Health Care Reform in the U.S.

Plasma Protein Therapies for Hemophilia: Good News on Safety, the Access Battle Remains

PPTA Interview: Michel Raguet Discusses C1 Inhibitor Deficiencies

Healthy Donors: The Cornerstone of Plasma Protein Therapies
Intelligence and speed without compromise

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Express™ is a software upgrade for the PCS® 2
Express decreases collection time by an average of 20%
Express' intelligent algorithm optimizes flow rate throughout the procedure

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Improve donor experience by decreasing collection time
Improve center production throughput
Improve inventory management
Improve device management

Optimize your center through the use of eQue™, eLynx™, and Express™
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<th>Event</th>
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<td>February 4 – 5</td>
<td>3rd Annual Congress of European Association for Haemophilia and Allied Disorders</td>
<td>Edinburgh, United Kingdom</td>
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<td>March 9 – 12</td>
<td>International Symposium on Intensive Care and Emergency Medicine</td>
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<td>2nd Pan-European Conference on Haemoglobinopathies</td>
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<td>5th European Conference on Rare Diseases</td>
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<td>March 16 – 17</td>
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<td>March 18 – 20</td>
<td>VI International Conference on Rare Diseases and Orphan Drugs (ICORD 2010)</td>
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<td>May 26-27</td>
<td>International Plasma Fractionation Association (IPFA)/PEI 17th Workshop</td>
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<td>June 10 – 13</td>
<td>15th Congress of the European Hematology Association</td>
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<td>June 15-16</td>
<td>Plasma Protein Forum</td>
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<td>June 26 – July 1</td>
<td>XXXIst International Congress of the ISBT</td>
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<td>July 10 – 14</td>
<td>Hemophilia 2010 World Congress</td>
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<td>August 22 – 27</td>
<td>14th International Congress of Immunology, Hosted by The Japanese Society of Immunology (JSI)</td>
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<td>October 6 – 9</td>
<td>International Organization for Primary Immunodeficiencies Biennial 2010</td>
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<td>October 10</td>
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<td>October 21–24</td>
<td>XI European Symposium on Platelet and Granulocyte Immunobiology</td>
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PPTA held a well-attended and highly successful 2009 Source Business Forum in New Orleans, Louisiana in conjunction with the annual meeting of the AABB. During the meeting, Association updates were provided on regulatory issues and the Source Industry Image and Credibility Campaign. In addition, a panel on “The Industry’s Cornerstone: Plasma Donor Care and Customer Service,” was well received. PPTA looks forward to another successful Source Business Forum next year in Baltimore, Maryland, USA on October 10, 2010.

VISITORS to DonatingPlasma.org can more easily find their local plasma donation center now with an improved search feature. PPTA, which developed the website to raise awareness of plasma donation, unveiled the tool in September, seeking to build on the importance of providing up-to-date information to donors who provide plasma needed to manufacture lifesaving therapies. DonatingPlasma.org gets on average 18,000 unique visitors each month. Visitors will find an organized, user-friendly, and more comprehensive website. The new site includes online web mapping powered by Google Maps, which allows browsers to locate plasma donation centers in a more efficient manner and view a high-resolution street map, specifically pinpointing the address. In addition, browsers will now be able to search for a center by zipcode, city, state or country. The newly designed site can be found at www.DonatingPlasma.org.

**GLOSSARY OF TERMS**

| ABRA | American Blood Resources Association |
| ASP | Average Sales Price |
| BLA | Biologic License Application |
| CER | Comparative Effectiveness Research |
| DSH | Disproportionate Share Hospital |
| EMEA | European Medicines Agency |
| FDA | U.S. Food and Drug Administration |
| GAO | Government Accountability Office |
| GPO | Group Purchasing Organization |
| HELP | U.S. Senate Committee on Health, Education, Labor and Pensions |
| HBV | Hepatitis B Virus |
| HCV | Hepatitis C Virus |
| HIV | Human Immunodeficiency Virus |
| IABS | International Association for Biologicals |
| IQPP | International Quality Plasma Program |
| IVIG | Intravenous Immunoglobulin |
| QSEAL | Quality Standards of Excellence, Assurance and Leadership |
| vCJD | Variant Creutzfeldt-Jakob Disease |
| WHO | World Health Organization |
MY NAME IS DOTTIE TRIPP.
I am PPTA’s associate, Global.
I have worked for PPTA for over eight and a half years, the first two in what was known as the American Blood Resources Association (ABRA), now PPTA’s Source division and now in PPTA’s Global division. In my position, I focus on providing administrative support to Jan M. Bult, the President of PPTA and as a liaison for the Global Management Committee and Global Board of Directors, organizing meetings and disseminating information.
I also administer the Quality Standards of Excellence, Assurance and Leadership (QSEAL) program.

Tell us about your background.
I was born in Washington, D.C., but I have been fortunate enough to have lived in various areas of the country before moving back to Maryland and working for PPTA. In fact I wanted to work at PPTA so much, I commuted from Delaware every day for three months! No job that I have ever held has been the same—from medical transcriptionist for a local hospital all the way through to a nuclear power plant and specialty chemical company. Each has been an enriching experience. I have been married to a most patient man, Alan, for 26 years. We have no children (unless you count the two dogs).

What is your proudest professional achievement?
Being asked to support the President of PPTA, Jan M. Bult. Jan likes to tell the story that when he said he wanted me to work for him, I asked him how long I had to think about it. Needless to say, that was not an option, and the rest is history. It has been inspiring to work for someone who is so passionate about the work we do on behalf of patients.

What is most rewarding about working in this industry?
Working with the PPTA staff and members has been a joy. Since I was diagnosed with cancer almost four years ago, I have received nothing but caring support and encouragement from everyone. I think this is what has helped me get through the constant chemotherapy and doctors. I consider myself very lucky, and I am very grateful. I don’t know how long I’ll remain on this earth, but I will continue to provide the best service possible to a wonderful group of people.

Dottie enjoys playing with her miniature collie and dachshund.
SELF-SUFFICIENCY: INTERESTING EXPERIENCES FROM FINLAND

Queens College at the University of Cambridge in the United Kingdom provided the serene and memorable backdrop for the latest International Association for Biologicals (IABS) Symposium on Advances in Transfusion Safety held in early July 2009.

In total, more than 100 experts from Europe, North America, Asia, the Middle East and Africa participated in a series of sessions. From the title of the meeting it is obvious that the main focus of the IABS and particularly this meeting was whole blood and the transfusion sector. Presented in two themes, the meeting looked at “Cutting Edge in Blood Safety” and “Issues in Developing Countries.” Of particular interest was the presentation by

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<th>Country</th>
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*It is expected that Jukka Rautonen’s presentation will be included in the report of the IABS meeting expected to be published in 2010.*
Juka Rautonen, Director of the Finnish Red Cross. Provocatively, Mr. Rautonen retitled his speech from "Self-sufficiency, free trade and safety" to "Self-sufficiency OR free trade and safety." This apparently subtle change is not without significance. It was noted that, "complaints and concerns [about self-sufficiency] only appear to arise when the incumbent producer is bypassed . . .". Developing this theme, data was presented that demonstrates some of the less obvious side effects of self-sufficiency. The sometimes blurry line between the collection of blood for transfusion, the separation of blood components and, from this, the availability of plasma for fractionation was demonstrated. Comparing a standard quantity of red blood cell units and platelets, the data showed the wide range in the price of blood.

The Finnish Red Cross experience with contract fractionation and the associated commitment to their blood donors to maximizing the quantity of immunoglobulins and other plasma proteins from their donations proved the most interesting. Mr. Rautonen, explained the decision to change the fractionation organization entrusted with fractionating Finnish plasma from one "that was providing less than three grams of immunoglobulin per liter to a new one contracted from January 2010 to provide more than five grams per liter." This means that in return for the "58 tons of plasma" for fractionation collected each year in Finland, the Finnish Red Cross will receive back over 300 kilograms of immunoglobulin, compared to barely 150 kilograms under the existing contract fractionation arrangement.

The therapeutic need for plasma proteins grows every year and still the high number of undertreated patients or those not even diagnosed persists. The extra 150 kilograms of immunoglobulin available to the Finnish health system reduces the demand from other sources. Apart from the obvious appeal of not wasting this quantity of this lifesaving medication, it demonstrates the true value of ensuring all plasma for fractionation is efficiently used and underlining the benefit of sustained investment in state-of-the-art production.

IABS (International Association for Biologicals) is an independent, non-profit scientific organization, which was founded in Lyon, France, in 1955 by a group of independent experts who identified an urgent need for an improvement in the quality and comparability of the data being exchanged between scientists working in research, development, production, standardization and regulation of human and veterinary biological products.

Charles Waller is PPTA’s vice president, PPTA Europe
While constant vigilance remains necessary, the efforts made by industry and regulators to enhance and maintain the safety of hemophilia therapies have resulted in a total absence of historical viral transmissions by these products in North America and Europe for almost two decades. The measures introduced to address the risks of the historically important agents—human immunodeficiency virus (HIV), hepatitis B virus (HBV) and hepatitis C virus (HCV)—have proven to be robust enough to deflect the entry of other emerging agents—such as West Nile Virus—which infected the blood supply, but did not affect chronic users of plasma protein therapies.

Prions were unknown when viral inactivation processes were developed and these abnormal proteins cannot be inactivated by the manufacturing steps which kill viruses without damaging the protein product. However, the purification methods that are used for many of the currently available hemophilia therapies contribute to removing a large amount of contaminating prions that may be in the blood of individuals exposed to variant Creutzfeld Jakob disease (vCJD). Authorities such as the U.S. Food and Drug Administration (FDA) in the U.S. and similar regulators in Canada, Europe and Australia have performed risk assessments, which take into account issues such as the amount of vCJD infective agent in blood and the capacity of a manufacturing process to clear prions in order to estimate the actual risk to which patients may have been exposed.

Patients have been troubled and confused as these estimates have varied greatly from country to country and from agency to agency. This has happened because the parameters used to calculate the risk, such as the amount of vCJD agent in blood and the number of persons in a —donor population that are infected, are very uncertain and each country and agency have their own views on what is an accurate estimate for these uncertain parameters. Most estimates agree that while the risk is small, it is, on a relative scale, higher for hemophilia patients who are exposed to a lot of product. With the high prion clearance of most modern concentrates, this risk becomes vanishingly small. It is probable that a patient with hemophilia found to have the vCJD prion in his spleen after he died from other causes in the United Kingdom (UK) was infected by a low purity Factor VIII product available in the UK at the time that the infection was highest in the population. It is important to emphasize that this product is not representative of most Factor VIII products available today, which are of higher purity and which have been shown to have high levels of prion clearance. As the possibility of testing for vCJD and removing vCJD with specific filters arises, the safety of products can be expected confidently to continue to increase.
Unfortunately, as the safety of therapies continues to increase, the promise they impart to patients who aspire to a normal life is dented through impediments to access. The continued thrust by the so-called “self-sufficiency” movement to exclude products from the market that are not sourced from national plasma sources threatens the life and well-being of many patients. In Europe, the capacity of all the countries of the European Union to manufacture FVIII from European plasma is less than two international units per head of population, a level which is completely unreflective of modern standards of care. For European countries, which are still dependant on plasma-derived therapies, this bodes ill if the ever-present threat embedded in the European blood directive to exclude other plasma sources is brought into effect. In other countries, products that would enhance patient care have been approved by the relevant regulatory agencies, only to be denied reimbursement and, therefore, access. Increasing access through competition with the entry of new players on the market is claimed to be the reason for the current debate on biosimilars and the consideration of factor concentrates as therapeutically equivalent drugs irrespective of their manufacture. This is an area fraught with risk for the patients, as factor concentrates, derived from a biological source and manufactured in a multitude of ways, can differ significantly in their final structure, composition and clinical effect. Treating the 250,000 kilo Dalton FVIII molecule like a 300 kilo Dalton generic pharmaceutical is misguided and dangerous, as has been stated by the European Medicines Agency, which has stated that hemophilia therapies cannot be considered as biosimilars. Moves to consider them as such in the United States, and to abbreviate the regulatory path for their scrutiny prior to market approval, is ill-advised.

“hemophilia care over the past 40 years has constituted a story of continual progress...”

As payers feel increasingly the effect of the global economic downturn, the pressure to scrutinize expensive hemophilia therapies and compare them to other possible therapeutic options is increasing. Obviously, ensuring that therapies are achieving the optimal effectiveness in patients is important. However, it is important to recognize that hemophilia care over the past 40 years has constituted a story of continual progress, and there is still much to be done. It is dangerous to compare interventions to the “current standard of care” when this standard is shifting as new and better products and therapeutic strategies are evolving rapidly. Some years ago the idea of full prophylaxis, of longer-acting factor therapies and of a possible cure through gene therapy, were all unthinkable. The “standard of care” 25 years ago was one unit of Factor VIII per head of population. These considerations need to be built into any comparative assessment of hemophilia therapies. So that the past becomes a basis for the present, and a launching pad for a better future.

Prof. Albert Farrugia is PPTA’s senior director, Global Access
Whether Bird or Swine Flu
Are you prepared?
FOUR YEARS AGO, THE TERM PANDEMIC INFLUENZA became part of our everyday vernacular. The pandemic pandemonium was triggered by the H5N1 influenza virus or bird flu that was spreading from birds to humans on a limited basis in parts of Asia. The severity of this particular strain raised concern with health officials as H5N1 began to appear sporadically in other parts of the world. Health officials began to emphasize that the world should brace for the first possible pandemic influenza of the 21st century.

What is pandemic influenza?
It is a global influenza outbreak, where everyone is susceptible. It occurs when there is a novel human influenza A subtype, which causes serious illness and spreads easily from human-to-human. The H5N1 virus does not spread easily from human-to-human. The lack of transmission provided the world time to plan for the possible crippling effects of a pandemic. The World Health Organization (WHO) in an effort to assist with pandemic planning developed a six-phased alert system that would signal the eminence of a pandemic. The United States and many European countries produced checklists, which serve as a springboard for pandemic planning, based on these phases. The question everyone began to wonder was whether we were prepared? This topic was debated nightly in the news, and numerous conferences were held to assist people with planning.

As Bird Flu Frenzy Subsides, Swine Flu Emerges
However, as the WHO pandemic alert level remained constant, the stories regarding H5N1 became intermittent, and slowly pandemic pandemonium died down. People began to place pandemic planning to the side until the spring of this year when an outbreak of a novel influenza virus caught some by surprise—swine flu. A few sporadic cases of swine flu or H1N1 had been identified in the United States, while an almost silent epidemic was building in Mexico. It was not until about 75 students at a New York school fell ill did the world take notice. It seemed within days of the increased attention, the virus had spread rapidly within Mexico and parts of the U.S.

WHO Alert Levels Quickly Climb
Quickly, health officials around the world moved from scenario development to response and mitigation. On April 26, 2009, the U.S. Department of Health and Human Services (HHS) issued the first of several nationwide public health emergency declarations. A day later the European Health Union advised Europeans to postpone non-essential travel to the U.S. and Mexico. Within weeks the WHO alert level that had remained stagnant moved from three to five. By June, the WHO declared that a global pandemic of H1N1 flu was underway.

FDA Approves Four Vaccines for H1N1
To mitigate the spread of the virus, vaccine development became essential. The U.S. Food and Drug Administration (FDA) announced the approval of four vaccines on September 15. The European Medicines Agency (EMEA) approved two vaccines for pandemic influenza on September 25. Health officials determined that certain priority groups who are at higher risk of medical complications from influenza should receive the vaccine first. Those groups comprise healthcare workers, pregnant women, caregivers for children younger than six months, people ages six months to 24 years-old, and persons aged 25 through 64 years old who have health conditions with certain medical conditions.

As of October 25, worldwide there have been more than 440,000 laboratory confirmed cases of pandemic influenza. These numbers do not reflect actual progression of the disease as some countries have stopped testing every case. Worldwide, the WHO attributes 5,700 deaths to the virus since April 2009. As H1N1 continues to spread, it is important to note that we all play a vital role in mitigating the spread of the disease. The keys to mitigation are vaccination of priority groups, robust hand-washing practices by everyone and people staying at home when sick. Continued vigilance by all is necessary to ensure a healthy population.

BRIDGET ELIS is PPTA’s assistant director, Regulatory Policy
Partnering for Rare Disease Therapy Development

**Policy Continuity and Funding**

For rare diseases threatened by economic downturn—EPPOSI calls for policy continuity and continued research to ensure the best quality health care in Europe.

For its 10th Workshop on Rare Diseases Therapy Development, the European Platform for Patients’ Organizations, Science and Industry (EPPOSI) appropriately chose as its host city, Brussels, the capital of the European Union, where 10 years ago the EU Regulation EC 141/2000 on orphan medicinal products was unanimously approved by the European Parliament.

The workshop brought together representatives from EU and member state institutions, patient groups, physicians, politicians, researchers and industry in the presence of Her Royal Highness Princess Astrid of Belgium. Topics addressed during the event included funding for rare disease research, earlier and timely diagnosis and patient access to orphan medicines and care given to the economic crisis in Europe.

Alastair Kent, Chair of EPPOSI, opened the event with an overview of the progress made over the past decade and reflected on the next 10 years and on upcoming challenges and opportunities for the treatment of rare diseases. Dr. Yolande Avondroodt, member of the Federal Parliament of Belgium, followed with an opening speech explaining progress made in Belgium towards the creation of a National Plan for Rare Diseases, which is expected to be implemented in 2011.

Commenting on the impact of the economic downturn on the rare diseases field, a representative from the Belgian National Health Institute (INAMI) explained how new paradigms in reimbursement mechanisms are under consideration, while reassuring participants that a recent survey indicated no particular threat from an economic standpoint on access to rare diseases therapies. In her speech, Ségolène Aymé, Orphanet, mentioned the increasing financial challenges facing the rare diseases sector and highlighted the "need to provide cost-effectiveness data on the reality of the rare diseases sector." During a live survey carried out during the event, an overwhelming majority of the participants agreed that too much attention was being given by policymakers on the cost per person when discussing rare diseases therapy funding.

Later in the congress, it was pointed out that cost containment measures should target the financial “wastage,” which occurs on a daily basis with a number of inefficacious
mainstream pharmaceuticals being misused, but still granted reimbursement. Therapies that treat rare diseases, which are most often lifesaving or life-enhancing, and still only represent a modest proportion of general health care budgets, should be prioritized regardless of the economic environment. The increasing use of Health Technology Assessments (HTAs) to assess the clinical added value of orphan drugs and as a cost containment measure was also highlighted.

During a session focusing on sustainable access to orphan drug products at the national level, Larry Warren spoke on behalf of Alpha Europe and the recently created Platform of Plasma Protein Users (PLUS), to highlight the challenges facing patients affected by rare plasma related disorders. In his speech, he stressed the importance of ensuring a sustained access to plasma protein therapies in Europe. While orphan drugs are used to treat rare diseases, other therapies, such as plasma protein therapies, also are used to treat rare diseases and are faced with similar challenges, although they do not have an orphan drug status. PLUS will be organizing its first stakeholder meeting to discuss these issues on January 7-8, 2010 in Dublin, he said. Mr. Warren also pointed out the discrepancies with regard to the availability of alpha-1 antitrypsin deficiency therapies, which varies from member state to member state.

In conclusion, the following recommendations were made during the workshop:

- Additional targeted policy measures and incentives need to be identified to promote R&D in the field of rare diseases and orphan drugs;
- Doctors’ awareness and education needs to be raised in order to improve the chances for early diagnosis of rare diseases, and for enabling more research;
- Continuation of the orphan drug regulation 141/2000 received strong support as orphan drug development and availability could not rely on a free market to attract investments and drive innovation for rare diseases;
- European collaboration for the assessment of clinical added value of orphan medicines was strongly supported and participants called for immediate creation of the Working Party at the EMEA;
- Orphan medicines should be conditionally reimbursed in Member States upon approval at EU level, subject to revision when more data become available, based on the revised report on the clinical added value;
- Rare cancers must continue to be included in public policies for rare diseases and orphan medicines;
- Transparency about pricing, budgets and total impact of orphan medicines needs to be improved; and
- Priority needs to be given to setting up Centers of Expertise and European Reference Networks for diseases for which orphan drugs are approved, to speed up access and promote diagnostic and care standards.

Johan Prevot is the director of Health Policy, PPTA Europe
**SINCE PRESIDENT OBAMA TOOK OFFICE,** the Administration and Congress have maintained a focus toward passing some version of health care reform legislation. Because many Americans would argue that the United States’ health care system—from coverage to delivery—is fundamentally broken, the nation’s capital has been focused on little else since the summer. Congress has been resolute in its efforts to craft legislation that includes a sweeping system wide change intended to cover the approximately 46 million uninsured, end discriminatory practices of the insurance industry and overhaul the delivery system.

America’s escalating trillion dollar deficit is unsustainable, and President Obama has been clear—health care expenditures that are climbing nearly 20 percent annually must be brought under control in order to attain a meaningful chance of economic recovery. The goals are laudable. Pass a bill that will achieve cost savings; provide meaningful coverage; result in high quality health care; eliminate waste; improve patient access; and improve affordability—and the funding must be sustainable.

**House Passes Landmark Health Reform Bill**
The efforts of Congress and the Administration have resulted in a historical outcome—on Saturday, November 7, 2009, the U.S. House of Representatives passed comprehensive health care reform legislation that would achieve many of President Obama’s chief goals that he highlighted during his Presidential campaign, and has reinforced in recent months.

The legislation, H.R. 3962, which narrowly passed by a vote of 220-215, includes the heavily debated “public option” that proponents believe will help provide meaningful coverage for those currently without insurance. The Republican victories in recent gubernatorial elections in Virginia and New Jersey caused many Congressional Democrats take stock of their own reelection challenges, as evidenced when 39 Democrats choose to vote against H.R. 3962. Only one Republican, freshman Joseph Cao, voted in support of the bill.

**Senate Moves Forward; Challenges Remain**
The Democrats are attempting to take full advantage of their power position of controlling the House, Senate, and the White House for the first time since early in President Clinton’s first term more than 16 years ago and are optimistic that something similar to the House bill will ultimately become law. Late
HEALTH CARE REFORM

By Julie Birkofer
in the evening on November 18, Senate Majority Leader Harry Reid (D-NV) released the health reform bill, Patient Protection and Affordable Care Act, filed as a substitute amendment to the House-passed legislation. The following Saturday, the Senate voted along party lines to begin full debate. The bill intends to extend health benefits to 31 million Americans who currently are not insured at a cost of $848 billion over 10 years. Now that the Democrats have sidestepped a Senate filibuster, it will take 51 votes to pass the bill out of the chamber. Once the Senate passes its version of health care reform, it is likely a conference committee will convene to reconcile the differences between the two bills. Hurdles remain, however.

Notwithstanding the incredible achievements of the passage of House and Senate bills, the political realities in the Senate, the lack of full Democratic Caucus support in the House, and the incredibly contentious issue of whether federal funds should cover abortions indicate that much work remains for lawmakers in order to present President Obama with a bill that he can sign into law.

Industry Advocates to Preserve Patient Access

There are provisions within health care reform that would cause a sea change in how Americans receive health care. PPTA and its member companies have been focused on several aspects of the legislation that would directly affect the industry as a whole. In addition to PPTA, several recombinant manufacturers outside of the PPTA membership also have a stake in how the legislation would affect patient access to blood clotting factors. PPTA’s membership is

340B Drug Pricing Program

Designed to support federally funded clinics and hospitals that serve a large percentage of low income or uninsured patients, the 340B program offers covered entities the opportunity to purchase pharmaceuticals at steep discounts based on the minimum Medicaid outpatient drug rebate percentage. These hospitals and clinics are then able to resell these drugs to patients at or near market value, so the patients do not directly benefit from the discount. PPTA is concerned that expanding this program, which has already grown by more than 1,000 percent in the last decade, without an equitable improvement of program integrity could create both short-term and long-term patient access impediments.

Legislation in the Senate would expand the 340B program by increasing the types of entities eligible to qualify for 340B pricing, mandating that manufacturers sell product to 340B covered entities, extending 340B pricing to inpatient sales, and relaxing in certain instances the current prohibition against disproportionate share hospitals (DSH) using group purchasing organizations (GPOs) to purchase covered outpatient drugs. The bill would also require a study of the 340B program by the Government Accountability Office (GAO) within 18 months of enactment. The proposed study would examine, among other things, whether mandatory sales of certain products to 340B covered entities could hinder patient access to these therapies through any provider.

Like the Senate bill, H.R. 3962 also would add new covered entity types and mandate sales. The House bill would not, however, extend 340B pricing to inpatient sales, nor would it create exceptions to the DSH GPO prohibition. The GAO study also is not included in H.R. 3962.

Comparative Effectiveness Research (CER)

Because an interoperable health information technology system will soon be a reality in the U.S. as a result of provisions in the economic stimulus bill signed into law earlier this year, there is unlimited potential for CER as a key component of a rapid learning network tool for physicians. While federally funded CER has been occurring for more than a decade, the creation of an independent CER entity has been a top priority for both the Administration and Congress. CER, however, has the potential to affect access to plasma protein therapies if study outcomes are used to support national coverage determinations or restrictive formularies.

Fortunately, the Senate bill, would help preserve patient access by requiring the new CER institute, each time there
is a proposed CER study on a rare disease, to appoint an “expert advisory panel for rare diseases” to assist in the design of such research study and determine “the relative value and feasibility of conducting such research study.” The panel would include practicing and research clinicians, patients and patient representatives with experience in the relevant topic, project, or category for which the panel is established. Additionally, this panel would be permitted to include a representative of each manufacturer of each medical technology that is included in the relevant research topic project or category for which the panel is established.

The House bill, however, does not include a similar protection for patients with rare diseases.

Pathway for Biosimilars
Both the House and Senate health care reform bills include a provision creating an abbreviated Food and Drug Administration (FDA) approval pathway for biologicals that can prove biosimilarity to an innovator product. Such a pathway obviously raises considerable patient safety concerns. Interestingly, the European Medicines Agency (EMEA), which already has a process for biosimilars in place, has stated that it will not accept an abbreviated application for a biosimilar referencing IVIG or blood clotting factors (both plasma-derived and recombinant). Congress has unequivocally indicated, however, that it will not carve out any product classes in legislation.

Of significant concern to PPTA is that neither bill would require FDA to promulgate product class-specific guidance on biosimilarity, interchangeability, and immunogenicity prior to consideration and approval of an abbreviated BLA. The key point of contention among stakeholders in the overall debate surrounds the number of years of non-patent market exclusivity to which the innovator product should be entitled. Both the House and Senate bills contain 12 years of such exclusivity.

Congress will optimize its cost savings from biosimilars by modifying Medicare reimbursement to create new classes of reimbursement for interchangeable biosimilars and non-interchangeable biosimilars. Generally, under the House bill, interchangeable biosimilars would be reimbursed according to the volume-weighted ASP plus six percent of it and the reference product, while non-interchangeable biosimilars would be reimbursed according to their own volume-weighted ASP plus six percent of the reference product’s ASP.

Learn more: If you would like to join PPTA’s advocacy for patient access to plasma protein therapies, contact Kym Kilbourne at 443-458-4682 or via email at kkilbourne@pptaglobal.org.

Julie Birkofer is PPTA’s vice president, North America. Jay Greissing and Kym Kilbourne contributed to this article.
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Samuel is no stranger to spending his life helping those in need. When he began donating, he was working for Gateways to Better Living, an organization that helps individuals diagnosed with mental retardation and developmental disabilities. He was 22 years-old when he learned that he could help others by donating plasma. When Samuel first ventured into the plasma center, he left without donating because he was a bit nervous and apprehensive about the process. A couple of days later, Samuel’s drive to help others gave him the inspiration he needed to overcome his reservations, and he successfully donated plasma on this visit. He never imagined back then that he would still be donating plasma regularly more than a decade later.

Samuel goes on to say he equates donating his plasma to, “two hands washing each other.” He explains that while he is helping someone in need, the compensation he receives can be used to pay off a bill or to help make the holidays a little merrier. While he finds the atmosphere at the center a positive one, he also enjoys the camaraderie between the staff and donors.

Alvin, Samuel’s younger brother, began donating after his 18th birthday with some encouragement from Samuel. Now 29, Alvin says donating plasma gives him a good feeling, plus he enjoys visiting the center and has built relationships with the staff and other donors as well.

Both brothers have contributed to various specialty programs through the years, and added that it gave them even more satisfaction knowing that their plasma is being used for additional products.

While they had always hoped that no one they knew would experience a need for a lifesaving plasma-derived therapy, about five years ago that is exactly what happened. Their two-year-old godson grabbed a coffee pot and sustained burns over 35 percent of his body. The boy received a plasma-derived therapy to help aid his recovery. This solidified their belief that what they are doing is well worth their time and commitment.

Biotest Pharmaceuticals provided this article to The Source.
Maintaining a cadre of healthy donors is essential for the manufacture of lifesaving plasma protein therapies. A donor's good health is important to ensure safe and effective final therapies for patients, but it is also of paramount importance to protect the donor's health. Aspects of donor safety and how plasma companies provide oversight for donor health were recently discussed with corporate medical directors. These medical directors serve PPTA as the Medical Directors Task Force and address specific issues related to the donors and donation experience for the association. The medical directors are responsible for setting medical policies for their companies and providing training and oversight of clinical/medical personnel at the plasma collection centers. First and foremost, the medical directors agree that a donor's health and safety are most important.
Donor health is a primary consideration in the donor selection process. Prospective donors are screened using a health history questionnaire and a physical examination designed to ensuring that the donor is healthy, both for the plasma donated and for the donation procedure. During this process, donors are provided information about plasma donation including: general health parameters, tests that are performed both to ensure the safety of the plasma collected and that the donor is healthy to donate, and any risks associated with donating plasma (inform consent). The one-to-one opportunity for the prospective donor to be interviewed and examined by the center’s clinical/medical personnel is considered most important in determining the donor’s fitness for donation. This time also is used to help educate the donor about the center’s deferral policies as they relate to health. For example, the donor is informed that the trained center staff will monitor the donor’s plasma protein levels to ensure that the donor replaces proteins lost in the plasma donation. If the plasma protein drops below a certain level, the donor will be deferred from donating until an acceptable plasma protein level returns.

In addition to monitoring protein levels, the center personnel provide guidance on the importance of maintaining a healthy diet with adequate protein and fluids. This helps minimize the possibility of the donor’s level dropping below the acceptable level and encourages donors to make healthy food choices. Donors are asked about medical treatments and medications, as this information may point to an underlying condition that would indicate a potential difficulty with the donation. While the donor answers a donor history questionnaire at each donation, it is in the context of the physical examination (performed initially before a donor starts a donation program and at least annually thereafter) that valuable information is obtained about the donor’s health that helps the center determine whether the donor is healthy enough to donate and provides the center the opportunity to educate the donor about how to maintain a healthy lifestyle.

One of PPTA’s voluntary standards is the Donor Education Standard. This standard requires that plasma collection centers provide information to the donor regarding risk behaviors (protecting the safety of the plasma) and also encourages that information be provided on steps to be taken by the donor to have a healthy lifestyle (helping to protect the donor.) This information may include pointers on nutrition, hydration, and smoking cessation.

It is important to note that donor education is of paramount importance. However, center staff are careful not to cross the line between education and diagnosis. Whenever a question arises as a result of the physical examination, test results or medical history, the donor is referred to his personal physician. In fact, it is common practice to include the donor’s physician in deciding whether the donor can start or continue a plasmapheresis program whenever there is a question of whether or not the donor is healthy to donate. If a prospective donor does not have a personal physician, he is referred to local clinics.

Concern about the safety of the donor continues to the plasmapheresis procedure itself. Donors are constantly observed and monitored while donating. Plasma donation is a very safe process, in large part because of the care exerted by the staff and the elaborate safety and quality measures that have been developed through regulation, voluntary industry standards, and best industry practices.

Donors are the cornerstone of our industry. Without donors committed to participate, there would be no plasma protein therapies for the patients whose lives depend on it. Keeping donors healthy through education and monitoring is an important function of the medical staff of the collection centers. Healthy donors are in everyone’s best interests, and nothing is taken more seriously by plasma collection facilities than the safety and welfare of plasma donors.
Can you tell us more about angioedema due to C1 Inhibitor deficiency?

Angioedema due to C1 inhibitor deficiency can be either hereditary or acquired and manifests as spontaneous edema (swelling) of the skin, the face, the extremities and, most worryingly, on the intestinal and laryngeal mucous membrane. Laryngeal edema, if untreated, can cause death by asphyxiation.

Three different types of angioedema exist and the most common (type 1) can be diagnosed by testing levels of C1 inhibitor, a protein found in human plasma. C1 inhibitor levels are extremely low in people affected by type 1 angioedema, which is the most common form.

During these last few years, two very effective treatments for angioedema have become commercialized. The first, a C1 Inhibitor concentrate (the missing blood protein) that is administered intravenously, is a plasma-derived product used to treat angioedema attacks. This treatment stops the development of the edema within a few hours, and prevents it from recurring during the days that follow. A second form of treatment is a medicine that blocks the activity of bradykinin, a vasodilator substance naturally present in human blood, but at higher levels in people with angioedema. It helps efficiently in blocking the onset of angioedema attacks.

When patients are properly diagnosed and treated, their quality of life is very good, and it is possible for them to forget about the disease almost completely. Unfortunately, this is not the case for all patients, and especially not those who have not yet been diagnosed. What has been noticeable for some time is that patients are starting to have a good knowledge of the different treatment options, as well as an increased dialogue with their physicians, in order to find the most suitable treatment for them.

Can you tell us more about HAEI and its work?

HAEI is an umbrella organization that represents 13 countries with active patients’ organizations. It was founded in 2004, after several meetings between national association representatives. At the time, it seemed natural to gather various national patient organizations together as they pursued the same objectives—e.g., increased awareness and improved access to safe and efficient treatment. The advantage of an umbrella organization is better liaison with various stakeholders such as physicians, research centers, the industry, health authorities and so on.

Unfortunately, due to a lack of coordination, the association did not grow and progress as we had originally wished. However, this should change in future months, thanks to the support of the industry; our President, Anthony J. Castaldo; and our new Executive Director, Henrik Boysen, who will take things in hand to accelerate the projects’ pace.

One of HAEI’s main priorities is to inform patients about the range of treatments available to them. The chief difficulty is that the level of access to treatments differs from one country to another, according to each country’s medical infrastructure. Another priority for HAEI is to help countries with no patient organizations to create their own. This process generally happens with the help of patients and physicians and, once done, HAEI provides guidance to newly-founded associations on how to improve access to treatment.

The Source | Winter 2009
When did your work with AMSAO start?
I created AMSAO in 1997, with the help of some of my family members who were equally concerned with this disease. Originally, our main priority was to get access to information about the disease, the available treatments, the location of specialized physicians, the state of the research and greater understanding of the disease in general. At that time, finding this kind of information was hard, even for the patients themselves. The main problem was a lack of expertise among health care professionals in France.

Today, with the support of specialized health care professionals, AMSAO provides information to patients regarding their treatment options, as well as advice on how to tackle the disease and information regarding the state of research at the European level on the identification of complex mechanisms developing angioedema. These are patients’ main priorities, especially finding a personalized treatment in order to get the best quality of life despite the disease. This is done through specialized reference centers.

In the past years the European Union and subsequently national governments in Europe have been implementing new policies to increase rare disease diagnoses and treatment.

What was the impact of these policies for patients and for patients’ organizations?
European Union policies have motivated Member States to address the rare diseases issue in Europe.

In France, for example, this effort resulted in the creation of a (specialized) medical reference center in Grenoble.

This center brings together a wide variety of medical experts, such as genetic scientists, clinicians, biologists, etc. This multidisciplinary approach makes research progress faster. Moreover, the center is very active at the European level by sharing its research advances and monitoring other countries’ progress. Following the creation of the reference center in Grenoble, seven branches have been established in France, creating a network across the country. These centers work closely with AMSAO, in order to diffuse information regarding scientific advances efficiently and effectively to patients.

What has been your proudest achievement in your work?
Through AMSAO’s work, my proudest achievement was to make C1 Inhibitor available to ambulatory patients in France. Traditionally, patients needed to go to a hospital to get the drug administered and, at the time of AMSAO’s creation, most hospitals did not have this medicine available. This proved to be a relief for patients as they could access the treatment whenever needed.

Laura Savini is PPTA’s national affairs assistant, Europe
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AGENDA

TUESDAY 16 MARCH 2010
Session 1: Keynote session
- Pandemic preparedness
- State of the industry
- FIND-ID: The role of immunodeficiency centers

Session 2: Health care funding
- Consequences of the financial crisis on health care funding
- HTAs - The European perspective
- U.S. developments in health care reform
- A patient’s perspective
- A physician’s perspective

Session 3: Rare diseases policies, from the EU to the member state
- Rare diseases: How can the EU help the member states?
- EU Parliament recommendations for member states
- Impact of EU policies on member states: The patient’s viewpoint
- National healthcare budgets and rare diseases
- Germany: Actions on rare diseases

Session 4: Regulation: Critical considerations
- Regulatory leadership: Combatting regulatory creep
- EDQM progress report towards international harmonization
- European initiative for better regulation: Did it work?
- How can science provide regulatory relief?
- Clinical trials for small patient populations - thinking outside the box

WEDNESDAY 17 MARCH 2010
Session 5: Beyond normal source plasma
- Hyperimmunes: The latest developments
- Collecting hyperimmunes: Ethical and regulatory aspects
- Convalescent plasma
- Collecting plasma and blood: A working model
- Regulation: A barrier to self-sufficiency

Session 6: Getting the plasma we need
- Plasma demand in 2015
- The European Commission’s perspective
- Plasma collector’s perspective
- Patient’s perspective

Session 7: Therapy developments
- CIDP
- ITP
- “Gold standard” for hemophilia care
- Regime of hemophilia care in Russia: How did you get there?
- Albumin

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IN MY VIEW

QUALITY AND SAFETY OF THERAPIES ARE PARAMOUNT

I AM WRITING THIS COLUMN in an airplane on my way from Australia to Japan. I have a one-day stop-over in Bangkok and will use that time to meet with Thai authorities to talk about the quality and safety of plasma protein therapeutics.

Quality and safety are two of the most important factors to be considered when it comes to choice of therapy. Government purchasers are understandably cost-conscious, but when a country decides to work with tenders it should also insure that the resulting therapies it receives meet the strongest criteria that are set for therapies licensed in regions like Europe and North America.

Thailand puts a lot of importance in the World Health Organization (WHO) and European Medicines Evaluation Agency (EMEA) guidelines. The WHO guidelines on manufacturing are rather vague, not very specific and tailored to support developing countries. The EMEA, however, is very specific when it comes to quality and safety. A lot of attention is paid to the plasma that is used in the manufacturing process and detailed information needs to be provided about all centers where the plasma is collected. European and U.S. Food and Drug Administration (FDA) inspectors visit each center in Europe and the United States on a regular basis to ensure compliance with stringent regulatory requirements. But when a country decides to go with therapies manufactured in China, then it is difficult to see how that company can comply with the requirements knowing that none of their therapies has gone through the European regulatory process.

All of PPTA's global member companies have their therapies licensed in multiple countries and comply with these requirements. In addition, the voluntary standards programs—the International Quality Plasma Program or IQPP (for plasma) and the Quality Standards of Excellence, Assurance and Leadership, or QSEAL, (for therapies) — provide additional evidence that our companies are serious about their commitment to quality and safety.

I understand that price is an important consideration when it comes to tenders, but the quality and safety of therapies must be the driving force. The criteria primarily should be set on quality and safety of the therapies. I remember that a few years ago I met with health authorities in Mexico City. Unsolicited, we were told about an experience they had with a Chinese company that was bringing albumin to their country. The authorities had some concerns and decided to perform inspections on the product. Even though several specifications were checked and were within the required range, the authorities continued to have concerns and decided to send an inspection team to the manufacturing plant in China. During that inspection, multiple violations of good manufacturing practices were discovered and the result was that the import license was suspended. I hope this will not happen again.

The member companies in PPTA take their job seriously and can easily meet the requirements as set forth by the Thai authorities. One thing must be understood—quality and safety come at a price. Competing on price is good and healthy, but quality and safety should not be sacrificed.
IN MY VIEW
Quality and Safety of Therapies Are Paramount

PPTA INTERVIEW
Michel Raguet
Discuss C1 Inhibitor Deficiencies

Healthy Donors:
The Cornerstone of Plasma Therapies
Maintaining Cadre of Healthy Donors Is Essential
for Manufacture of Plasma Protein Therapies

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