRICS* 38, 38-43 (2006); see also Letter from Jordan Orange, M.D. and Kathleen Sullivan, M.D., to Anne Jacques, Dir. Clinical Pharmacy Servs., Highmark (Feb. 28, 2011) (describing the clinical differences among the brands of immune globulin) (on file with author).

³ Utilization controls such as step therapy, fail first, or prior authorization channel patients to the least costly treatment option or to the least costly therapy in a given therapeutic class. While perhaps sound policy in some contexts, these utilization controls can pose severe health risks for plasma protein patients who require access to the specific therapy that has proven to optimally interact with their biological characteristics. For an example of the dangerous and costly adverse events that can occur by preventing access to the therapy best suited for the patient's needs, see the European Medicines Agency (EMA) finding that switching patients with hemophilia from one Factor VIII product to another can give rise to the development of inhibitors by that patient, undermining the patient's hemostasis, and diminishing the efficacy of that patient's previously sound treatment regimen. The European Medicines Agency, *EMA Completes the Review of Recombinant Factor VIII Products and Inhibitor Development* (July 31, 2007), at http://www.ema.europa.eu/docs/en_GB/document_library/Public_statement/2009/11/WC500011389.pdf

While PPTA recognizes the need to control escalating prescription drug costs, utilization controls subjecting patients to therapies unsuited for their specific needs has the potential to increase adverse events, raising the cost of health care, and threatening the health of patients.

Plasma Protein Patients Require a Timely and Transparent Appeals Process

Plasma protein therapy requires patients to receive regular infusions or injections for the duration of their lives. Depending on the disease and its severity, patients requiring plasma protein therapies may receive one infusion a month⁴ or as many as three a week.⁵ For many patients, a delay in their plasma protein therapy treatment regimen can result in severe and potentially life-threatening health consequences.⁶ Recognizing the significance that delays in treatment pose for plasma protein therapy patients, PPTA urges HHS to include within its future regulations and guidance, standards that will ensure the swift and transparent resolution of claims denials, with special consideration for rare disease patient populations.

Specifically, PPTA urges HHS to establish standards that obligate insurers to confer with the patient's physician, and prior to the denial, provide objective and clinically valid reasons for the denial. Given the intent of the ACA to provide individuals access to health insurance without discrimination, PPTA believes it is appropriate and necessary for the Department to establish regulations and guidance that go beyond what is currently required of insurance plan appeals processes, and provide the special protection that is necessary for the safe and effective care of individuals with rare diseases. Principally, HHS should stipulate denials for patients with rare, chronic, life-threatening diseases that require regular treatments to be expeditiously executed and communicated in clear and understandable terms. HHS EHB regulations should also outline minimum standards of transparency for appeals of claims denials, providing contracted timeframes for patients that rely on regular treatments as part of their life-sustaining regimens.

Access to Specialty Services and Physicians Represents a Medical Necessity

Because plasma protein therapies predominantly are used to treat rare diseases, the medical profession has evolved such that physicians treating these rare diseases build a specialized expertise for their diagnosis, treatment, and management.⁷ Accordingly, patients treated with plasma protein therapies rely on unencumbered access to the specialized services, and physicians who have specialized knowledge of the diagnosis, treatment, and management of their disease or

⁴ See Bonnie Kirschenbaum et al., Maximizing Efficiencies and Economic Benefits of IVIG, Pharmacy Practice News (2009) (Quoting Dr. Marc Riedl, MD, MS, Assistant Professor of Medicine at UCLA's David Geffen School of Medicine as stating that, "patients with PID typically receive an infusion of IVIG about once a month, unless they opt for the subcutaneous therapy, which is administered weekly.")

⁵ See National Hemophilia Foundation's Medical and Scientific Advisory Council (MASAC) recommendation #179. Available at <http://www.hemophilia.org/NHFWeb/Resource/StaticPages/menu0/menu5/menu57/masac179.pdf>. (Stating that optimal treatment for individuals with severe hemophilia A or B includes regular—three times per week—infusions of Factor to prevent bleeding.)

⁶ See e.g. OFFICE OF THE ASS'T SEC. FOR PLANNING & EVALUATION, U.S. DEP'T OF HEALTH AND HUMAN SERV., ANALYSIS OF SUPPLY, DISTRIBUTION, DEMAND, AND ACCESS ISSUES ASSOCIATED WITH IMMUNE GLOBULIN INTRAVENOUS (IGIV) (2007) (*Reporting increased rates of hospitalizations and related adverse events resulting from interruption to IVIG continuity of care stemming from changes in Medicare reimbursement*).

⁷ See e.g. C. Sabba, A rare and misdiagnosed bleeding disorder: hereditary hemorrhagic telangiectasia, 3 Journal of Thrombosis and Haemostasis, 2201-2210 (October 2005) (finding that once a diagnosis for a rare disease, such as HHT, is established, patients need access to physicians with specialized knowledge in the cause, symptoms, and either established or experimental treatments for the disease).

disorder.⁸ For example, individuals with hemophilia should have in network access to physicians at Federally Qualified Hemophilia Treatment Centers for their hemophilia care. PPTA urges HHS to include within its future regulations and guidance protections that ensure that medically necessary access to these specialists is guaranteed, and that plans are prohibited from effectively creating barriers to specialists through the establishment of higher cost-sharing for specialists or the use of clinically invalid reasons for denying specialist claims. Plasma protein therapy patients represent a unique segment of the general patient population that requires access to specialized treatment. By recognizing the need for unencumbered access to specialized care in the future EHB regulations and guidance, HHS will ensure that plasma protein patients who suffer from chronic illnesses are protected from burdensome cost-sharing mechanisms and ensured access to the care that best suits their individual needs.

Nondiscrimination Regulations Must Be Explicit and Binding

The ACA requires that coverage decisions may not discriminate based on age, disability, or expected length of life.⁹ In its Bulletin, HHS recognized the need to ensure that coverage is provided in a nondiscriminatory way, however, in its EHB regulations PPTA urges the Department to implement binding regulations that clearly stipulate the prohibition of policies that discriminate based on age, disability, or expected length of life. PPTA further urges HHS to establish strict standards of oversight to be followed by states ensuring that the plans administered within their borders are complying with the nondiscrimination provisions of the EHB regulations.

To protect against possible discrimination, PPTA urges HHS to require plans to:

- Disclose all information that is pertinent to deductible, co-payment, and co-insurance rates applied to in-network and out-of-network covered services;
- Disclose all limitations on services;
- Abstain from applying specialty tier pricing;
- Abstain from any substitution of certain therapies considered to be clinically non-interchangeable.

Chronically ill plasma protein patients face high recurring medical costs, and are thus acutely and immediately affected by any policy that discriminatorily raises the cost of their care. For example, specialty tiering, where often the most expensive medications are assigned high cost-sharing values, places a significant and disparate financial burden on patients with chronic illnesses. PPTA thus urges HHS to establish both strong prohibitions against discrimination by any plan, and state-based mechanisms of oversight to ensure these prohibitions are consistently followed.

⁸ *Id.*

⁹ See Patient Protection and Affordable Care Act (“PPACA”) § 1302, Pub. L. No. 111-148 (2010).

Increases in Cost-sharing Affecting Chronically Ill Plasma Protein Patients Should be Subjected to Heightened Scrutiny

Long-term health care studies have demonstrated that uniform increases in cost-sharing without consideration for the clinical status of the individual patients can have negative impacts on patient health and increase the likelihood of hospitalization in the long-term.¹⁰ These negative effects are amplified for chronically ill plasma protein patients facing high recurring medical costs of plasma protein therapies. PPTA urges HHS to establish within its final regulations and guidance standards for calculating the clinical implications that an increase in cost-sharing may have on chronically ill patients. The Association further urges HHS to require the findings of these calculations to be published prior to an increase in cost-sharing for benefits used by chronically ill patients. By providing standards for transparency in cost-sharing determinations, HHS will allow for the consideration of the clinical status of individual patients, improving long-term outcomes for patients suffering from lifelong diseases.

Conclusion

PPTA recognizes that the implementation of the essential health benefit provisions will represent an important milestone in the overall progress towards achieving the ACA's intended purpose of providing effective and affordable coverage to a greater number of Americans. Accordingly, PPTA stresses the need for HHS to implement regulations that protect the unique needs of plasma protein patients and provide federal oversight of these protections. Without protections for patients with rare diseases and the oversight to maintain those protections, HHS risks undermining the core purpose of the ACA to provide health insurance coverage to individuals who otherwise would be unable to acquire coverage that meets their unique needs.

The Association appreciates the opportunity to provide comments on the Essential Health Benefits Bulletin and looks forward to working the Agency on future rulemaking. If you have any questions, please contact Kym H. Kilbourne at 202-789-3100 or kkilbourne@pptaglobal.org or Everett Crosland at ecrosland@pptaglobal.org.

Sincerely,



Julie A. Birkofer
Senior Vice President, North America, PPTA

Attachment: PPTA State Health Insurance Exchange Principles

¹⁰ See Amal Trivedi et al. Increased Ambulatory Care Copayments and Hospitalizations among the Elderly, 362 N Engl J Med. 4 (2010); Dana Goldman et al. Pharmacy Benefits and the Use of Drugs by the Chronically Ill, 291 JAMA 19 (2004).

PPTA STATE HEALTH INSURANCE EXCHANGE PRINCIPLES

The Plasma Protein Therapeutics Association (PPTA) represents the world's leading manufacturers of plasma-derived and recombinant biological therapies, collectively known as plasma protein therapies, and the collectors of source plasma. These critical therapies are infused or injected by more than 1 million people worldwide to treat a variety of rare, life-threatening diseases and serious medical disorders. PPTA members produce in excess of 80 percent of the plasma protein therapies used in the United States today and more than 60 percent worldwide.

Lifesaving therapies produced by PPTA members include clotting factor therapies for individuals with bleeding disorders, immunoglobulins (IG) to treat complex diseases in persons with compromised immune systems and neurological disorders, and therapies for individuals who have alpha-1 anti-trypsin deficiency, which typically manifests as adult onset chronic obstructive pulmonary disease and substantially limits life expectancy.

State Health Insurance Exchanges

State Health Insurance Exchanges will be a marketplace where individuals are going to be able to purchase comprehensive health insurance coverage from an approved health plan. Individuals will purchase these products with the expectation that they will provide them with access to the care they need. And given that the federal government is compelling the purchase of these products, the administrators of the state exchanges have a fiduciary duty to ensure that the plans meet the needs of their state residents.

This will be difficult given the different health profiles of all the individuals that will be served through the exchange. Especially difficult will be making sure the health plans meet the needs of individuals with rare, chronic conditions. The state administrators would do these individuals a great service by requiring the health plans to meet the standards of care established by those with expertise in treating these individuals. Numerous medical groups have established these guidelines and they are easy to find.

The standards established for the medically appropriate care of individuals who rely on plasma protein therapies have some common principles. PPTA suggests that as you develop the rules governing your state's health exchange that you consider the principles below.

Patients need affordable health care insurance. PPTA believes patients deserve access to appropriate public and private health insurance coverage regardless of health or disability, employment status, age, or medical predisposition. Specifically, PPTA urges state governments to adopt legislation and/or regulations that protect patients from health insurance industry practices that impose punitive cost-sharing requirements upon patients with rare, chronic diseases and disorders.

An example of such proactive law is Chapter 2010-536, Laws of New York. Enacted in 2010, this new law prohibits health plans from imposing cost-sharing, deductibles, or co-insurance obligations greater than those for any non-preferred brand drugs or their equivalents. It will protect patients from cost-sharing policies that make their life-saving therapies cost prohibitive.

Patients need access to quality providers. Not every provider has the training and experience necessary to provide these patients with quality care. Nearly all of the diseases and disorders treated with a plasma protein therapy require a physician with a sub-specialty in the specific disease. For this reason, PPTA urges legislatures, regulators, and Medicaid agencies to implement standards of service that require health plans, and others that coordinate care for patients with rare, chronic diseases and disorders to meet the quality standards established by medical panels such as the Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation (NHF)—a leading patient organization for persons with bleeding disorders in the United States.

Patients need unfettered access to drugs and biologicals. PPTA supports patient access to all medically appropriate, life-saving plasma protein therapies. Because of significant clinical and manufacturing differences, an individual patient may tolerate or respond to one therapy better than another in the same class. Consequently, such therapies are not therapeutically equivalent, pharmaceutically equivalent, or bioequivalent. They are not one-size-fits-all, interchangeable therapies.

An individual with hemophilia should have access to the full range of FDA-licensed clotting factor concentrates prescribed by the patient's treating physician, who typically specializes in the treatment of their specific bleeding disorder. In fact, the U.S. Food and Drug Administration (FDA) has approved the various clotting factor therapies [Factor VII, VIII, IX and X and von Willibrand Disease] for distinct clinical indications. The therapies are neither clinically nor therapeutically interchangeable. In addition, some therapies are derived from human plasma, while others are made utilizing recombinant DNA technology, created from genetically modified cell lines.

Moreover, the MASAC has stated in its Guideline #159, "Clotting factor therapies are neither pharmacologically nor therapeutically equivalent and vary based upon purity, half-life, recovery, method of manufacture, viral removal and inactivation processes, potential immunogenicity, and other attributes. 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."¹

¹ MASASC Recommendation #159 (last visited August 14, 2008), available at <http://www.hemophilia.org/NHFWeb/MainPgs/MainNHF.aspx?menuid=57&contentid=179>

In addition to blood clotting factors, the products in other plasma protein therapy categories are not pharmaceutically or therapeutically equivalent. Specifically, each IG therapy has been approved by the FDA for distinct clinical indications and each has distinct contraindications. For example, each IG therapy has a significantly different shelf life, and each is prepared and administered in a specific manner. Storage requirements vary. Sugar content varies.

In each case, these distinct therapies require different dosages and well-defined regimens, and they may be appropriate or effective only for specific populations or for particular individuals within those populations. Treating plasma protein therapies as interchangeable directly contradicts the determinations made under FDA guidelines, which have undergone years of review.

Because of the uniqueness of each therapy, PPTA opposes any limitation of access to plasma protein therapies based on comparative effectiveness models by government and private health insurance plans for patients who have chronic, life-threatening diseases and disorders.

SASC11020, June 8, 2011