Healthcare Delivery
Lost in Red Tape?

Treating Children: A Team Sport

IG Treatment: Infusing at College

Diagnosing an Antibody Deficiency

The Skin Cancer & PIDD Connection
GAMUNEX®-C
Immune Globulin Injection (Human) 10% Caprylate/Chromatography Purified

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use GAMUNEX®-C safely and effectively. See full prescribing information for GAMUNEX-C.

GAMUNEX-C, (Immune Globulin Injection (Human) 10% Caprylate/Chromatography Purified)
Initial U.S. Approval: 2003

WARNING: ACUTE RENAL DYSFUNCTION and FAILURE
See full prescribing information for complete boxed warning.

- Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur with immune globulin intravenous (IGIV) products in predisposed patients.
- Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. GAMUNEX-C does not contain sucrose.
- For patients at risk of renal dysfunction or failure, administer GAMUNEX-C at the minimum concentration available and the minimum infusion rate practicable.

---------INDICATIONS AND USAGE---------
GAMUNEX-C is an immune globulin injection (human) 10% liquid indicated for treatment of:

- Primary Humoral Immunodeficiency (PI)
- Idiopathic Thrombocytopenic Purpura (ITP)
- Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

---------CONTRAINDICATIONS---------
- Anaphylactic or severe systemic reactions to human immunoglobulin
- IgA deficient patients with antibodies against IgA and a history of hypersensitivity

---------WARNINGS AND PRECAUTIONS---------
- IgA deficient patients with antibodies against IgA are at greater risk of developing severe hypersensitivity and anaphylactic reactions. Have epinephrine available immediately to treat any acute severe hypersensitivity reactions.
- Monitor renal function, including blood urea nitrogen, serum creatinine, and urine output in patients at risk of developing acute renal failure.
- GAMUNEX-C is not approved for subcutaneous use in ITP patients. Due to a potential risk of hematoma formation, do not administer GAMUNEX-C subcutaneously in patients with ITP.
- Hyperproteineemia, with resultant changes in serum viscosity and electrolyte imbalances may occur in patients receiving IGIV therapy.

---------ADVERSE REACTIONS---------
- PI – The most common adverse reactions (≥5%) with intravenous use of GAMUNEX-C were headache, cough, injection site reaction, nausea, pharyngitis and urticaria. The most common adverse reactions (≥5%) with subcutaneous use of GAMUNEX-C were infusion site reactions, headache, fatigue, arthralgia and pyrexia.
- ITP – The most common adverse reactions during clinical trials (reported in ≥5% of subjects) were headache, vomiting, fever, nausea, back pain and rash.
- CIDP – The most common adverse reactions during clinical trials (reported in ≥5% of subjects) were headache, fever, chills, hypertension, rash, nausea and asthenia.

To report SUSPECTED ADVERSE REACTIONS, contact Talecris Biotherapeutics, Inc. at 1-800-520-2807 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------DRUG INTERACTIONS---------
- The passive transfer of antibodies may transiently interfere with the response to live viral vaccines, such as measles, mumps and rubella. Passive transfer of antibodies may confound serologic testing.

---------USE IN SPECIFIC POPULATIONS---------
- Pregnancy: no human or animal data. Use only if clearly needed.
- Geriatric: In patients over 65 years of age do not exceed the recommended dose, and infuse GAMUNEX-C at the minimum infusion rate practicable.

Thrombotic events have occurred in patients receiving IGIV therapy. Monitor patients with known risk factors for thrombotic events; consider baseline assessment of blood viscosity for those at risk of hyperviscosity.

Aseptic Meningitis Syndrome (AMS) has been reported with GAMUNEX-C and other IGIV treatments, especially with high doses or rapid infusion.

Hemolytic anemia can develop subsequent to IGIV therapy due to enhanced RBC sequestration. Monitor patients for hemolysis and hemolytic anemia.

Monitor patients for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI]).

Volume overload

GAMUNEX-C is made from human plasma and may contain infectious agents, e.g., viruses and, theoretically, the Creutzfeldt-Jakob disease agent.

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Important Safety Information for GAMUNEX-C

Gamunex-C, Immune Globulin Injection (Human), 10% Caprylate/Chromatography Purified, is indicated for the treatment of primary humoral immunodeficiency disease (PI), idiopathic thrombocytopenic purpura (ITP), and chronic inflammatory demyelinating polyneuropathy (CIDP).

Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur with immune globulin intravenous (IGIV) products in predisposed patients. Patients predisposed to renal dysfunction include those with any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. Gamunex-C does not contain sucrose. For patients at risk of renal dysfunction or failure, administer Gamunex-C at the minimum concentration available and the minimum infusion rate practicable.

Gamunex-C is contraindicated in individuals with acute severe hypersensitivity reactions to Immune Globulin (Human). It is contraindicated in IgA deficient patients with antibodies against IgA and history of hypersensitivity.

Gamunex-C is not approved for subcutaneous use in patients with ITP or CIDP. Due to the potential risk of hematoma formation, Gamunex-C should not be administered subcutaneously in patients with ITP.

Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving IGIV therapy.

Thrombotic events have been reported in association with IGIV. Patients at risk for thrombotic events may include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, coagulation disorders, prolonged periods of immobilization and/or known or suspected hyperviscosity.

There have been reports of noncardiogenic pulmonary edema [Transfusion-Related Lung Injury (TRALI)], hemolytic anemia, and aseptic meningitis in patients administered with IGIV.

The high dose regimen (1g/kg x 1-2 days) is not recommended for individuals with expanded fluid volumes or where fluid volume may be a concern.

Gamunex-C is made from human plasma. Because this product is made from human plasma, it may carry a risk of transmitting infectious agents, e.g., viruses, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

After infusion of IgG, the transitory rise of the various passively transferred antibodies in the patient’s blood may yield positive serological testing results, with the potential for misleading interpretation.

In clinical studies, the most common adverse reactions with Gamunex-C were headache, fever, chills, hypertension, rash, nausea, and asthenia (in CIDP); headache, cough, injection site reaction, nausea, pharyngitis, and urticaria with intravenous use (in PI) and infusion site reactions, headache, fatigue, arthralgia and pyrexia with subcutaneous use (in PI); and headache, vomiting, fever, nausea, back pain, and rash (in ITP).

The most serious adverse reactions in clinical studies were pulmonary embolism (PE) in one subject with a history of PE (in CIDP), an exacerbation of autoimmune pure red cell aplasia in one subject (in PI), and myocarditis in one subject that occurred 50 days post-study drug infusion and was not considered drug related (in ITP).

*CIDP=Chronic inflammatory demyelinating polyneuropathy; PI=Primary immunodeficiency; ITP=Idiopathic thrombocytopenic purpura.


You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see adjacent page for brief summary of GAMUNEX-C full Prescribing Information.
Healthcare Delivery: Lost in Red Tape?
“Despite good intentions by all, many of the patients may never get the help they need for many reasons, all of which lie in the workings of a healthcare system that fails to focus on the patient, but instead results in a rationing of healthcare.”

Finding a Championship Team to Treat Your Child’s Immune Deficiency
“Without a doubt, parents of children with immune deficiencies need championship teams — of physicians. And, our quest to put together the best team possible can sometimes be a long, arduous process.”

How an Antibody Deficiency Diagnosis Is Made: Cases 2 and 3
“These cases illustrate the variability that a virus such as EBV can have on the immune system, and its potential role in causing antibody deficiencies.”

Connect with Other IG Living Readers through Monthly Teleforums!
IGL’s Readers Group Teleforums allow readers to connect with others to share their experiences living with chronic diseases. Here’s how you can participate:

- Email IG Living to be added to our email invitation list for the teleforums.
- IG Living will send you invitations to let you know when the two-per-month, hosted, toll-free teleforums will be held, as well as what topic relevant to the IG community will be discussed.
- The moderated, hour-long calls will be filled on a first-come, first-served basis and will be limited to 15 readers.

In addition to connecting with others, IG Living’s patient advocate can help you determine if there’s a patient organization support group in your area. Or, she can help you to start an IGL Readers Group of your own. To join a group or start one in your area, visit www.IGLiving.com and click on IGL Readers Groups.

Sign up for the Teleforums now by emailing rrhodes@IGLiving.com or calling (800) 843-7477, ext. 1362.
Editorial

Patient Dissatisfaction:
A Serious Reality

The unfortunate reality of our healthcare system is that most patients report that for every good experience they’ve had, there are an equal number of, if not countless more, poor experiences. Patients with chronic illnesses and their caregivers will be the first to confirm this reality, even if the care they currently receive is satisfactory or very good.

Quite a lot of research has been conducted relating to patient satisfaction with our healthcare system. In 2009, Advocacy for Patients with Chronic Illness Inc. and the Center for Managing Chronic Disease published a study titled Living with Chronic Illness: A Prescription for Advocacy. The study reported on a survey conducted between March 2008 and March 2009 of more than 1,500 patients with chronic illnesses and their experiences as patients. In particular, it reported on the obstacles they face and the strategies they use to try to surmount those obstacles. Among all respondents, care coordination was a significant issue. Half of respondents reported that their doctors do not communicate with each other to coordinate care, and 70 percent said they have to put in a lot of effort to manage healthcare providers and coordinate their own care. In addition, 34 percent of respondents reported that a healthcare provider had given up on them, and 58 percent felt that a doctor they saw did not understand their disease.

This disconcerting reality is not a one-sided issue. Indeed, it is not just patients who realize there is a lack of coordinated care to treat their rare and serious diseases; physicians have a keen awareness of this reality as well. In this issue, we look at both sides.

First, from a healthcare provider’s standpoint, Dr. Sue Romanick, a rheumatologist, gives us a very detailed look at what doctors often must deal with when treating patients with difficult-to-diagnose and difficult-to-treat conditions. Her heartfelt description of her journey to treat one young man shows that even with the best intentions, the workings of our healthcare system oftentimes prevent physicians from providing care in the manner they desire. These physicians frequently are left with very difficult decisions that pit their practices against patients’ best interests.

Next, Mark Haggard, father of two children with primary immune deficiency disease, describes how parents of chronically ill children struggle to get the best care for them. Likening the challenge to putting together a championship team, he provides some glaring examples, as well as useful tips to help parents ensure that their healthcare team is all on the same page of the playbook.

A lack of care coordination is a serious reality that begs to be solved. As the authors of the Living with Chronic Illness study assert, it is hoped that with changes in our healthcare system that move patients into different delivery systems, such as patient-centered medical homes and accountable care organizations, these burdens will eventually lessen.

To your health,

Ronale Tucker Rhodes, MS, Editor
Home Run Articles for Rare Diseases

Just could not help myself to say that there are two, not one but two, home runs in the February-March 2011 issue of IG Living for neuropathy patients. Matt Hansen has done it again in his article Understanding and Treating Multifocal Motor Neuropathy. [It is] an outstanding article, and I find myself so grateful that professionals are bringing such challenging medical conditions from the dark basement of medicine to the clear light of day. [It] is encouraging [for] neuropathy patients, and [it] challenges the status quo for neurological illnesses that must receive more attention in research and clinical training at the medical school level if we are ever to advance our ability to diagnose and care for these patients.

Kris McFalls hit a home run with her article An Overview of Immune Globulin Dosing. The only thing that we had [about] IVIG dosing for my chronic inflammatory demyelinating polyneuropathy (CIDP) beginning in 2004 was the struggling relationship between my responses to treatment, the neurologist who did not have much information on dosing, and Medicare, [which] wanted to deny the treatment as medically unnecessary while my illness was preventing me from breathing. If it had not been for other CIDP patients who had gone this route before and who offered great advice and insight into how to resolve the issues, the process may have killed me. ... Without my IVIG treatment today, I would not be here and for that I am grateful. The statement that we need more research on dosage needs to be screamed from the hilltops of medicine for the patients and doctors who struggle together to get it right when treating patients with little dosing information [and] knowing that one size of IVIG does not fit all.

— Lieutenant Colonel Eugene Richardson, USA (Retired), MDiv, EdM, MS
Founder/President of The Neuropathy Support Network
Executive Producer of the DVD “Coping with Neuropathy”

The article [titled] Understanding and Treating Multifocal Motor Neuropathy in your February-March 2011 issue was especially interesting and helpful. I don’t often see much information on this rare condition and [I] credit IG Living and the article’s author, Matthew David Hansen, for giving attention to this condition. I made copies of the article and shared them with some family and friends to help them understand my condition. Thank you for your high-quality publication.

— Kelly L. Caffey
Clarem ore, Okla

I just started receiving your magazine, and I am very happy with it. I find it so informative and sensitive to the needs of the immunosuppressed patients and family. I have a daughter with common variable immune deficiency. Keep up the good work.

— Mrs. Perez
Florida

Once again, IG Living comes through for my family. My daughter (who is in remission from cancer) was on the brink of delivering her baby last week. I just happened to have my latest copy of IG Living magazine, which had the fantastic article on severe combined immune deficiency. ... Since I wanted my grandson tested ASAP (my son has common variable immune deficiency and the family is riddled with autoimmune diseases), the article provided the doctor with the needed information to perform the test. Thank you, and my grandson is healthy!

— Tammy Frye Ryan

IG Living Blog Helps Others

Just wanted to drop you a note to say thank you to all those involved with IG Living. The subjects addressed in the blog are helpful and informative for anyone living with chronic immune diseases whether on IVIG or not. Though there may not be cures, there can be healing.

— Robert Brandt

The Editor replies:

The staff at IG Living post a new blog each Friday. We encourage all our readers to read the blog at www.IGLiving.com/blogengine and to post comments. If you are interested in contributing to the blog with an original post, contact us at editor@IGLiving.com.

Your feedback, opinions, suggestions and anything else you’d like to share are important! Email us at editor@IGLiving.com or visit www.IGLiving.com and go to the Be Heard/Feedback page to send your comments.
CSL Behring has published its Key Issues Dialogue — Access to Care, which addresses many of the practices that impede access to care for people with rare and serious medical disorders, as well as possible solutions. The dialogue is the most recent in the ongoing series that analyzes critical issues of importance to patients who use human plasma-derived and recombinant coagulation factor therapies and to caregivers and healthcare providers. In the dialogue, participants engage in a frank and open exchange about a wide range of issues, including evidence-based medicine, cost versus coverage decisions, step therapy, defensive medicine and tort reform, consumers’ responsibility to question necessity and cost, and the vulnerability of people with rare diseases to cost shifting through copays. The dialogue can be viewed at www.cslbehring.com/docs/554/284/FINAL%2010_14_11.pdf.

A new study shows that vitamin D is needed to activate the immune system’s response to tuberculosis (TB). Published in Science Translational Medicine, the study shows that vitamin D is necessary for the T cells, which respond to threats as part of the body’s adaptive immune system, to produce a protein called interferon that directs cells to attack the bacteria. Previous studies by the same research team found that vitamin D played a key role in producing a molecule called cathelicidin, which helps the innate immune system kill the TB virus. “At a time when drug-resistant forms of tuberculosis are emerging, understanding how to enhance natural innate and acquired immunity through vitamin D may be very helpful,” says Barry Bloom, former dean of the faculty at the Harvard School of Public Health and co-author of the study.

The findings could lead to new treatments for the lung disease that kills 1.8 million people per year. They also could be crucial to treat the disease in parts of the world like Africa, since people with dark skin tend to be more susceptible to TB and also are more likely to have vitamin D deficiencies.

**Resource**

CSL Behring Publishes Dialogue on Access to Care

**Research**

Vitamin D Activates Immune Response to Tuberculosis

**Partnership**

Angel Flight Northeast Partners with Jeffrey Modell Foundation

Angel Flight Northeast (AFNE) is partnering with the Jeffrey Modell Foundation’s (JMF) Roots & Wings program, which provides travel and related support for families whose children have been identified with a potentially life-threatening illness and require a lifesaving treatment. Under the partnership, both organizations will launch a nationwide campaign to ensure that primary immunodeficiency (PIDD) patients throughout the U.S. are able to access the medical care they need within the Jeffrey Modell Centers Network of 100 diagnostic and research centers. AFNE will serve as the U.S. clearing house for all national flight requests for patients with PIDD and their families.

“We are honored to be partnering with the Jeffrey Modell Foundation,” said Larry Camerlin, founder and president of AFNE. “JMF’s commitment to serve as a tireless, compassionate advocate on behalf of PI patients and families ensuring they have access to excellent and comprehensive care aligns perfectly with Angel Flight’s mission to provide free flights of healing and hope to patients and their families in need. Together, we can change lives one flight at a time.”
**Insurance**

**Medicare Part B Premiums Lower Than Projected for 2012**

The U.S. Department of Health and Human Services (HHS) announced that Medicare Part B premiums in 2012 will be $15.50 lower ($99.90 vs. $106.60) than previously projected and the Part B deductible will decrease by $22 to $140. In addition, because of the Affordable Care Act, people with Medicare also receive free preventive services and a 50 percent discount on covered prescription drugs when they enter the prescription drug “doughnut hole.” In 2010, 1.8 million people with Medicare received cheaper prescription drugs, while nearly 20.5 million Medicare beneficiaries received a free annual wellness visit or other free preventive services.

The majority of people with Medicare have paid $96.40 per month for Part B since 2008, due to a law that freezes Part B premiums in years when beneficiaries do not receive a cost-of-living adjustment (COLA) in their Social Security checks. In 2012, these people with Medicare will pay the standard Part B premium of $99.90, amounting to a monthly charge of $3.50 for most people with Medicare. But this increase will be offset for almost all seniors and people with disabilities by the additional income they will receive for COLA. The average COLA for retired workers is about $43 per month.

HHS also announced a $1 increase in Medicare Part A monthly premiums, as well as a $24 increase in the Part A deductible. For more information about Medicare premiums and deductibles for 2012, go to https://www.csm.gov/apps/media/fact_sheets.asp.

**Legislation**

**EEOC Issues Final Regulations Interpreting the ADA Amendments Act**

Effective May 24, final regulations published by the Equal Employment Opportunity Commission (EEOC) protect many more employees from disability discrimination in the workplace than had previously been the case under the courts’ narrow interpretations of the Americans with Disabilities Act (ADA) and the ADA Amendments Act (ADAAA).

According to an EEOC press release, “The ADAAA and the final regulations keep the ADA’s definition of the term ‘disability’ as a physical or mental impairment that substantially limits one or more major life activities; a record (or past history) of such an impairment; or being regarded as having a disability. But the law made significant changes in how those terms are interpreted, and the regulations implement those changes.”

The regulations provide a list of principles to guide the determination of whether a person has a disability, including that an “impairment need not prevent or severely or significantly restrict performance of a major life activity to be considered a disability.” Whether an impairment is a disability should be construed broadly, to the maximum extent allowable under the law. And, with one exception (ordinary eyeglasses or contact lenses), “mitigating measures,” such as medication and assistive devices like hearing aids, cannot be considered when determining whether someone has a disability. Impairments that are episodic (such as epilepsy) or in remission (such as cancer) are disabilities if they would be substantially limiting when active.

The regulations also clarify that the term “major life activities” includes “major bodily functions,” such as functions of the immune system, normal cell growth, and brain, neurological and endocrine functions. And, not every impairment will constitute a disability. Examples of impairments that should easily be concluded to be disabilities, such as HIV infection, diabetes, epilepsy and bipolar disorder, are provided.

Last, the regulations make it easier for individuals to establish coverage under the “regarded as” part of the definition of “disability.” Establishing such coverage used to pose significant hurdles, but under the new law, the focus is on how the person was treated rather than on what an employer believes about the nature of the person’s impairment.

Research
Cancer Drug May Treat Chronic Fatigue Syndrome

A recent study suggests that the cancer drug Rituxan (rituximab) may be an effective treatment for chronic fatigue syndrome, as well as supports the theory that chronic fatigue syndrome is an autoimmune disease. Rituxan is a biologic drug that lowers levels of B cells in the immune system, known as B cell depletion. In the double-blind, placebo-controlled study, published in October in PLoS ONE, Rituxan showed improvement between two and seven months in 10 out of 15 participants, despite early B cell depletion. According to the researchers, that’s consistent with autoimmune activity due to gradual elimination of autoantibodies created by B cells. For four participants, improvement continued even after they stopped taking Rituxan. None of the participants experienced serious side effects. In addition to cancer, Rituxan is being investigated for multiple autoimmune diseases, including rheumatoid arthritis and lupus.

Grant
CSL Behring Awards $40,000 Advocacy Grant

CSL Behring has awarded a $40,000 advocacy grant to the American Plasma Users Coalition (A-PLUS) through its Local Empowerment for Advocacy Development (LEAD) program. The grant will be used to create the A-PLUS State Exchange Project, which will educate state advocates on the development of state insurance exchanges, including federally defined essential health benefits that establish the minimum requirements of exchanges. The project also will help state advocates educate patients about implementation of the exchanges and how they can participate to ensure that access to specialized care and treatments will be maintained in the plans offered through the state insurance exchanges. A-PLUS Partners include Alpha-1 Association, Alpha-1 Foundation, Committee of Ten Thousand, GBS/CIDP Foundation International, Hemophilia Federation of America, Immune Deficiency Foundation, Jeffrey Modell Foundation, National Hemophilia Foundation, Patient Services Inc., and Platelet Disorder Support Association.

LEAD grants support the grass-roots advocacy efforts of organizations that help people who use plasma-derived or recombinant therapies to manage rare and serious medical disorders. CSL Behring has awarded more than $600,000 in grants to patient organizations since the LEAD program was established in 2008.

People and Places in the News

Immune Design Corp. has appointed Wayne R. Gomboz, PhD, as its new chief development officer who will oversee product development and manufacturing for the company’s therapeutic vaccine product candidates. Gomboz previously was the vice president of pharmaceutical operations at Omeros Corp.

Abbie Cornett, Nebraska state senator and current board of trustee chairperson for the Alliance for Biotherapeutics, has assumed the additional role of president for the Alliance following the recent department of the executive director. The Alliance was formed in 2007 under the name The Alliance for Plasma Therapies to advocate for patients in need of specialty biotherapeutics.


**Research**

**Vitamin D May Improve Lupus Patients’ Immune Systems**

Recognizing the connection between systemic lupus erythematosus (SLE) and the disturbance of regulatory T cells, T helper lymphocytes and B cells, researchers at the Internal Medicine Department of the Pitie-Salpetriere Hospital in Paris, France, studied 24 people with SLE to determine their vitamin D status and whether vitamin D supplementation would be well-tolerated and potentially beneficial to their immune systems. Only patients with no or mild lupus activity were included in the study, and all study participants were taking a stable dose of prednisone and/or immunosuppressive drugs.

In the study, 20 of the 24 patients (around age 30) had low levels of vitamin D and received vitamin D supplementation (100,000 IU of cholecalciferol) each week for four weeks followed by the same amount each month for six months. Researchers evaluated each participant at the beginning of the study, at two months and again at six months to see how well they were tolerating the supplementation and how it was affecting their immune systems. They also analyzed the blood lymphocytes of each participant at the three time points to monitor the evolution of regulatory T cells, T helper lymphocytes and B cells under vitamin D therapy.

Researchers found that serum 25(OH)D levels dramatically increased with vitamin D supplementation, reaching normal values at two months and six months. The clinical activity of lupus did not change significantly, and none of the patients showed a flare of the disease or required an increase in corticosteroids or immunosuppressive drugs. However, the levels of anti-DNA antibodies, which are abnormal, and pathogenic antibodies produced by B cells decreased at two months and six months. In addition, the number of regulatory T cells increased with vitamin D supplementation at both two and six months, with a similar trend for both naive and activated memory regulatory T cells, which represents two subsets of regulatory T cells. This increase also was associated with an increased expression of molecules associated with their suppressive function.

**Medicines**

**FDA Approves First MS Oral Treatment**

The U.S. Food and Drug Administration (FDA) has approved Gilenya, the first oral treatment for multiple sclerosis (MS). For years, the only treatments for patients with MS had to be injected. In MS, the body’s immune system attacks myelin, a substance that protects nerves. Gilenya works by holding certain immune cells in the lymph nodes so they can’t reach the myelin. In clinical studies, Gilenya reduced MS relapses by 54 percent compared with a placebo and by 52 percent compared with another common injectable drug. However, because there are not many patients yet on the drug, the long-term effects are unknown. And, Gilenya can cause serious side effects such as slowed heart rate, liver problems, headaches and a buildup of fluid in the eye. Currently, four other oral medications are in the final phase of clinical testing that could soon become FDA approved.

**Clinical Trials Update**

The Bill & Melinda Gates Foundation has given Seattle Biomedical Research Institute an $8.9 million grant to support some systems biology-style research to help speed up the hunt for a new malaria vaccine.

The National Institutes of Health has awarded Kineta $1 million under a phase two contract with the National Center for Research Resources to help identify new drug candidates for infectious, cardiovascular, neurological, metabolic and autoimmune diseases.
Renal dysfunction and acute renal failure occur more commonly in IGIV (human) products in predisposed patients.

- Renal dysfunction, acute renal failure, osmotic nephrosis, and death may be associated with Immune Globulin Intravenous (Human) (IGIV) products in predisposed patients.
- Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. Octagam 5% liquid does not contain sucrose.
- Administer IGIV products at the minimum concentration available and the minimum infusion rate practicable.

**ADVERSE REACTIONS**

Most common adverse reactions with an incidence of >5% during a clinical trial were headache and nausea. To report SUSPECTED ADVERSE REACTIONS, contact Octapharma at 1-866-766-4860 or FDA at 1-800-FDA-1008 or www.fda.gov/medwatch.

**DRUG INTERACTIONS**

- The passive transfer of antibodies may confound the results of serological testing.
- The passive transfer of antibodies may interfere with the response to live viral vacancies.

**HOW SUPPLIED**

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**CONTRAINDICATIONS**

- Anaphylactic or severe systemic reactions to human immunoglobulin.
- Immunoglobulin A (IgA) deficient patients with antibodies against IgA and a history of hypersensitivity.
- Patients with acute hypersensitivity reaction to corn.

**WARNINGS AND PRECAUTIONS**

- Hyperproteinemia, increased serum viscosity and hyponatremia occur in patients receiving IGIV therapy.
- Thrombotic events have occurred in patients receiving IGIV therapy. Monitor patients with known risk factors for thrombotic events; consider baseline assessment of blood viscosity for those at risk of hyperviscosity.
- Aseptic Meningitis Syndrome has been reported with Octagam 5% liquid and other IGIV treatments, especially with high doses or rapid infusion.
- Hemolytic anemia can develop subsequent to IGIV therapy due to enhanced RBC sequestration.
- IGIV recipients should be monitored for pulmonary adverse reactions (TRALI).
- The product is made from human plasma and may contain infection agents, e.g. viruses, and theoretically, the Creutzfeldt-Jakob disease agent.

**Recent Major Changes**

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**INDICATIONS AND USAGE**

Octagam® [Immune Globulin Intravenous (Human)] 5% Liquid Preparation

Initial US Approval: 2004

**DOSAGE AND ADMINISTRATION**

<table>
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<tr>
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<tr>
<td>PI</td>
<td>300-600mg/kg</td>
<td>0.5mg/kg/min</td>
<td>3.33mg/kg/min Every 3-4 weeks</td>
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**WARNINGS AND PRECAUTIONS**

- Ensure that patients with pre-existing renal insufficiency are not volume depleted; discontinue Octagam 5% liquid if renal function deteriorates.
- For patients at risk of renal dysfunction or thrombotic events, administer Octagam 5% liquid at the minimum infusion rate practicable.

**CONTRAINDICATIONS**

- IgA deficient patients with antibodies against IgA are at greater risk of developing severe hypersensitivity and anaphylactic reactions.
- Epinephrine should be available immediately to treat any acute severe hypersensitivity reactions.
- Monitor renal function, including blood urea nitrogen and serum creatinine, and urine output in patients at risk of developing acute renal failure.
- Falsely elevated blood glucose readings may occur during and after the infusion of Octagam 5% liquid with some glucometer and test strip systems.
IMPORTANT SAFETY INFORMATION

Octagam® is contraindicated in individuals with intolerance to immunoglobulins, especially in immunoglobulin A (IgA) deficiency, when the patient has IgE mediated antibodies to IgA. Immune Globulin Intravenous (Human) (IGIV) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Other possible side effects with Octagam include: aseptic meningitis, hemolysis, transfusion-related acute lung disease (TRALI) and thrombotic events.

Immune Globulin Intravenous (Human) products have been reported to be associated with various minor reactions, such as headache, chills, backache, chest pain, fever, allergic reactions, arthralgia, dizziness, and changes in blood pressure, cutaneous reactions and/or nausea and vomiting. Cases of reversible aseptic meningitis and migraine and isolated cases of reversibly hemolytic anemia and reversible increases in liver function tests have been observed with Octagam. Immediate anaphylactic and hypersensitivity reactions are a remote possibility.

As with all medicine made from human plasma, the risk of spreading infections agents, including viruses, cannot be completely eliminated.

Some types of blood glucose testing systems falsely interpret the maltose contained in Octagam as glucose. This has resulted in falsely elevated glucose readings and, consequently, in the inappropriate administration of insulin, resulting in life-threatening hypoglycemia.

References
1. Octagam®, Immune Globulin Intravenous (Human) 5% Liquid Preparation, complete Prescribing Information. 2009.

Please see Highlights of Prescribing Information
IT’S STRESSFUL ENOUGH to have kids go away to college, but throw in a chronic disease that requires expensive and sometimes complicated treatments, and it can quickly become overwhelming. While college students cannot take their parents with them, they also should not be forced to stay home for the sole purpose of undergoing infusions. After all, kids merely want to be free and to fit into their new environment. So, they should be encouraged to think like Garret Moore, a senior in high school contemplating college choices, who says: “My treatments are not a consideration when it comes to choosing a college. I plan to make my college choice, and then make my treatments work around it.”

The more independent kids are before they leave home, the more likely they are to be compliant with immune globulin (IG) therapy once they are gone. Julia Scott agrees. She used her newfound independence to stop her treatments shortly after she went away to college. She has since regretted her decision: “As kids get older, it is important to involve them in the decision process. It is important for doctors to address the kids directly and help them to feel like their thoughts and feelings matter. Give them choices so that instead of things happening to them, they are happening with them.”

Parents can help kids become as independent as possible. The best way to find out how much kids know and how they will behave once they are out of sight is to let them run the show while they are still at home. For instance, by the end of their senior year, kids in need of IG should be able to schedule their infusion appointments, order their supplies and keep an infusion log and health diary on their own.

Discuss Privacy
Respecting a child’s right to privacy while minimizing the risks to their health is a delicate balancing act. Teenagers are quick to set boundaries for privacy, especially where parents are concerned. On the other hand, parents know they can only ensure their kids are safe by staying involved. After all, it is all parents’ natural instinct to protect their children no matter how old they get. But, parents of kids with chronic disease have the added responsibility of making sure that others are educated about their kids’ disease to protect their kids from unwanted infections — even if that embarrasses their kids.

Unfortunately, this invades one of the most important privacy issues for kids: their desire to blend into the crowd and not be seen as different. My son Konner became very private about his disease when he went away to college; he didn’t feel it was anyone’s business but his own. Looking back on that decision, Konner recently told me: “I wish I had been more open with my roommates because they were kind of slobs. I think they would have been a little better and would have stayed away from me more when they were sick if they had known. Plus, in hindsight, it would have been nice to have had some support when I was doing infusions.”

When considering the privacy issue, it is especially important for parents to remember that the balance tips toward the kids’ side of the equation once they reach the magical age of 18. On that day, parents no longer have untethered access to their kids’ medical records and are not able to make medical decisions for them without express written permission. On the other hand, kids need to remember that revoking all parental access may result in
newfound financial responsibilities. If they expect their parents to continue picking up the tab, they had better find a way to compromise on some issues before making regrettable decisions. Therefore, having discussions about privacy issues and how to accommodate both the kids’ wishes and the parents’ needs should occur long before the 18th birthday.

Privacy becomes especially important when discussing college housing. Understandably, parents may want single dorm rooms with a private bathroom for their kids with a chronic illness. And while some colleges may accommodate these parents’ request due to their kids’ disability, being segregated may not be what the student wants. In addition, housing choices also may depend on the infusion needs of the student.

Home-Based Infusions
While going home for infusions may not be an option for students whose school is far away, that does not mean they cannot continue with home-based infusions. However, they do need to be proficient with all aspects of their home-based therapy three to six months prior to their first day on campus. As Amy Ehlers, PharmD, BCPS, pharmacist-in-charge for NuFACTOR Specialty Pharmacy, explains: “It’s important to have the students comfortable with all of the aspects of

Helpful Resources
• In Case of Emergency (ICE) App for iPhone: www.kavapoint.com/index.php/ieemergency-pro
• ICE for Blackberry: appworld.blackberry.com/webstore/content/2281
• Free personal electronic health record for patients with a primary immune disease: primaryimmune.org/patients-and-families/idf-ehealthrecord
• Online personal electronic health records: www.microsoft.com/en-us/healthvault
• Free NuFACTOR wallet emergency medical card, health diary and infusion log: nufactor.com/IGHHealthTools.aspx?Section=Resources

Imagine caring for your child with hemophilia with no factor, refrigerator, running water, electricity, or transportation to a clinic. This is the reality for thousands of families in developing countries. For just $20 a month, you can help an impoverished child with hemophilia. Become a sponsor today!

www.saveonelife.net / contact@saveonelife.net
Caring for people with hemophilia around the world—one at a time.
the infusion long before they get to college, especially when the parents may be several hours away. This should include basic troubleshooting of pumps, ordering supplies, planning ahead for holiday breaks and reporting any changes in health and/or medications.”

With home-based therapy, students with primary immune deficiency diseases (PIDD) have a choice of subcutaneous IG (SCIG) or intravenous IG (IVIG). SCIG, in particular, allows students with PIDD more flexibility with their infusion schedule. It also gives them increased autonomy from medical providers because, once trained, they can self-infuse SCIG independently. And, with SCIG, infusions are usually once a week instead of every two to four weeks.

**Respecting a child’s right to privacy while minimizing the risks to their health is a delicate balancing act.**

Students also can be successful with home-based therapy with IVIG — sometimes without even changing infusion providers. Families that want to stick with the same provider should explore their options several months before the start of college. Some providers are able to contract with local nurses to provide care at the students’ residence. Some college campuses have student health centers that may allow students and their nurses to infuse at the center. And, some infusion providers have infusion suites in their local branch offices where students can go for therapy. While this option is technically not in the home, the therapy is still performed by homecare providers.

Despite the fact that college residential space is typically limited, students will require space to store their home infusion supplies. Therefore, solutions for an organized but compact storage device used exclusively for supplies need to be considered. Plastic carts with drawers on rollers work particularly well. Another storage option is a hanging garment bag with pockets that zip. It also is important to keep in mind that having a clean environment helps lessen the risk of infection in people with chronic illness, and students’ cleaning habits are not likely to be any different at college than they were at home. To make things simple for students, consider sending along disposable cleaning wipes, garbage bags, paper plates and hand sanitizer.

If the IG brand needs refrigeration, students may want to purchase a small refrigerator so that the drug can be kept separate from the communal refrigerator. Private storage lessens the risk of damage to the drug and can provide some security, which is important because not all health insurers will replace IG if a vial is accidentally destroyed. To add an extra layer of protection, the homeowners insurance policy should be checked to determine whether accidental breakage of IG vials is covered. If not, renters insurance should be considered.

**Clinic- or Hospital-Based Infusions**

Students who prefer to keep their infusion life separate from their college life or those who tend to have side effects during infusions may prefer to receive infusions in a doctor’s office or as an outpatient at a hospital infusion clinic. This kind of care provides a higher level of medical supervision, which also may give parents peace of mind. Even so, this kind of infusion has its drawbacks. Students may find it difficult to get reliable transportation to and from the medical facility. And, while many large universities have medical centers nearby, smaller campuses may not have that service. Additionally, receiving an infusion at a clinic or hospital necessitates that a local doctor be responsible for prescribing the medication. Probably even more important, insurance companies that cover students at home may have a more limited network in the campus area. Regardless, most obstacles can be overcome by preparing well ahead of time.

Students need to start by speaking with their insurance company to find infusion providers near campus. Some insurance companies will provide subscribers with a case manager who can assist in this process. Once a list of infusion providers has been compiled, some of them should be called and asked the same questions: Which IG products do they carry? What days and times can they schedule infusions? Which doctors order infusions at their facility?

Hospitals and infusion clinics generally do not allow a doctor without privileges to prescribe IG at their facility. And, because college kids frequently return home for holidays and summers, to maintain good continuity of care, it will
be important for their home physicians to stay involved with their care even while they are away at college. Physicians can do this by assisting students in finding a local physician near campus who is willing to oversee infusions, by cosigning prescriptions and providing local support as needed. It also is important to make sure that the insurance authorization for infusions is obtained at the home infusion clinic, as well as at the clinic used at school. To make things go easier, students should schedule appointments to see their home physicians while on break and their college physicians at the beginning of each school year.

Advice for All Students

No matter where infusions take place, the most important thing is to be sure they take place on schedule. Additionally, here are a few tips for all students: First, they need to become familiar with the paperwork that comes with doctor visits. This includes learning how to read an insurance card, fill out new-patient forms, and keep a current list of their doctors, medications and diagnoses. Second, parents should consider providing students with copies of their latest lab results. Third, doctors seeing college students for the first time may appreciate a letter of introduction from the treating physician with information about health history, medications and typical needs for treatments. Fourth, students should keep this kind of information in their own files. Tech-savvy students can download medical information onto their smartphones or to a flash drive kept on their keychains. Last, students should always carry an emergency card or medic alert tag of some kind that lists emergency contact information. Again, many cell phones and smartphones have an app for that.

For most students, the goal of college is to maximize their academic potential so that, upon graduation, they can compete in what is now a highly selective job market. By preparing early to take on the responsibility for their own healthcare, students in need of IG can make their treatments a manageable part of their college life, allowing them to enjoy all their life successes for a very long time.

Kris McFalls is the patient advocate and a staff writer for IG Living magazine.
Immunology 101:
How an Antibody Deficiency Diagnosis Is Made: Cases 2 and 3
By Terry O. Harville, MD, PhD

IN THE OCTOBER-NOVEMBER issue, I presented one case of how an antibody deficiency diagnosis is made. However, there are several case examples that demonstrate the ways in which this type of diagnosis is made, two more of which I present in this column. To review, an antibody deficiency may exist 1) as a “quantitative deficiency” of IgG (the serum IgA and/or IgM may also be deficient), along with a “functional antibody deficiency” (deficiency in the ability to make antibodies in response to immunization with a vaccine), or 2) as a “functional antibody deficiency” with normal, or near-normal, immunoglobulin serum levels. A patient with a quantitative deficiency may be diagnosed with “hypogammaglobulinemia” (low immunoglobulin levels) or “agammaglobulinemia” (essentially absent immunoglobulin levels), and a patient with a functional antibody deficiency may be diagnosed as having “specific antibody deficiency” (SAD), since the quantitative levels are normal.

Case 2: Hypogammaglobulinemia with Apparent Progression to CVID, No Recovery

A 29-year-old woman presented with recurrent respiratory infections and fatigue as her primary complaints. On examination, she had very small tonsils. In addition, her spleen was slightly enlarged, and many lymph nodes were enlarged (prominent in the neck and groin). Laboratory evaluation indicated her serum IgG to be approximately 600 mg/dL (considered somewhat low by most laboratories), with undetectable serum IgA levels, but with high-normal serum IgM levels. Pre-/post-immunization studies using diphtheria-tetanus toxoid vaccination revealed essentially normal responses. In contrast, more than half of the pneumococcal serotype titers had very low levels, and had no post-immunization increase. However, in the remaining half, some responsiveness was noted, and some of these responses were normal. Interestingly, the patient had always been healthy until approximately age 23, when she developed an illness that was subsequently diagnosed as mononucleosis, Epstein-Barr virus (EBV). Since then, she reports that she has been “going downhill,” and she has become much worse over the past year or so.

EBV infects B lymphocytes. The immune system fights this virus by killing the infected B lymphocytes. But, sometimes, it does too good a job and essentially kills all the B lymphocytes. This can then result in a reduced ability to make appropriate and useful antibodies.

Further testing revealed the patient had very high antibody titers to EBV, suggesting that her immune system was continuing to battle EBV. And, she had very low levels of B lymphocytes. Therefore, it was plausible that her immune system, responding to the EBV infection, was “killing off” her B lymphocytes, which was subsequently resulting in her “hypogammaglobulinemia” with functional antibody deficiency.

While rare, this scenario may explain some forms of antibody deficiency in individuals who have previously been healthy. To determine if this diagnosis is correct, we could question the apparent discrepancies in the laboratory values. For example, even though she has few B lymphocytes, her IgG level is only somewhat low, and her
IgM level is actually on the high side of normal. Further, she had normal antibody production with diphtheria-tetanus toxoid immunization, and she had some responsiveness with pneumococcal vaccination. One explanation is that she has some long-term “memory” B lymphocytes that have not become infected with EBV and that have evaded immune destruction. Also, because everyone continuously produces B lymphocytes within the bone marrow to replenish the normal loss of B lymphocytes, it’s possible that her “new” B lymphocytes may have helped in immunoglobulin production prior to becoming infected and then presumptively were killed by her immune system.

An important question regarding this patient is whether her immune system will improve or whether it will further decline with eventual complete loss of B lymphocytes and antibodies. Either circumstance could occur. As we saw in Case 1, phenytoin likely led to B lymphocyte loss and eventually to common variable immune deficiency. In this case, EBV may be the culprit that is resulting in a complete loss of B lymphocytes (and their function), which has resulted in hypogammaglobulinemia and will subsequently result in agammaglobulinemia. Alternatively, after some time of “recovery,” the immune system may “heal,” once again demonstrating normal B lymphocytes, normal immunoglobulin levels and normal antibody function.

Case 3: Apparent Common Variable Immunodeficiency, but with Full Recovery

A 21-year-old man presents with a history of having an antibody deficiency, and is on intravenous immunoglobulin (IVIG) replacement therapy. He wants to become a fireman/paramedic, so he is requesting re-evaluation of his immune system, hoping that he can discontinue IVIG to facilitate his career goals.

He has a complex history. As a young teenager (some seven years earlier), he began having fevers, and he had an enlarged spleen and enlarged lymph nodes. After a computed tomography (CT) scan revealed multiple large lymph nodes in his abdomen, he was diagnosed with lymphoma. Surgery was performed to remove abdominal lymph nodes and to biopsy his spleen in order to “stage” his lymphoma and to decide on the appropriate therapy. However, the histopathologic evaluation of the tissue failed to demonstrate lymphoma or any other cancer. But, the evaluation did reveal evidence of EBV infection. Indeed, he had a severe case of mononucleosis. As in Case 2, his serum immunoglobulin levels decreased, and he had decreased ability to respond to pneumococcal polysaccharide antigens. Therefore, he was diagnosed with CVID, and he was started on IVIG therapy. Overall, he did well with his therapy, remaining infection-free.

At age 21, his serum immunoglobulin levels were essentially normal. While the IVIG treatment could explain a normal IgG level, his IgA and IgM levels also were normal, even though his records indicated some five years earlier they had been very low; IVIG does not replenish IgA or IgM. In late spring of that year, his IVIG was discontinued. When he came back four months later for pre-/post-immunization studies, he had normal antibody responses to diphtheria-tetanus toxoid vaccination, but this can be normal in some patients with partial antibody deficiency. Most telling was that he had reasonable responses to pneumococcal polysaccharide antigen immunization. More than half were relatively good, but the other half were mediocre responses, below what would be anticipated with “totally” normal immunity.

Because he had remained infection-free while off IVIG and he felt quite well, with normal serum levels and some normal post-immunization antibody responses, the plan was to remain off IVIG and re-evaluate in six months. At that time, his pre-immunization pneumococcal antibody titers had improved, with most in the normal range, which may occur with normal immunity as the immune system is essentially “kick-started” into function. Further, his post-immunization pneumococcal antibody titers were very, very good.

In contrast to Case 2, where the patient appeared to be evolving further into an antibody deficiency with the likelihood of being diagnosed with CVID at some point, Case 3 recovered normal immune function over the same time period of approximately seven years. These cases illustrate the variability that a virus such as EBV can have on the immune system, and its potential role in causing antibody deficiencies.

Next time, we will continue with additional case presentations that illustrate how a diagnosis of a functional antibody deficiency is made. ■

TERRY HARVILLE, MD, PhD, is medical director of the Special Immunology Laboratory at the University of Arkansas for Medical Sciences, and a consultant for immunodeficiencies, autoimmunities and transplantation.
The story of one physician’s journey to coordinate care for a child is a worrisome example of the ways in which the healthcare system is configured for potential failure.

By Sue Romanick, MD
What happens when a patient gets caught in limbo due to reimbursement issues, a lack of treating physicians or simply because his or her medical condition can’t be explained? These are situations that occur more frequently than many realize, causing significant frustration for both the physicians seeking to treat and the patient who is left without answers. Despite good intentions by all, many of the patients may never get the help they need for many reasons, all of which lie in the workings of a healthcare system that fails to focus on the patient, but instead results in a rationing of healthcare. One such example of this is a patient who has caused me to see this issue very clearly.

The Patient: Undiagnosed

Mr. B is a very unusual gentleman. This was apparent from the beginning. First, he managed to steal my heart within minutes of meeting him. Second, he had baffled his physicians with his medical condition for more than two years. Finally, he broke through the usual barrier to get into my clinic. I don’t usually accept his type of patient, so to speak. Why? Mr. B is only 10 years old.

Also unusual was his letter of introduction that had preceded his visit to my office. His eye doctor was, in fact, begging that I urgently evaluate him. Apparently, Mr. B had been dropped from his other doctor’s practice due to “lack of clear diagnosis.” At first glimpse, this would probably make some sense. Who would argue with their doctor who says: “If I don’t know what your diagnosis is, then I can’t treat you.” But, the fact is that his team of providers had already delivered comprehensive treatment over a two-year period. This had included not only dramatic in-hospital care but also multiple high-risk medications with costs totaling more than $15,000 per year. Moreover, over time, some of these medications had caused Mr. B to balloon to such a weight that they gave him the appearance of being severely “cushingoid” (medical jargon for collateral damage in the form of excessive weight gain or an unsightly redistribution of fat). Medically, this can mean severe obesity. To a youngster, this meant loss of self-esteem and being at risk for bullying and harassment. At least, that would be the usual part. But as I said, Mr. B was quite unusual. Which brings us to his physical examination.

When I asked Mr. B to cover his right eye and tell me how many of my fingers he could see on my left hand, his head began to roll around on his neck in a most disconcerting, unusual way. What he was desperately trying to do was to adjust the angle of his left eyeball to see around a very large patch of complete blindness, a hole of sorts, which he called his “purple patch.” But, of course, wherever he gazed, the purple patch followed. Like a curse, he couldn’t escape it. Over time, Mr. B had grown accustomed to using what was left of his peripheral vision to be able to make out shapes. I knew that he no longer had the eye pain that had originally signaled his eye problem. Yet even I could feel his current pain as he struggled to see with his left eye.

As much as I wanted to mount my white horse and ride into the arena, swoop up Mr. B and save him, I simply couldn’t.

He could have played on my heartstrings and I would have dutifully melted. But, as I said, Mr. B was unusual. When I murmured that I would like to look into his eyes with my ophthalmoscope, he replied with booming confidence punctuated by a winning smile: “I know the drill!” It was as if each of his words seemed to be patting me on the shoulder to reassure me: “It’s OK, Doctor, you’re going to be fine.” (It was I who was going to be fine?) It was precisely at that moment that I made a commitment to help Mr. B, no matter what. So, the journey started, and I found myself drawn into the jungle of primary care providers, specialists and the potential dangers of insurance and malpractice companies.

The Journey: Who Is Responsible?

The first step was to understand the problem. There was, however, a rather important detail. Time was already running out. I knew that, without continuing his medication, Mr. B could lose the sight in his right eye as well. So, I needed to get going on this.

Back to the problem: code word “obscure.” As a rheumatologist and specialist in adult internal medicine, I am used to conditions that defy placement in neat little categories. The autoimmune conditions can lurk in the shadows, spring forth at will, pop up in different places at different times, and pick on the sick and vulnerable. Stated
differently, try placing a neat label on a moving target. Professionally, we use terms such as “undifferentiated connective tissue disorder” or “mixed connective tissue disease” or “undifferentiated spondyloarthropathy,” to name a few of my favorites. It’s really quite simple: By the time you have uttered these terms, the patient has adopted either glassy eyes or a rather forlorn look on his or her face. Translated from the medical lingo, these terms mean: “Your condition doesn’t fall into any neat category and could change for the better or change for the worse,” sounding like the cryptic answers uttered to poor Alice in the story of *Alice in Wonderland*. Yet, the medical truth could be explained using a pictorial analogy. There is a popular illustration that originated in India depicting blind men each touching a different part of the same elephant and only that specific part. The lesson here is that if each man is asked to describe what an elephant is, then the descriptions may differ dramatically. That also is true for autoimmune conditions.

To my disappointment, in a room filled with members from both ranks, even from different countries, it appeared impossible to reach a clear consensus as to who is responsible for what.

For example, having certain eye problems could be the first sign of an autoimmune condition. Over time, this condition could spread, say, to the joints or the spine, or it could cause rash or affect the hair. The list goes on and on. The fact that Mr. B had only eye involvement, in my estimation, didn’t exclude a widespread (“systemic”) condition. In fact, this young gentleman’s blood tests showed evidence of inflammation in the blood (an elevated sedimentation rate), as well as evidence of an increased level of a substance produced by the liver in response to significant inflammation in the body (an elevated c-reactive protein). These tests showed that more than the eyes were involved. I am sorry to say that this made the distinction between which doctors ought to be claiming responsibility for Mr. B’s treatment plan a little blurry, pardon the pun. And, yes, the actual diagnosis was obscure. But do we treat words on paper, or do we treat a process that may cause a patient to go blind if we stand by and do nothing?

The way I see it, my job as a rheumatologist is to out-smart the condition. Yet, what do you do when the enemy lurks within your own defense system? Picture a widespread network with surveillance units infiltrating normal day-to-day operations. If a rogue unit breaks away and causes problems, you want to go after it. But if you can’t isolate it from the rest of the system, you could have a problem. Simply put: Damage your immune system and you could have a big problem.

Initially, I felt an extreme sense of frustration that Mr. B had been dropped from one of the main branches of his medical team. This branch was in charge of choosing, administering and following Mr. B’s strong medications. Believing initially that a mistake had been made, I contacted my medical colleagues involved. To my shock, I was able to verify that, indeed, a letter of rejection had been sent to Mr. B’s family. The explanation given to me was simple: The diagnosis was obscure, limited to the eyes, and should be treated by the eye doctor. But there was a ringer here. The condition fell out of the realm of conditions usually treated by eye doctors because of the need to have familiarity with the other organ systems in the body that the medications can adversely affect. Also, as many autoimmune conditions can pop up in different organ systems at different times in the future, I felt it was important to keep a close eye on the patient.

As much as I wanted to mount my white horse and ride into the arena, swoop up Mr. B and save him (which is, of course, the feeling that propelled me toward a medical career in the first place), I simply couldn’t. Being a board-certified adult rheumatologist, I am not “approved” to treat children. I am not a pediatric rheumatologist. Yet I found myself in action in 2009, as part of a lobbying effort on Capitol Hill, meeting with lawmakers and their staff to speak up for patients with arthritis and autoimmune disorders. One of the main talking points was the severe shortage of pediatric rheumatologists nationwide, making access to medical care difficult for children with autoimmune disorders. Sadly, there simply aren’t enough pediatric rheumatologists to go around. Mr. B’s family did some research. They would have to transfer his care out of state. However, that was not an option with the family’s financial situation.
I returned to the notion of patient selection. The hallowed halls of my deep memories shuddered. A few years ago, I urgently called a specialist colleague to ask for help with a patient who I feared was in imminent danger of a full stroke. To my shock, the receptionist at the other clinic announced that they could not make an appointment because of the patient’s insurance. Curious, I pressed on with questioning. The insurance was a so-called capitated insurance, sometimes referred to as an insurance in which doctors lose money if they see patients too often. My patient at that time was out of luck. That clinic’s weekly quota of patients having that specific insurance had been already met! Well, exactly what was the quota they had set? Answer: only two patients per week.

On another occasion, I needed to refer a delightful grandmotherly type for urgent knee surgery. My staff dutifully got on the phone and started to scratch off names on a long list of orthopedic surgeons. It was my first introduction to physicians refusing to see Medicare patients. I calculated in my own mind how many years I had left until I, myself, might need surgery. In the event getting myself an appointment at a ripe old age would be an issue, I began to plan ways I could get more mileage out of my own tires. But Mr. B was not in such a fortunate position to come up with his own treatment plan.

It appears that, in the current healthcare climate, a kind of patient selection bias is at play among providers, allowing some children to start or continue treatment, while forcing others to leave medical treatment facilities. I held a copy of the rejection letter in my hand that had been sent to Mr. B’s family. I also knew that his parents had discussed this letter in front of him. I worried not only about Mr. B’s health and eyesight, but also about the blow that had been dealt to his self-esteem. Indeed, it was a mature young man who had announced to me: “I know the drill.” He knew more than the drill, which I found to be very, very sad.

Very coincidentally, in May, I was invited to a meeting as “the” token adult rheumatologist in the presence of pediatric rheumatologists and ophthalmologists representing at least four countries. The point of the meeting was to try to come up with a consensus regarding the treatment of children with autoimmune eye disease, the kind of disease that can rob children of their eyesight. The issues were not simply whether certain medications work effectively, but which type of doctor should be calling the shots about treatment. A hotly debated issue was whether the eye specialists or the rheumatologists (the “aches, pains and immune specialists”) should take responsibility for prescribing and monitoring higher-risk medications for these young patients with eye disease. The eye doctors have the training to use fancy equipment to identify diseases in the eyes and are trained to perform a highly skilled examination. On the other hand, the (pediatric) rheumatologists understand the complexities of the high-risk medications and are experienced in prescribing and monitoring them, as well as looking for signs of disease popping up in other parts of the body. Rheumatologists might see patients with skin, joint, eye, heart, liver, muscle, kidney and brain diseases. To my disappointment, in a room filled with members from both ranks, even from different countries, it appeared impossible to reach a clear consensus as to who is responsible for what.

The Solution: Coordinating Forces

But where did that leave Mr. B (or myself, for that matter)? Without being officially trained as a specific children’s rheumatologist, how could I erect a MASH unit on the battleground? Mr. B’s eye doctor was also passionate about saving him and his eyesight. It had been at her urging that Mr. B found his way into my clinic in the first place. Ah, yes, a familiar request: “Dr. So-and-So just called, asking if you can’t just squeeze in this patient on short notice… please?” So, the story continued, after hours, even from home, as I began identifying members for our new team and began making contacts.

If you want to coordinate forces, you need good communication. Walkie-talkies may have been fine on old battlefields, but they are insufficient for this modern-day
healthcare team. Being new at this, I had to learn from scratch. My initial ground rules were simple: Identify team members. Establish communication.

The infrastructure of communication has included letters, phone calls, faxes, emails and in-person meetings, while we have been strengthening, albeit slowly, our sense of teamwork. Goal-setting has included trying to minimize medication where possible to minimize side effects. Mr. B’s family was asked to find a new pediatrician with whom they could “bond” and who was willing to review lab tests from a pediatric perspective and regularly evaluate Mr. B in person. The eye specialist agreed to follow the potentially elusive eye changes every few weeks and keep us all informed. I agreed to assume the prescribing and monitoring of three high-risk medications, as long as there was a clear “all-way” instead of “two-way” flow of information between all team members, including immediate summaries of each clinic visit to alert us of any need to deal with flares of the condition. Meanwhile, I had extensive discussions with Mr. B’s previous medical team that had managed him over the previous two years to understand the rationale, dosing and effects to date of the multiple high-risk medications. Mr. B’s parents were given instruction on how to maintain open communication with the other team members and, to date, have proved very compliant in bringing Mr. B to all appointments. This is not an easy feat. I live in a different city than he does. And, oh yes, to preserve medical confidentiality, I suggested Mr. B take this name as a kind of nickname. In return, I made him the team captain.

When the vision of a young boy hangs in the balance, do we allow ourselves to get lost in red tape?

Interpretation of the concept of “uncertainty” of a particular diagnosis may lead to decreased accessibility of care not necessarily for the protection of the patient, but for the protection of the doctor who is afraid of being sued for malpractice. In other cases, there are simply not enough doctors to go around. Of course, poor reimbursement for medical services might be the actual behind-the-scenes stumbling block behind poor accessibility to healthcare. The bottom line is that the delivery of healthcare appears to be rationed.

Unusual steps were taken, the majority outside of regular clinic hours, to allow Mr. B to continue medical treatment. Certainly, it takes time to set up a type of team that may never have been set up before. Most providers these days have less time as they are forced to learn new ways for documenting visits and to leave a paper or electronic trail in a patient’s medical chart. Meanwhile, reimbursement for services is shrinking. Pressures of being audited by insurance companies looking to recoup money paid out for services already delivered further pollute the ideal, altruistic environment.

On a personal level, it is uncomfortable to disagree with one’s colleagues in terms of diagnosis or diagnostic terminology. It can be even more uncomfortable to disagree with their delivery of healthcare. Given the debate I witnessed at the meeting addressing pediatric autoimmune eye disease, plenty of controversy remains as to which doctor should take responsibility for what. Yet, when the vision of a young boy hangs in the balance, do we allow ourselves to get lost in red tape? Do we rush to protect ourselves and perhaps our own free time, while keeping our own eyes on the proverbial bottom line? Or, are we willing to make a commitment and follow it through without any thought for reimbursement? These decisions are becoming increasingly difficult. It depends on your view. That is, if you can see clearly.

The Worrisome Realities

A lot of issues have been raised in Mr. B’s situation that haven’t been fully explored. Certainly, this case illustrates some of the worrisome realities in this current atmosphere of healthcare. Lack of accessibility to healthcare is not simply a case of having or not having health insurance.

SUE ROMANICK, MD, is board-certified, as well as recertified in both general internal medicine and rheumatology. She was involved with immunology research on cell clones at the German Cancer Research Institute in Heidelberg, Germany, and has worked in immunology and plasmapheresis at the University of California, San Francisco. Dr. Romanick is a public speaker and has spoken for the Arthritis Foundation, University of Washington and Overlake Hospital in Bellevue, Wash. She also has participated in lobbying efforts on Capitol Hill to support arthritis patients, both young and old, at the request of the American College of Rheumatology. She runs her own private practice clinic in Bellevue, Wash.
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People who have primary immune deficiency diseases (PIDDs) are susceptible to a number of life-threatening health complications. One that should not get overlooked is skin cancer. According to the Skin Cancer Foundation, skin cancer is the most common form of cancer in the United States, with two million people diagnosed each year. Normally, when abnormal skin cells pop up, the immune system attempts to knock them out. But those with PIDDs have weakened immune systems that aren’t up for the fight, and the cancerous abnormal cells multiply. To make matters worse, the cancer and the chemotherapy wear out the already-taxed immune system even more, making it a vicious cycle.

**PIDD and Increased Cancer Risk**

Because the survival rates for those with PIDD have increased in recent years, due in large part to effective immunoglobulin (IG) replacement therapies, researchers

Research shows that PIDD patients have a 60 percent greater chance of developing cancer, and a handful of specific indications account for the majority of cases.
have turned their attention to the higher rates of cancer among PIDD patients. According to a 2008 report in the journal *Anticancer Research*, cancer is the second-leading cause of death, after infection, for children and adults with some form of PIDD. The type of cancer occurring often depends on the patient's type of immunodeficiency, their age, as well as the kind of viral infections contracted. However, the most common type of cancer in PIDD patients is lymphoma, an immune-system-related malignancy. And, according to the Immunodeficiency Cancer Registry (ICR) database at the University of Minnesota, the most common malignancies for those with PIDD are non-Hodgkin’s lymphoma (48.6 percent) and Hodgkin’s disease (10 percent).

Research from the early 1990s suggests that approximately 25 percent of those with PIDD will develop cancer during their lifetime, a jump from the estimate of 2 percent to 10 percent reported in 1972, when treatment options were far less advanced. Based on estimates from patients in Australia, those with PIDD are estimated to have a 60 percent higher chance of cancer than the general population.

**According to a 2008 report in the journal Anticancer Research, cancer is the second-leading cause of death, after infection, for children and adults with some form of PIDD.**

There are approximately 150 subtypes of PIDD, only a few of which are correlated with cancer formation. According to the ICR, patients with ataxia telangiectasia (A-T) and common variable immunodeficiency (CVID) account for more than half of PIDD-related cancer cases, and one-third of cancer cases occur in patients with Wiskott-Aldrich syndrome (WAS), severe combined immunodeficiency (SCID) and selective IgA deficiency. A number of risk factors make PIDD patients more susceptible to cancer, including an impaired ability to respond to agents toxic to cells’ genetic materials, a decreased ability to remove pathogens, overactive inflammation responses and impaired control over virus-infected cells.

As with other forms of malignancies, CVID and A-T are associated with higher rates of skin cancer. In CVID, sufferers have low levels of antibodies, which make it difficult for them to stave off infections. Those with CVID sometimes contract systemic bacterial infections like meningitis and get frequent skin infections. In addition to skin cancer, CVID patients may also develop breast, prostate, gastrointestinal tract and lymphoid system cancers. Patients with A-T, a systemic disorder that affects the nervous system, have motor skills trouble, which leads to balance problems, as well as slurred speech and dilated blood vessels in their eyes and skin. A-T patients have a 37-fold higher risk of developing cancer than the rest of the population, according to the National Cancer Institute. In addition, they have a 10 percent chance of getting leukemia and lymphoma, and they are at risk for cancers of the stomach, brain, ovary, liver, larynx, parotid gland and breast.

**Decreasing Cancer Risk**

To decrease the risk factor of skin cancer, PIDD patients should heed the common-sense advice that applies to everyone: First and foremost, limit sun exposure. Not only does the sun cause skin cancer, it also further weakens the immune system. The Centers for Disease Control and Prevention recommends taking cover in the shade from 10 a.m. to 4 p.m., when the ultraviolet rays are the strongest.
If individuals do go out in the sun during that time, they should protect themselves by wearing a wide-brimmed hat, sunglasses that block the UVA and UVB rays (wrap-around shades are the best at preventing sunlight from seeping in) and loose-fitting clothing made with a tightly woven material. Using sunblock with an SPF of 15 or higher also will help shield exposed skin, and it’s important to do so even on cloudy days and during the winter. Slather on the lotion a half-hour before going outside and then reapply every two hours. Of course, it should go without saying that tanning beds should be avoided completely.

**Although not a lot of research is available on the link between skin cancer and PIDD, one promising avenue is vitamin D.**

However, what will go a long way in preventing skin cancer is to take care of the underlying problem, the immunodeficiency. Keeping the immune system in tip-top shape is a priority, so PIDD patients should be sure to practice good hygiene — such as using a mild soap to keep the skin clean and brushing teeth twice daily — and eat nutritious meals. Patients should also keep up their standard practices to ward off infections, like receiving regular IG treatments (or subcutaneous infusions) and steering clear of large crowds and people who have colds. Another alternative that can thwart a possible chronic infection is the use of long-term antibiotics in low doses, which will require a doctor’s prescription.

Therapies offered for PIDD patients often are the same for other persons with the same kind of malignancy. However, shorter time in chemotherapy may be called for, given these patients’ already-weakened immune systems. In addition, PIDD patients will need to work even harder to protect themselves from bacteria and other viruses while being treated.

The Cancer Research

Although not a lot of research is available on the link between skin cancer and PIDD, one promising avenue is vitamin D. A team of researchers found that the natural hormone is connected to immune reactions and could protect against cancer and autoimmune diseases. These researchers examined how the body stops the growth of pathogens and discovered the white blood cells that are integral to the body’s ability to fight infections cannot function without adequate levels of vitamin D. However, that doesn’t mean PIDD patients should freely bask in the sun just yet; the incidental sun exposure one gets from walking to the car or to the office is probably enough, and if not, there are vitamin D supplements available over the counter and through prescriptions. It is hoped that researchers will uncover more ways vitamin D can help PIDD patients fight cancer more effectively.

**JENNIFER KESTER is a San Diego-based writer and editor specializing in health and lifestyle issues.**

**Sources**


AGAMMAGLOBULINEMIA

CONGENITAL AGAMMAGLOBULINEMIA

in predisposed patients. Renal dysfunction and acute renal failure occur more commonly in patients receiving IgIV products containing sucrose. Gammmaplex does not contain sucrose. For patients at risk of renal dysfunction or failure, administer Gammmaplex at the minimum infusion rate practicable. See full prescribing information for complete boxed warning.

Gammmaplex is contraindicated in patients who have had a history of anaphylactic or severe systemic reactions to human immune globulin and in patients with selective IgA deficiency and in patients with a history of hypersensitivity.

In patients at risk of developing renal failure, monitor urine output and renal function including blood urea nitrogen (BUN) and serum creatinine. Hyperproteinemia, increased serum viscosity, and hypernatremia may occur in patients receiving IgIV therapy. Thrombotic events may occur following treatment with Gammmaplex and other IgIV products. Monitor patients with risk factors for thrombotic events, including a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, coagulation disorders, prolonged periods of immobilization and/or known/suspected hyperviscosity.

Aseptic meningitis syndrome (AMS) may occur infrequently with IgIV treatment. AMS usually begins within several hours to 2 days following IgIV treatment. Discontinuation of IgIV treatment has resulted in remission of AMS within several days without sequelae. AMS may occur more frequently in association with high doses (2 g/kg) and/or rapid infusion of IgIV. Hemolysis and hemolytic anemia can develop subsequent to IgIV treatments. Noncardiogenic pulmonary edema may occur in patients following IgIV treatment (i.e. transfusion-related acute lung injury [TRALI]). Monitor patients for pulmonary adverse reactions (TRALI). Test product and patient’s serum for anti-neutrophil antibodies.

Gammmaplex is derived from human plasma. The risk of transmission of infectious agents, including viruses, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated.

In clinical studies, the most common adverse reactions with Gammmaplex were headache, fatigue, nausea, pyrexia, hypertension, myalgia, pain and vomiting.

Please see the Brief Summary of Prescribing Information, including boxed warning, on the reverse.

Important Safety Information

Gammmaplex is indicated for the replacement therapy of primary humoral immunodeficiency (PI). This includes, but is not limited to, the humoral immune defect in common variable immunodeficiency, X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome and severe combined immunodeficiencies.

WARNING: Renal dysfunction, acute renal failure, osmotic nephropathy and death may be associated with the administration of Immune Globulin Intravenous (Human) (IgIV) products in predisposed patients. Renal dysfunction and acute renal failure occur more commonly in patients receiving IgIV products containing sucrose. Gammmaplex does not contain sucrose. For patients at risk of renal dysfunction or failure, administer Gammmaplex at the minimum infusion rate practicable. See full prescribing information for complete boxed warning.

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Please see the Brief Summary of Prescribing Information, including boxed warning, on the reverse.

Report adverse reactions to adr@bpl.co.uk

REFERENCES

For product information and inquiries, please call (866) 398-0825 or email BPLinfo@LashGroup.com
Immune Globulin Intravenous (Human), 5% Liquid

BRIEF SUMMARY

CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION PRIOR TO USE

INDICATIONS AND USAGE

Gammalux®, Immune Globulin Intravenous (Human), 5% Liquid, is indicated for the replacement therapy of primary humoral immunodeficiency (PI). This includes, but is not limited to, the humoral immune defect in common variable immunodeficiency, X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome and severe combined immunodeficiencies.

CONTRAINDICATIONS

Gammalux, Immune Globulin Intravenous (Human), 5% Liquid, is contraindicated in patients who have had an anaphylactic or severe systemic reaction to human globulin and in IgA-deficient patients with antibodies to Iga.

WARNINGS

Use of Immune Globulin Intravenous (IGIV) products, particularly those containing sucrose, have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephropathy and death. Patients at risk of acute renal failure include those with any degree of pre-existing renal insufficiency, diabetes mellitus, advanced age (above 65 years of age), volume depletion, sepsis, paraproteinemina, children who are overweight or are receiving known nephrotoxic drugs. Gammalux does not contain sucrose. For patients at risk of renal dysfunction or failure, administer Gammalux at the minimum infusion rate practicable.

See WARNINGS AND PRECAUTIONS and DOSAGE AND ADMINISTRATION sections in the Package Insert for important information intended to reduce the risk of acute renal failure.

Because this product is made from human plasma, it may contain infectious agents, e.g. viruses and, theoretically, the Creutzfeldt-Jakob (CJD) agent that can cause disease. The risk has been reduced by screening plasma donors for prior exposure, testing donated plasma and inactivating or removing viruses during manufacturing. Despite these measures, Gammalux carries an extremely remote risk of transmission of viral diseases. The physician should discuss the risks and benefits of this product with the patient, before prescribing it to the patient.

All infections suspected by a physician possibly to have been transmitted by this product should be reported to (866) 398-0825 or email BPLInfo@LastGroup.com on behalf of Bio Products Laboratory Ltd.

Gammalux, Immune Globulin Intravenous (Human), 5% Liquid, should only be administered intravenously.

PRECAUTIONS

General

The product should be used promptly after piercing the cap. Any partially used or unused product should be discarded. Visually inspect each bottle before use. Do not use if the solution is cloudy or turbid. Solution that has been frozen should not be used.

Hypersensitivity

Severe hypersensitivity reactions may occur. In case of hypersensitivity, discontinue Gammalux infusion immediately and institute appropriate treatment. Medications such as epinephrine should be available for immediate treatment of acute hypersensitivity reactions.

Renal dysfunction/failure

Ensure that patients with pre-existing renal deficiency are not volume depleted before infusion of IGIV. Periodic monitoring of renal function and urine output is particularly important in patients considered to be at increased risk of developing acute renal failure. Renal function, including blood urea nitrogen (BUN) and serum creatinine, should be assessed before administering Gammalux and at appropriate intervals thereafter. If renal function deteriorates, consider discontinuing Gammalux.

Information for patients: Patients should be instructed to report the following signs and symptoms to their healthcare professional: decreased urine output, sudden weight gain, fluid retention/edema, and/or shortness of breath (which may suggest kidney damage).

Hyperproteinemia, increased serum viscosity, and hyponatremia

Hyperproteinemia, increased serum viscosity and hyponatremia may occur in patients receiving IGIV therapy. Consider baseline assessment of blood viscosity at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/ markedly high triglycerol levels, or monoclonal gammopathies. For patients judged to be at risk of developing thrombotic events, administer Gammalux at the minimum rate of infusion practicable.

Thrombotic events

Thrombotic events may occur following treatment with IGIV products. Patients at risk include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, coagulation disorders, prolonged periods of immobility, and/or known suspected hyperviscosity. Baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/ markedly high triglycerol levels, or monoclonal gammopathies. For patients judged to be at risk of developing thrombotic events, administer Gammalux at the minimum rate of infusion practicable.

Aseptic meningitis syndrome (AMS)

Aseptic meningitis syndrome (AMS) may occur infrequently with Immune Globulin Intravenous (IGIV) treatment, usually beginning within several hours to 2 days after IGIV. AMS may occur more frequently with high doses (2 g/kg) and/or rapid infusion of IGIV. Discontinuation of IGIV treatment has resulted in remission of AMS within several days without sequelae.

Hemolysis

IGIV products can contain blood group antibodies (hemolysins) that coat red blood cells (RBCs) in vivo with immune globulin, resulting in a positive direct antoglobulin test (DAT). Acute hemolysis has been reported with IGIV. Delayed hemolytic anemia can develop due to BPS sensitization. IGIV recipients should be monitored for clinical signs and symptoms of hemolysis (See WARNINGS AND PRECAUTIONS: Monitoring: Laboratory Tests).

Transfusion-related Acute Lung Injury (TRALI)

Noncardiogenic pulmonary edema (Transfusion-related Acute Lung Injury (TRALI)) may occur in patients following IGIV treatment. Symptoms (fever, severe respiratory distress, pulmonary edema, hypoxemia but normal left ventricular function) typically appear within 1 to 6 hours following infusion. If TRALI is suspected, test for anti-neutrophil antibodies in both the product and the patient’s serum (See WARNINGS AND PRECAUTIONS: Monitoring: Laboratory Tests). Management includes oxygen and appropriate ventilatory support.

Laboratory Tests

For appropriate monitoring, see previous sections on Renal, Hyperproteinemia, Hemolysis and TRALI.

Drug Interactions:

Passive transfer of antibodies may transiently interfere with the immune response to live virus vaccines such as measles, mumps, rubella and varicella (SEE PATIENT COUNSELING INFORMATION IN PACKAGE INSERT).

Pregnancy Category C

Animal reproduction studies have not been conducted with Gammalux. It is not known whether Gammalux can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Gammalux should be given to a pregnant woman only if clearly needed.

ADVERSE REACTIONS

General

Gammalux, Immune Globulin Intravenous (Human), 5% Liquid, contains no reducing carbohydrate stabilizers (e.g. sucrose, maltose) and no preservative.

Postmarketing Experience

The following adverse reactions have been identified during post-approval use of IGIV products.

Intusion reactions: hypersensitivity (e.g., anaphylaxis), headache, diarrhea, tachycardia, fever, fatigue, dizziness, malaise, chills, flushing, urticaria or other skin reactions, wheezing or other chest discomfort, nausea, vomiting, rigors, back pain, myalgia, arthralgia and other symptoms of anaphylaxis.


Cardiovascular: Cardiac arrest, thromboembolism, vascular collapse, hypotension, anaphylaxis.

Neurological: Coma, loss of consciousness, seizures, tremor, asceptic meningitis syndrome.

Intestinal: Stevens-Johnson syndrome, epidermolysis, erythema multiforme, dermatitis (e.g. bullous dermatitis).

Hematologic: Pancytopenia, leukopenia, hemolysis, positive direct antiglobulin (Coombs) test.

Gastrointestinal: Hepatic dysfunction, abdominal pain.

Primary Humoral Immunodeficiencies (PI)

In a multicenter, open-label, non-randomized clinical study, 50 subjects with primary humoral immunodeficiency received 703 infusions with Gammalux. Doses ranged from 279 to 799 mg/kg every 21 days (mean dose 465 mg/kg) or 28 days (mean dose 458 mg/kg), for up to 12 months. At some time during the study, all 50 subjects had an adverse event (AE) and in twenty-four subjects (48.0%) it was considered product-related.

The temporally associated AEs that occurred in more than 5% of subjects during a Gammaplex infusion or within 72 hours after the end of an infusion, irrespective of causality are given in the table below:

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Subjects (%)</th>
<th>Infusions (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>18 (36%)</td>
<td>53 (7.5%)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>8 (16%)</td>
<td>9 (1.3%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>7 (14%)</td>
<td>10 (1.4%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>6 (12%)</td>
<td>7 (1.0%)</td>
</tr>
<tr>
<td>Pain</td>
<td>5 (10%)</td>
<td>5 (0.7%)</td>
</tr>
<tr>
<td>Chills</td>
<td>3 (6%)</td>
<td>5 (0.7%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3 (6%)</td>
<td>9 (1.3%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 (6%)</td>
<td>4 (0.6%)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>3 (6%)</td>
<td>3 (0.4%)</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>3 (6%)</td>
<td>3 (0.4%)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>3 (6%)</td>
<td>5 (0.7%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3 (6%)</td>
<td>3 (0.4%)</td>
</tr>
</tbody>
</table>

Five subjects (10%) experienced seven serious AEs. Two of these serious AEs were considered related to Gammaplex treatment (thrombosis and chest pain). Three other subjects withdrew from the study due to the following AEs: paresthesia, bronchospasm and pregnancy.

During this study, no subjects tested positive for infection due to human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), or Parvovirus B19.

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Bio Products Laboratory

a commitment for life

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**Ask Kris**

By Kris McFalls

**Patti:** My doctor who diagnosed my primary immune disease uses this billing code for my IG treatment: 279.00. Since I am getting close to Medicare age, I wonder if this code can be used when I am covered by Medicare?

**Kris:** Medicare Part B accepts only five codes for treatment of a primary immune disease with immune globulin. Code 279.00 is not covered. Medicare codes include:

- 279.04: congenital hypogammaglobulinemia (includes agammaglobulinemia: Bruton’s type; and agammaglobulinemia: X-linked)
- 279.05: common variable immunodeficiency (includes dysgammaglobulinemia: acquired, congenital and primary; hypogammaglobulinemia: acquired primary; hypogammaglobulinemia: congenital non-sex-linked; and hypogammaglobulinemia: sporadic)
- 279.12: Wiskott-Aldrich syndrome
- 279.2: combined immunity deficiency (includes agammaglobulinemia: autosomal recessive; agammaglobulinemia: Swiss-type; agammaglobulinemia: X-linked recessive; severe combined immunodeficiency [SCID]; thymic: alymphoplasia; thymic: aplasia or dysplasia with immuno-deficiency) (excludes thymic hypoplasia 279.11).

It will be important to have a conversation about this with your doctor before you are eligible for Medicare.

**Kevin:** I have been infusing subcutaneous immune globulin (SCIG) in my home for a few years now. After a recent change to a different provider, I was informed I am using too many Sharps containers. I was instructed to cut the needles off of the tubing and place only the needles in the Sharps container. I was also told to place the glass IG vials in the recycling and throw everything else into the trash.

I’m puzzled by these instructions because my former provider taught me to place all tubes, spikes, needles, used gauze and tubing into Sharps containers as they are a biohazard. Which provider is correct?

**Kris:** Each state has its own medical waste regulations. And, regulations for home medical waste differ from those required of healthcare facilities.

Regulations in Rhode Island, where you reside, specifically say to “never put medical waste or containers of medical waste in the recycle bin.” Therefore, your provider’s instructions to put empty vials of IG in the recycling are probably ill-advised. Furthermore, just because something is legal for you to do as a homeowner does not make it the best practice for a medical practitioner to teach. To find out what waste disposal procedures your state will tolerate, you should contact your state regulators.

To read more about medical waste rules in your state, go to www.epa.gov/waste/wyl/stateprograms.htm.

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**Kris McFalls** has two adult sons with chronic diseases treated with IG. She is formerly a physical therapist assistant, and currently is IG Living’s full-time patient advocate.
Let’s Talk!

By Trudie Mitschang

When the editorial team received a letter from Brent Vreeland last September, we knew we wanted to share his story with our readers. Brent is among the thousands of caregivers in this country who suffer silently with the effects of immune disease. Brent is a caregiver for his wife of 31 years, Brenda, and they have three grown children and nine grandchildren. Chronic illness became the third party in their relationship in 2009, and its constant presence has taught them both what it means to love “in sickness and in health.”

Trudie: What inspired you to write to us?
Brent: We subscribe to your magazine and, to date, I had read very little from the spouse’s or caregiver’s perspective. I wanted to share some insight into what we face when a family member is diagnosed with a horrible, chronic illness.

Trudie: Tell us about Brenda’s diagnosis.
Brent: My wife was diagnosed with necrotic myelitis in October 2009, several months after our local hospital had dismissed her symptoms as side effects from Lipitor. Within two months, she had gone from simply being weak to being unable to use her arms and legs. After the diagnosis at the University of Michigan Hospital, she was admitted for physical and occupational rehabilitation, and after seven weeks, she was allowed to return home in a wheelchair.

Trudie: What did you do to step into the role of caregiver?
Brent: Prior to Brenda’s diagnosis, I was clueless about immune system diseases. I’ve had to get up to speed pretty quickly. We now put all of her medications on a computer spreadsheet and link it to every medical procedure and surgery so we can keep medical personnel up-to-date.

Prior to Brenda’s diagnosis, I was clueless about immune system diseases. I’ve had to get up to speed pretty quickly.
various doctors prescribe so I can know what good and bad effects to expect from each medication.

Trudie: How has Brenda’s illness impacted your family?

Brent: This whole thing has been difficult for everyone, especially the kids. I know it bothers Brenda that she can’t attend all of the events for our grandkids because she’s just not well enough. But this experience has definitely brought the two of us closer.

“\textbf{I learned you really have to take the bull by the horns and demand the answers you need, even if it means driving seven or eight hours to a quality medical facility with better physicians.}”

Trudie: What is your greatest challenge as a caregiver?

Brent: The helpless feeling you get when you realize that sometimes there’s not a lot you can do. Once, Brenda developed a horrific infection and I had to administer the antibiotics, but when episodes like that flare up and your loved one is in pain or vomiting, you just want to make things better, and you can’t.

Trudie: How do you avoid caregiver burnout?

Brent: It’s tough. I’m a retired teacher and I work part time with at-risk children, so I try to stay busy. Brenda and I have a place up in northern Michigan where we like to go and get away when her health permits.

Trudie: What do you want off your chest?

Brent: These immune diseases are so rare and some of the doctors you meet can be so flippant. I’ll never forget that first doctor saying, “Oh, it’s just the Lipitor,” without even running any tests! I learned you really have to take the bull by the horns and demand the answers you need, even if it means driving seven or eight hours to a quality medical facility with better physicians.

Trudie: What have you learned through this journey?

Brent: That you do what you have to do. You’re going to learn to set up IV lines and how to give shots. You’re going to learn medical lingo and how to do research. You learn what love really is — holding your wife’s head while she throws up, helping her learn to bathe and use the restroom again. You learn you get a little ticked off when you see someone young and able take the handicapped spot you really need. Every day, I learn something new.

Trudie: What advice do you have for others?

Brent: Don’t be complacent, and don’t accept everything you’re told. Become an active learner about whatever disease state you’re facing. Also, be confident enough to ask questions, or be willing to say to the doctor: “I don’t understand that.” Also, I’ve found that it doesn’t help to walk around like “gloomy Gus”; you have to look for the positive in each situation. Right now, Brenda is so much better and she’s been able to go back to work as our local township treasurer; we’re thankful for that.

Trudie: Have you had any issues with insurance companies?

Brent: No, we’ve been very fortunate so far. We easily spend $20,000 a month on healthcare, and we’ve only had one issue where a $600 claim was not covered.

Trudie: Any final thoughts for our readers?

Brent: I hope people in my same boat are helped by hearing my story. I just want them to know they are not the only ones suffering through this.

Trudie Mitschang is a staff writer for IG Living magazine.
I AM VERY open about telling others about my autoimmune condition. The hardest part is trying to explain my treatment. Immunoglobulin (IG) is quite a mouthful to pronounce, let alone spell. Then, I have to explain how it works. At first, I tried using all the medical terms to describe IG and how it helps me. Besides mangling all the technical words and even confusing myself about what I just said, I could see the other person drifting off. I also found I was getting depressed over the actual medical process of what I was going through.

So, I decided a while ago to be true to myself and tell it like it is from my perspective. There’s a reason the term “arts and sciences” exists. I’m already living the science, so why shouldn’t I get creative with the arts side? After all, if life is a movie and we are the stars of our own film, then I want all aspects of my life to be colorful. Dr. Seuss states it best: “I like nonsense; it wakes up the brain cells. Fantasy is a necessary ingredient in living; it’s a way of looking at life through the wrong end of a telescope. Which is what I do, and that enables you to laugh at life’s realities.”

Watching John Hughes films about the various cliques in school and how their stories play out through love, betrayal, angst and humor has had a profound impact on my life. I try to visualize my IG infusions with that same cinemagraphic scope:

Imagine the inside of my body as a high school dance. There are all types of social cliques in attendance. My nerve endings are what are being served at the party buffet table (quite the healthy snack). The Rebel Nerve Eaters attending the dance declare: “This party is lame! We like eating nerve endings more than dancing anyway.” They head over to the party buffet table and chow down nonstop — to my detriment. Then, in flows the cool, pretty foreign exchange students: the IG Girls. They only have eyes for the Rebel Nerve Eaters and sweetly say: “We want to dance with you.” The Rebel Nerve Eaters are drawn to them: “You’re so cute and different. Plus, we really do like to dance.” Unable to resist them, the Rebel Nerve Eaters stop munching and go off with the IG Girls, giving the buffet table (my nerves) a rest. For a while, they dance carefree, have fun and fall in love. But at some point, the IG Girls’ party shoes get tired, they start flirting with other guys and someone starts turning up the bright gym lights. The Rebel Nerve Eaters feel rejected and hungry again, so back to the party buffet they go. That’s when I need another infusion. My happy ending depends on the IG Girls “infusing” life into the party and falling in love with the Rebel Nerve Eaters.

I have to face enough reality with my chronic illness: tests, medicines, medical bills, physical ailments, infusions, etc. I figure a little dose of imagination never hurt anyone. I’m already special with the neurological condition I have. How I make it part of my life and share it with others is my choice — as it is for all others with chronic illness. So the next time you’re asked what IG is or how it helps you, just speak from the heart. I know I feel better just being myself and not trying to sound like a doctor.

Now, cue the ‘80s music. My demyelinating macrophages want to get their boogie on, and the cute IG Girls just hit the dance floor! ☀️

STACY OLIVER was diagnosed in 2008 with multifocal motor neuropathy (MMN). She is the assistant director of the Center for the Writing Arts at Northwestern University, a jewelry and accessory artist (www.dancingstones jewelry.com), and she is working on her secret super hero identity as Neuropathy Girl.
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**Bottoms Up!**

*By Cheryl L. Haggard*

**I’M GERMAN.** I love all things Deutschland: volkswagens loaded with Blaupunkt stereo equipment, Octoberfest (I’m not a lush, but it wouldn’t surprise me if my lab reports confuse “B” cells for “brew” cells), Hummel figurines, accordion music, cuckoo clocks from the Black Forest und apple strudel. The first word for most English-speaking toddlers is “mama” or “dada”; mine was “prost!” (translation: “cheers!”). To top it off, I needed therapy in kindergarten because I didn’t understand why the cafegymatium didn’t include potatoes with my graham crackers and milk.

My dowry isn’t just clocks that drive you crazy and belching after gulping Glögg. I also hold credentials from the Hoxmeier, Gildemeister and Schwander School of Medical Opinion and Pharmaceuticals. I graduated in the top of my class, majoring in organic remedies with a minor in guilt. We are the ones who make no excuses for telling you, while waiting in line at the pharmacy no less: “That rash of yours will be gone in a flash with spring water and fireplace ash!”

I was the only third-grader at Eagle Elementary who knew the purpose of a wet nurse (just Google “women-nursing-someone-else’s-child” and then you’ll know). And, when I was having trouble getting my milk to come in after birthing our first, Aunt Sophie brushed the lactation nurse aside and demanded that the hospital “needs to feed these girls beer! Don’t you know the yeast and hops in a good ale stimulates milk production?” I thought I overheard Aunt Sophie, while shaking her head, calling my lactation specialist a “dumb Kopf.”

We Germans aren’t just good at lactation, but just about anything that ails. American culture has the BRAT (banana, rice, applesauce and toast) diet for the intestinal bug. Not good enough for us, however! The Hoxmeier, Gildemeister and Schwander School of Medical Opinion and Pharmaceuticals will tell its patients to “mix some fresh dirt into whatever liquid beverage suits you.” With that, your malady will dry up almost instantly, despite the fact you have concrete bowels. Gross, but effective.

Like many of you, our family spent hours and hours inside “traditional” doctors’ offices looking to anyone with a clue on how to heal my primary immune deficient disease (PIDD) kids. Our kids gave gallons of blood samples, took quarts of antibiotics by the teaspoonfuls, and produced enough green goo out of their sinuses to keep a building from falling over. In fact, I was seriously thinking about pitching a tent in my kids’ pediatrician’s office, since we were there every week. Sound familiar? And if a week passed and I didn’t have to go to the doctor with at least one of the kids, I wouldn’t know what to do with myself!

Whether it was my mama gut or good denial, I didn’t call on my heritage to heal my sick babies. We were so far gone from how I was medically treated by the Dr. Wack-a-Doodles...
that their ancient antidotes didn’t even cross my mind. So when intravenous immune globulin (IVIG) was introduced to our PIDD kids, I was elated that we finally had hope and an organic (human plasma cells, how organic can we get?) therapy that might break the unending cycle of synthetic antibiotic use. However, after Caleb’s first infusion, I was skeptical. I don’t remember how long it took, but I do recall this: Before his next infusion, which was scheduled four weeks later, I think the only curative he took was Flinstones multivitamins.

I’ve told countless others our family’s story about how IVIG saved the lives of our son Caleb and his sister, Molly, as well as improved the quality of my father’s life until his death in 2009. And, because my adult life has been a platform for encouraging healthy folks to donate plasma and for spreading the good news about strides made in the immune-autoimmune community, I’d forgotten about my indoctrination into the Hoxmeier, Gildemeister and Schwander School of Medical Opinion and Pharmaceuticals. After all, the old had passed and the new had come. I had been won over by modern medicine, or so I thought.

“How long have you had that cough?” my best friend, Lori, asked, as she blew steam away from her coffee confection.

“Oh, about a week or so, why?” I sputtered.

“I don’t know, I’m just a little concerned that’s all,” she said.

“Why don’t you come by the office and we’ll squeeze you in to see Dr. Schwartz?”

It’s nice to have a best friend who is also in the medical field. Lori is not only a mom, but a medical professional. What this means is she has just enough worry and nagging abilities to convince you to see a highly respected family physician.

“Well, OK. Only if I see Dr. Schwartz, though,” I hacked. “He’s the best. I don’t wanna see that herbal-pushin’ PA.”

Later that day, I found myself sitting on the examination table in Dr. Schwartz’ practice. While I smacked my legs against the table as if I was 5½, I nervously played with the “protective paper” my kids draw on. It had been a while since seeing a family practitioner, and I was a little leery of what he might say. I didn’t want to waste his time or mine just for a silly little cough.

Two seconds later, Dr. Schwartz knocked on the door and waltzed into the room, with Lori tow ing behind.

“So Lori tells me you’re not feeling well,” Dr. Schwartz chimed.

I looked right into Lori’s eyes, and if I could have read her facial expression, it would have said: You are not wasting Dr. Schwartz’ time, so stop with the snippy ‘tude.

Dr. Schwartz examined my ears, my breathing, my reflexes (almost kicked Lori!) and then gently pushed the stick on my tongue so he could check my nonexistent tonsils.

“Say AHHHHHHH.”

“AHAAAAAAH,” I gagged.

Lori had to turn around to avoid bursting out in laughter as I almost dry-heaved on Dr. Schwartz’ designer shoes.

“Well, that was pleasant,” I said, trying to breathe in some sort of dignity.

Dr. Schwartz began writing a prescription on a watermarked pad. I felt relieved that I did indeed need something potent for my cough.

Dr. Schwartz handed me the script and instructed me: “Get on this right away. You’ve got a pretty good cough that thankfully hasn’t quite gotten to your lungs.” Then, Dr. Schwartz patted me on my leg and said: “I think you’ll be OK. A little rest and this concoction should do the trick.”

“Thanks for your time, Dr. Schwartz,” I said as he handed the chart notes to Lori.

“So, what did he give you?” Lori asked.

I studied the script that lay in my hand and began to read the words out loud, trying hard not to laugh:

“Take one tablespoon of honey, a squeeze of lemon and a shot of good brandy or Jägermeister. Bottoms up!”

“You know,” Lori started. “Dr. Schwartz’ mother is a physician in Germany and he’s been using a lot of her ‘old family secrets’ to treat our patients.”

I looked at the prescription that lay in my hands as if I was looking at my 102½-year-old Great Grandma and resolved: “Dr. Schwartz is a brilliant physician.”

“Yeah,” Lori agreed. “Dr. Schwartz is always telling us, ‘If it ain’t broke, don’t fix it.’”

CHERYL L. HAGGARD is a stay-at-home mom and has three children, two of whom have CVID. She and her husband, Mark, also operate Under the Hood Ministries at www.underthehoodministries.org.
PATIENTS DEALING WITH a lifetime of illness eventually adapt to what the disease does to their bodies. What they don’t easily adapt to is what the disease does to their lives. For instance, those transitioning moments in life that healthy individuals often breeze through and take for granted can be downright difficult for the chronically ill. Perhaps one of the biggest transitioning moments for everyone is moving into adulthood, which often means choosing a college and a career. And Keegan McFalls, who was diagnosed with common variable immune deficiency (CVID) at age 3, can tell you that these choices are no last-minute decisions; they are something he had to take great pains to plan for.

College Life

The fact that Keegan had been infusing immune globulin (IG) subcutaneously prior to college didn’t make his transition to college life too much easier. He still had to learn how to take responsibility for his own infusions while away from home, which also meant ordering his own supplies. In addition, infusing while living in a dorm was a big change from infusing at home. “I had to be a little more careful with my health,” says Keegan. “I didn’t always have as much energy as my friends. [And], I found that I tend to need a little more sleep than most of my friends, although I rarely got enough sleep anyway.”

His energy level played a big part in college life. Infusing 7.5 grams of IG once a week, Keegan would find that on weekends, when he was coming up on his next infusion, he would still get a little tired. “So, sometimes, I didn’t always want to go out and do something on Saturdays,” explains Keegan. His social life sometimes suffered, but that wasn’t all that was affected. Setting up his infusions took time, and that cut into his studying time — the time “when I could be doing homework.” And, he didn’t have the energy to work as well as study. So, he found that the most efficient way for him to earn money was to

Immune globulin (IG) is a miraculous therapy, and no one knows this better than patients who receive it for an immune-mediated disease. Indeed, without IG, these individuals would fail to make the transition from living in a constant state of illness, struggling to survive, to a healthy, happy lifestyle. That is what this column is about — the unique and sometimes extraordinary stories of people of all ages whose lives have positively transitioned with the help of IG. We want to hear your stories! Email us at editor@igliving.com.
work longer hours during the summer so he didn’t have to work during the school year.

Career Life

This past April, Keegan graduated with a Master of Accountancy degree, a career path that was not chosen lightly. Knowing that he needed health insurance to continue to receive IG treatment for the rest of his life, Keegan says he “went into accounting because I wanted a backup plan if I couldn’t get a normal business job.” The way he figured it, there will always be jobs in accounting, which means more likely than not he will not have to go without health insurance.

Fortunately, Keegan ended up really liking accounting. And, while the backup plan provided some extra peace of mind for him, Keegan’s desire to get a job that would provide stable health insurance is what steered him to a more stable career path. That didn’t make getting his career started any easier, however. Despite multiple interviews, he was coming up empty, and he couldn’t understand why he had received no job offers. He would get a first interview and it would go well, and then, after a background check, the recruiter would tell him they had decided to hire another candidate. “Even though, a lot of times, they would be less-qualified candidates,” says Keegan.

Keegan eventually realized that the problem was his illness: “I have a few articles about me on the Internet and about my disease,” he says, which he believes were discovered during the background checks and led to eliminating him as a candidate.

Luckily for Keegan, a career adviser at the school of accountancy gave him advice about how to handle his disease with potential employers and also helped him practice his interviewing technique. This past September, he landed a job as an auditor for a company that performs high-security work.

The fact that Keegan had been infusing immune globulin (IG) subcutaneously prior to going to college didn’t make his transition to college life too much easier.

Self-“Insured”

Once Keegan was hired, his next transition was to ensure that he was adequately insured. He says the main factors he needed to look at were the out-of-pocket maximum, ease of approval and the broadest provider network possible. “All of my company’s plans had the same maximum, so I looked at the last two parts,” explains Keegan. “I knew that my current [insurance] company was pretty good about approving IG, so I knew they were a safe bet.” Since Keegan had moved out of state for his job, he didn’t have an immunologist. That played into the last part of his decision. “I made sure to go with the insurance company with the largest number of in-network providers so I would have the best chance of finding a good immunologist in my insurance network.”

Because of his disease, Keegan also had to be concerned about sick leave and long-term disability. “I was able to buy some long-term disability from my employer, which did not require a health examination if done within the first 30 days of employment,” says Keegan. And, “I was able to create an FSA [flexible spending account] to help offset my deductible and out-of-pocket maximum.”

Since beginning his new job, Keegan informed the necessary company employees about his illness, but his supervisor and co-workers are not aware. Keegan says his company has been “really good” about providing coverage for his IG; the only part that was difficult was getting the copay figured out. But as far as his worklife goes, he wants to keep his illness to himself. “I have decided to not let [my co-workers] know for now,” explains Keegan. I will probably tell them later on, but while I am still new to the company, I’d rather they not know, just to be safe.”

Harder Decisions in Life

Eventually, every child must make decisions about education and career, but as Keegan’s story so amply describes, having a chronic illness makes those decisions much more complicated. In taking on these challenges early in life, he
Keegan McFall graduated in April with a Master of Accountancy degree, a career path that was chosen as a way to ensure he would likely always be gainfully employed. Keegan has learned the power of planning ahead and making proactive choices that will benefit him most long-term. As a result, he’s become more self-reliant than most healthy individuals at this life stage. According to Keegan, “I learned how big of a cost [IG] is to me. A big part of my expenses are my medical bills.” To compensate for this heavy challenge, Keegan made strategic choices about his own health insurance and leap: “I would say, look heavily at the benefits provided with the job offer,” says Keegan. “Good benefits can easily offset a job offer by $5,000 to $10,000.” His current health plan and FSA account are saving him much more money than if he had gone to work at another company without comparable benefits. “Also, learn to evaluate insurance companies,” he continues. “Talk to people with the same disease about their experiences to see what insurance companies will approve your medicine and what companies will make you work for it.” Last, Keegan recommends looking at how the employer treats health problems. “My employer does a really good job of trying to keep employees healthy,” he says. “They even have a program to help people with chronic diseases to reduce their costs,” not by canceling their medicine, but by getting them the treatment they need and working on plans to help reduce their health risks.

Because of what he has to deal with, he has learned to be a lot more self-reliant than most healthy individuals have to during this time.

RONALE TUCKER RHODES is the editor for IG Living magazine.
Finding a Championship Team to Treat Your Child’s Immune Deficiency

It can be difficult to find a championship team when dealing with nonspecialists, but it is possible.

By Mark T. Haggard

AS FOOTBALL SEASON came to a close last year, I was reminded of what it means to be a team and a team player. Specifically, I reflected on how a team is built and what separates a good team from a bad team. Championship teams — those that win Super Bowl and World Series games — have players who are each responsible for a specific role that, when combined, work for the greater good. In contrast, nonchampionship teams haven’t figured out how to work together; they are simply conglomerates of players wearing the same uniform. Without a doubt, parents of children with immune deficiencies need championship teams — of physicians. And, our quest to put together the best team possible can sometimes be a long, arduous process.

For the most part, the specialists caring for our children are good
people. They can empathize with our frustrations about our children’s disorders. They spend time with us, and they listen to our concerns. They greet us at conferences and introduce us to their colleagues, calling us by our first names. My children’s immunologist gave me his “back” line to reach him anytime. He gives his best effort for our team.

As a coach, I have had to challenge players to play better, and I’ve had to cut players who could not live up to the challenge. Putting together a team of doctors to treat our children’s immune deficiencies takes time, perhaps years. You may have to cut some people; you may get cut yourself. But, with perseverance, you will find a team and appoint a doctor captain. That’s what happened to us, and soon after, our team was assembled to provide us the high quality of care that we receive today.

Leanne’s Search for a Team
Leanne has had a difficult time finding doctors for her team. Her health issues started with seven years of infections and ulcers. She suspected an immune deficiency, but doctors were skeptical. She was hospitalized in 2007 with ulcers in her throat, esophagus and intestines and with a white blood cell count of almost zero. Doctors suspected that she had cancer, even when she told her doctors that she had a cousin with common variable immune deficiency (CVID) and that she would like to be tested for that. Instead, they brought in a number of cancer specialists. She became infected with C. difficile after taking the plethora of antibiotics prescribed to her. When they ran out of ideas, her team of doctors said: “You’re our mystery girl; we have no idea what is wrong with you.” After six weeks in the hospital, a nurse entered Leanne’s room with intravenous immune globulin (IVIG). “So do I have CVID?” Leanne asked. “Oh yeah,” the nurse replied. “I thought you knew.”

After being discharged from the hospital, Leanne stayed with the hematologist/oncologist assigned to her and received IVIG every four weeks at a center with cancer patients. “That really messed with my head,” she says. “I was thinking ‘IVIG today, chemo tomorrow.’” When she asked to change her prescription because of horrible side effects, they replied: “We don’t pick the brand; we just order from the pharmacy and they send what they send.” She then cut the hematologist and went to see an immunologist.

The ENT Leanne went to for her sinus infections recommended surgery after the second visit. She traded him for another ENT more familiar with CVID. Leanne’s primary care physician ignored her immune problems, simply telling her: “Well, you’re overweight and depressed.” When she asked to be referred to a gastroenterologist when diagnosed with mastocytosis (a skin disease that produces lesions and intense itching), her doctor denied her request and said: “That is what you have; just take your medicine.”

“CVID is the worst thing that could have happened to me,” Leanne says. “I have no faith in doctors. Not one of these specialists that saw me in the hospital would even tell me my diagnosis. No one sat down with me, explained my illness, my treatment options, possible side effects.” Leanne pleads for a doctor “who cares enough to be educated or doesn’t get their
toes stepped on when you try to give them info about your illness.” This unfortunate series of events has given her a jaded attitude toward the medical profession. “I envy CVID patients who have a team of great doctors,” she says. “I’m trying to get there, but four years later, I am still not there.”

Finding the Role Players

Many parents whose children have an immune deficiency have heard or experienced similar stories. Talking to doctors can be intimidating. In the vast majority of cases, they are more highly educated, and often, they speak in medical jargon that we do not understand. A few believe that our input is not worth their consideration. Nevertheless, our life, or that of our children’s, is in their hands. Doctors should be confident, but they should have enough humility to know where their specialty ends and when to send an issue to another doctor. “My son is not a test tube,” I often asserted. “Get him to a person who can treat him.”

According to Dr. Erika Lawrence, associate professor of psychology at the University of Iowa, when dealing with nonspecialists, it is important to be assertive. In spite of their tight schedule, she says, “we are still their patients, and we are paying for their services.” A good introductory sentence could be something like: “I want to make sure we are on the same page.” Dr. Lawrence urges parents not to let doctors leave the room: “Tell them that you have a series of questions that you want to ask.”

Dr. Lawrence also suggests that nonspecialists be educated about immune deficiencies. Like athletes watching film and learning about their next opponent, doctors should be willing to become educated concerning the opponents of our children’s immune systems. Parents should consider bringing in a one-page description of their child’s medical condition, and a list of the medications that they are taking. Nonspecialists also should be willing to contact the child’s immunologist, the “quarterback,” when problems arise. If not, the dysfunction of the team will severely compromise the child’s health.

Treating Immune Deficiencies: A Team Sport

Treating immune deficiencies is a team sport. Because of their ability to see the entire field, immunologists should be the quarterbacks, able to distribute important facts about the child’s condition to other team members. Other team members will play varying roles. Some members will be humble, carrying the load without saying much, getting something done and leaving you looking around wondering how it happened. Some will be arrogant, doing their touchdown dance, but bringing so much to the table that we know that we cannot work without them. Many are “role players,” doing what is expected of them. No matter what, though, we should not be afraid to cut doctors who do not give their best effort. When the team is all on the same page of the IG playbook, the result is a championship — a long life of good health.

MARK T. HAGGARD is a high school teacher and football coach, and has three children, two of whom have CVID. He and his wife, Cheryl, also operate Under the Hood Ministries at www.underthehoodministries.org.
Using Adaptive Equipment to Maintain Independence

By Kris McFalls

**IMMUNE-MEDIATED DISEASES** are sometimes accompanied by comorbidities that can lead to decreased range of motion, reduced muscle strength and hampered mobility. Pain, swelling and weakness in the upper extremities in particular can severely impact activities of daily living such as bathing, dressing and eating. And, those same issues in the lower extremities can affect balance and the ability to transfer safely from one position to another. While these symptoms are frustrating, there is help. People with chronic disease can continue to live an independent and fulfilling life with the help of specially adapted equipment.

Slippery When Wet  
The bathroom is the one place in a home where a person should be allowed to have a bit of privacy. For people with muscle weakness or balance issues, this also can be an especially dangerous place. The use of shower chairs, hand-held shower heads and nonskid appliques all are good safety measures to consider. In addition, properly installed grab bars in the tub and toilet area can help individuals maintain balance, especially for those who normally use a mobility device such as a cane or crutches, as these devices can be very dangerous on wet surfaces.

**People with chronic disease can continue to live an independent and fulfilling life with the help of specially adapted equipment.**

Dress for Success  
Dressing should not take so much energy that you need a nap once you are done. Likewise, painful joints should not force one to spend the entire day in pajamas. People who find dressing particularly taxing or who have problems with balance should start by dressing in a seated position. Doing so helps conserve energy and lessens the risk of injury from loss of balance. Those with arthritic finger joints or hands affected by nerve damage can use a button hook to allow them to continue to dress in a way that fits their style and comfort level.

Sturdy shoes are especially important for people with balance and coordination difficulties. Shoes secured with laces are safer because they provide more stability and support than a slip-on shoe. Traditional shoelaces, however, require good hand dexterity and can be difficult for those with chronic joint issues. Replacing traditional laces with elastic shoe laces can help solve the problem and still allow the user to wear a normal shoe.

Get Up and Go  
The ability to stand up is often taken for granted. People with lower extremity weakness and problems with balance know just how perilous and taxing this maneuver can be. Arguably, the most difficult transitions are the maneuvers needed to get in and out of an automobile. Twisting one’s body to get lower extremities in and out of the car can be made easier by using a swivel cushion. This allows the user to twist their body with less friction and straining of lower-back muscles. Pushing up out of the car can be made easier with the use of a bar that slides into the door latch. The user then has a secure bar to push on rather than an unstable door.

Get Evaluated First  
Before trying any of these suggestions, patients should meet with their doctor and a physical or occupational therapist to have their needs evaluated to ensure the proper equipment is ordered and safely used. With the proper support, they just may find that living with a chronic disease does not have to mean living a life dependent on others. With a few adaptations, those with a chronic illness can maintain their dignity and their independence.

**KRIS MCFALLS** is the full-time patient advocate for IG Living magazine.
Aids for Arthritis Inc.
The cushioned grip of the Good Grip Button Hook makes buttoning clothes easy. The built-up handle features flexible ribbing that adapts to any grip. Handle length measures 4 1/4 inches (10.8 cm), total length is 6 1/4 inches (15.9 cm), and the handle diameter is 1 1/4 inches (3.8 cm).
(800) 654-0707; www.aidsforarthritis.com/catalog/good-grip-button-hook.html

ArthritisSupplies.com
The Deluxe Swivel Seat Cushion provides 360 degrees of swivel action. It enables a person to rise from a seated position while helping to prevent arthritic hip and back strain caused by twisting of the torso, and it has 1 3/4 inches of soft foam cushion padding for added comfort. A ball-bearing roller mechanism allows the seat cushion to turn without binding. The durable flexible base with slip-resistant bottom contours to the seat and stays in place.
(877) 750-0376; www.arthritisupplies.com/site/371928/product/CDM1994

ArthritisSupplies.com
The Handybar locks securely and reliably into position to help individuals get into and out of a car. It is made of forged steel with corrosion-resistant plating, is easy to insert and remove, and is strong, durable and affordable. Measuring approximately 9 inches long, the Handybar is lightweight and compact, and it can be carried in a handbag or pack.
(877) 750-0376; www.arthritisupplies.com/site/371928/product/CMT96314

LifeSolutions Plus
The Deluxe Elastic Shoelaces allow enough stretch so that once tied, shoes can be slipped on and off without untlying the laces. They are designed for athletic shoes with five, six or seven sets of eyelets, are 3/8 inches wide and are easy to grip. The shoelaces are sold two pairs per package.
(877) 785-8326; www.lifesolutionsplus.com/deluxe-elastic-shoelaces-p-191.html

Lock Laces
Lock Laces is a patented “elastic lacing system” that features specially designed elastic laces combined with a spring-activated locking device. They can be worn with all styles of athletic shoes and casual lace-up shoes for any desired use, they never have to be retied during sports or activities, and they eliminate tying and untying of laces or double knots.
877) 445-2237; www.locklaces.com

Moen
Moen’s ADA-compliant chair features a host of options, including baskets, handles, hand-held shower heads, non-slip surface with built-in drainage and rubber feet for stability. The chair supports up to 300 pounds.
(800) 289-6636; www.moen.com/bathroom/safety/_/N-67x
General Resources
These organizations provide information about various disease states, which can be found by conducting a search of the disease state name.

- Advocacy for Patients with Chronic Illness: www.advocacyforpatients.org
- The Alliance for Biotherapeutics (fair access to plasma therapies): www.bioalliance.org
- American Autoimmune Related Diseases Association (AARDA): www.aarda.org
- American Chronic Pain Association (ACPA): www.theacpa.org
- Band-Aides and Blackboards: www.lehman.cuny.edu/faculty/jfleitas/bandaides
- Cleveland Clinic: www.clevelandclinic.org/health
- eMedicine from WebMD: emedicine.medscape.com
- FamilyDoctor.org: www.familydoctor.org
- Johns Hopkins Medicine: www.hopkinsmedicine.org
- KeepKidsHealthy.com (pediatrician’s guide to children health and safety): www.keepkidshealthy.com
- Mayo Clinic: www.mayoclinic.com
- National Infusion Center Association: www.infusioncenter.net
- National Institutes of Health: www.niams.nih.gov/hi/topics/pemphigus/pemphigus.htm
- National Organization for Rare Disorders (disease-specific support groups and virtual communities for patients and caregivers): www.rarediseases.org
- Office of Rare Diseases Research: rarediseases.info.nih.gov
- Patient Advocate Foundation (patient access to care, maintenance of employment and financial stability): www.patientadvocate.org
- WebMD (medical reference): www.webmd.com

Disease-State Resources
Ataxia Telangiectasia (A-T)
Websites
- A-T Children’s Project: www.atcp.org

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
Websites
- GBS/CIDP Foundation International: www.gbs-cidp.org
- The Neuropathy Association: www.neuropathy.org

Evans Syndrome
Online Peer Support
- Evans Syndrome Research and Support Group: www.evanssyndrome.org

Guillain-Barré Syndrome (GBS)
Websites
- GBS/CIDP Foundation International: www.gbs-cidp.org
- The Neuropathy Association: www.neuropathy.org
Online Peer Support
- GBS/CIDP Foundation International Discussion Forums: www.gbs-cidp.org/forums

Idiopathic Thrombocytopenic Purpura (ITP)
Websites
- ITP Support Association – UK: www.itpsupport.org.uk
- Platelet Disorder Support Association: www.pdsa.org

Kawasaki Disease
Websites
- American Heart Association (how the disease affects the heart): www.americanheart.org/presenter.jhtml?identifier=4634
- Kawasaki Disease Foundation: www.kdfoundation.org

The nonprofit Patient Services Incorporated, www.patientservicesinc.org, specializes in health insurance premium, pharmacy co-payment and co-payment waiver assistance for people with chronic illnesses. (800) 366-7741
Mitochondrial Disease

Websites
- United Mitochondrial Disease Foundation: www.umdf.org

Multifocal Motor Neuropathy (MMN)

Websites
- The Neuromuscular Center at Washington University: www.neuro.wustl.edu/neuromuscular
- The Neuropathy Association: www.neuropathy.org

Multiple Sclerosis (MS)

Websites
- All About Multiple Sclerosis: www.mult-sclerosis.org/index.html
- Multiple Sclerosis Association of America: www.msaa.com
- Multiple Sclerosis Foundation: www.msfacts.org
- National Multiple Sclerosis Society: www.nationalmssociety.org

Online Peer Support
- Friends with MS: www.FriendsWithMS.com
- MSWorld’s Chat and Message Board: www.msworld.org

Myasthenia Gravis (MG)

Websites and Chat Rooms
- Myasthenia Gravis Foundation of America (MGFA): www.myasthenia.org

Online Peer Support
- Autoimmune Information Network Inc.: www.aininc.org

Myositis

Websites
- The mission of The Myositis Association, www.myositis.org, is to find a cure for inflammatory and other related myopathies, while serving those affected by these diseases. (703) 299-4850

Online Peer Support
- The Cure JM Foundation www.curejm.com (760) 487-1079

- The Jeffrey Modell Foundation, www.info4pi.org, is dedicated to early and precise diagnosis, meaningful treatments and, ultimately, cures for primary immunodeficiency. (212) 819-0200

Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus (PANDAS)

Websites
- P.A.N.D.A.S. Network: pandasnetwork.org

Pemphigus and Pemphigoid

Websites
- The International Pemphigus and Pemphigoid Foundation: www.pemphigus.org

Peripheral Neuropathy (PN)

Websites
- The Neuropathy Association, www.neuropathy.org, is devoted exclusively to all types of neuropathy, which affects upwards of 20 million Americans. The Association’s mission is to increase public awareness of the nature and extent of PN, facilitate information exchanges about the disease, advocate the need for early intervention and support research into the causes and treatment of neuropathies. (212) 692-0662

Online Peer Support
- Neuropathy Action Foundation: www.neuropathyaction.org
- Calgary Neuropathy Association: www.calgaryneuropathy.com

Primary Immune Deficiency Disease (PIDD)

Websites
- The Immune Deficiency Foundation (IDF), www.primaryimmune.org, is the national patient organization dedicated to improving the diagnosis, treatment and quality of life of persons with primary immunodeficiency diseases through advocacy, education and research. (800) 296-4433

Online Peer Support
- The National Institute of Child Health and Human Development (NICHD), www.nichd.nih.gov, is part of the National Institutes of Health. Go to the “Health Information and Media” tab on the website and do a search under "Primary Immune Deficiencies (PIDD)"
- American Academy of Allergy, Asthma & Immunology: www.aaaai.org
- International Patient Organization for Primary Immunodeficiencies (IPPO): www.ipopi.org
- Michigan Immunodeficiency Foundation: www.midf.org
Sources

- National Institute of Child Health and Human Development (NICHD) (Click on “Health Information and Media” tab and search for “primary immunodeficiency”: www.nichd.nih.gov
- New England Primary Immunodeficiency Network: www.nepin.org
- Team Hope (for families and patients in New England): www.teamhope.info

Online Peer Support
- IDF Common Ground: www.idfcommonground.org
- IDF Discussion Forum: http://idffriends.org/forum
- IDF Friends: http://idffriends.org
- Jeffrey Modell Foundation Message Board: www.info4pi.org
- Rhode Island peer group: http://health.groups.yahoo.com/group/RhodeIslandPIDD

Scleroderma

Websites
- Scleroderma Foundation: www.scleroderma.org
- Scleroderma Research Foundation: www.srfcure.org
- Scleroderma Center: http://www.hopkinsmedicine.org/rheumatology/clinics/scleroderma_center.html

Online Peer Support
- CureZone.com: curezone.com/forums/f.asp?f=404
- International Scleroderma Network: www.sclero.org/support/forums/a-to-z.html

Stiff-Person Syndrome (SPS)

Websites
- American Autoimmune Related Diseases Association Inc.: www.aarda.org
- Autoimmune Information Network Inc.: www.aininc.org
- Living with Stiff Person Syndrome (personal account): www.livingwithspss.com
- Stiff Person Syndrome: www.stiffpersonsyndrome.net

Other Resources

Education and Disability Resources
  Provides protection for people with disabilities from certain types of discrimination, and requires employers to provide some accommodations of the disability.
- Individuals with Disabilities Education Improvement Act of 2004: http://idea.ed.gov/explore/home
- National Disabilities Rights Network: www.ndrn.org. This website offers a search tool to find resources in your state to assist with school rights and advocacy.
- Social Security: www.ssa.gov/disability
- U.S. Department of Education Website: www.ed.gov. This federal government website offers a parents section titled “My Child’s Special Needs.”
  Spells out your rights under Section 504 of the Rehabilitation Act.

Medical Research Studies
- ClinicalTrials.com: www.clinicaltrials.com
  This site has a registration form to request that you be notified about recruitment for future studies.
- ClinicalTrials.gov: www.clinicaltrials.gov
  A registry of federally and privately supported clinical trials conducted in the United States and around the world.

Food Allergies
- Allergic Disorders: Promoting Best Practice: www.aaaai.org
- American Partnership for Eosinophilic Disorders: www.apfed.org
- Food Allergy and Anaphylaxis Network: www.foodallergy.org
- World Allergy Organization: www.worldallergy.org

Product Information
- Influenza and the influenza vaccine: www.cdc.gov/flu or call (800) CDC-INFO: (800) 232-4636
- IVIG Flebogamma 5% DIF and 10% DIF: www.grifols.com/portal/en/US/products
- IVIG/SCIG Gammapard Liquid: www.gammagardliquid.com
- IVIG/Gammagard S/D: www.baxter.com/patients_and_caregivers/products/gammagard_sd_5.html
- IVIG/Gammaplex: www.gammaplex.com
- IVIG Privigen: www.privigen.com
- SCIG Hizentra: www.hizentra.com

Pump and Infusion Sets Websites
- EMEDE Corporation: www.safetymedicalproducts.com
- Graseby Marcal Medical: www.marcalmedical.com
- Intra Pump Infusion Systems: www.intrapump.com
- Micrel Medical Devices: www.micrelmed.com
- Norfolk Medical: www.norfolkm edical.com
- Repro Med Systems, Inc: www.rmsmedicalproducts.com
- Smith Medical: www.smiths-medical.com/brands/cadd

Have something to add to these pages? Please send your suggestions for additions to the IG Living Resource Directory to editor@IGLiving.com.
CSL Behring

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Hizentra®,

Immune Globulin Subcutaneous (Human), 20% Liquid

Before prescribing, please consult full prescribing information, a brief summary of which follows. Some text and references refer to full prescribing information.

1 INDICATIONS AND USAGE

Hizentra is an Immune Globulin Subcutaneous (Human) (IGSC), 20% Liquid indicated as replacement therapy for primary humoral immunodeficiency (PI). This includes, but is not limited to, the humoral immune defect in congenital agammaglobulinemia, common variable immunodeficiency, X-linked agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.

4 CONTRAINDICATIONS

Hizentra is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of human immune globulin or to components of Hizentra, such as polysorbate 80.

Hizentra is contraindicated in patients with hyperprolinemia because it contains the stabilizer L-proline (see Description [11]).

Hizentra is contraindicated in IgA-deficient patients with antibodies against IgA and a history of hypersensitivity (see Description [11]).

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity

Severe hypersensitivity reactions may occur to human immune globulin or components of Hizentra, such as polysorbate 80. In case of hypersensitivity, discontinue the Hizentra infusion immediately and institute appropriate treatment.

Individuals with IgA deficiency can develop anti-IgA antibodies and anaphylactic reactions (including anaphylaxis and shock) after administration of blood components containing IgA.

Patients with known antibodies to IgA may have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions with administration of Hizentra. Hizentra contains ≥50 mcg/mL IgA (see Description [11]).

5.2 Aseptic Meningitis Syndrome (AMS)

AMS has been reported with use of IGIV or IGSC. The syndrome usually begins within several hours to 2 days following immune globulin treatment. AMS is characterized by the following signs and symptoms: severe headache, nuchal rigidity, drowsiness, fever, photophobia, painful eye movements, nausea, and vomiting. Cerebrospinal fluid (CSF) studies frequently show pleocytosis up to several thousand cells per cubic millimeter, predominantly from the granulocytic series, and elevated protein levels up to several hundred mg/dL. AMS may occur more frequently in association with high doses (>2 g/kg) and/or rapid infusion of immune globulin product.

Patients exhibiting such signs and symptoms should receive a thorough neurological examination, including CSF studies, to rule out other causes of meningitis. Discontinuation of immune globulin treatment has resulted in remission of AMS within several days without sequelae.

5.3 Reactions Reported to Occur With IGIV Treatment

The following reactions have been reported to occur with IGIV treatment and may occur with IGSC treatment.

Renal Dysfunction/Failure

Renal dysfunction/failure, osmotic nephropathy, and death may occur with use of human immune globulin products. Ensure that patients are not volume depleted and assess renal function, including measurement of blood urea nitrogen (BUN) and serum creatinine, before the initial infusion of Hizentra and at appropriate intervals thereafter.

Periodic monitoring of renal function and urine output is particularly important in patients judged to have a potential increased risk of developing acute renal failure. If renal function deteriorates, consider discontinuing Hizentra. For patients judged to be at risk of developing renal dysfunction because of pre-existing renal insufficiency or predisposition to acute renal failure (such as those with diabetes mellitus or hypovolemia, those who are overweight or use concomitant nephrotoxic medicinal products, or those who are over 65 years of age), administer Hizentra at the minimum rate practicable.

Thrombotic Events

Thrombotic events may occur with use of human immune globulin products. Patients at increased risk may include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, hypercoagulable disorders, prolonged periods of immobilization, and/or known or suspected hyperviscosity. Because of the potentially increased risk of thrombosis, consider baseline assessment of blood viscosity in patients at risk for hyperviscosity, including those with hyperglobulins, factoring chylomicronemia/markedly high triglycerides (triglycerides), or monoclonal gammopathies. For patients judged to be at risk of developing thrombotic events, administer Hizentra at the minimum rate practicable.

Hemolysis

Hizentra can contain blood group antibodies that may act as hemolysins and induce in vivo coating of red blood cells (RBCs) with immunoglobulin, causing a positive direct antiglobulin (Coombs') test result and hemolysis. Delayed hemolytic anemia can develop subsequent to immune globulin therapy due to enhanced RBC sequestration, and acute hemolysis, consistent with intravascular hemolysis, has been reported.

Monitor recipients of Hizentra for clinical signs and symptoms of hemolysis. If these are present after a Hizentra infusion, perform appropriate confirmatory laboratory testing. If transfusion is indicated for patients who develop hemolysis with clinically compromising anemia after receiving Hizentra, perform adequate cross-matching to avoid exacerbating on-going hemolysis.

Transfusion-Related Acute Lung Injury (TRALI)

Noncardiogenic pulmonary edema may occur in patients administered human immune globulin products. TRALI is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever. Typically, it occurs within 1 to 6 hours following transfusion. Patients with TRALI may be managed using oxygen therapy with adequate ventilatory support.

Monitor Hizentra recipients for pulmonary adverse reactions. If TRALI is suspected, perform appropriate tests for the presence of anti-neutrophil antibodies in both the product and patient's serum.

5.4 Transmissible Infectious Agents

Because Hizentra is made from human plasma, it may carry a risk of transmitting infectious agents (e.g., viruses, and theoretically, the Creutzfeldt-Jakob disease [CJD] agent). The risk of infectious agent transmission has been reduced by screening plasma donors for prior exposure to certain viruses, testing for the presence of certain current virus infections, and including virus inactivation/removal steps in the manufacturing process for Hizentra.

Report all infections thought to be possibly transmitted by Hizentra to CSL Behring Pharmacovigilance at 1-866-915-6958.

5.5 Laboratory Tests

Various passively transferred antibodies in immunoglobulin preparations may lead to misinterpretation of the results of serological testing.

6 ADVERSE REACTIONS

The most common adverse reactions (ARs) observed in ≥5% of study subjects receiving Hizentra were local reactions (i.e., swelling, redness, heat, pain, and itching at the injection site), headache, vomiting, pain, and fatigue.

6.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, AR rates observed in clinical studies of a product cannot be directly compared to rates in the clinical studies of another product and may not reflect the rates observed in clinical practice.

The safety of Hizentra was evaluated in a clinical study for 15 months in subjects with PI who had been treated previously with IGIV every 3 or 4 weeks. The safety analyses included 49 subjects in the intention-to-treat (ITT) population. The ITT population consisted of all subjects who received at least one dose of Hizentra (see Clinical Studies [14]).

Subjects were treated with Hizentra at weekly doses ranging from 66 to 331 mg/kg body weight during the wash-in/wash-out period and from 72 to 379 mg/kg during the efficacy period. The 49 subjects received a total of 2264 weekly infusions of Hizentra.

No deaths or serious ARs occurred during the study. Two subjects withdrew from the study due to ARs. One subject experienced a severe injection-site reaction one day after the third weekly infusion, and the other subject experienced moderate myositis. Both reactions were judged to be "at least possibly related" to the administration of Hizentra.

Table 2 summarizes the most frequent adverse events (AEs) experienced by at least 4 subjects, irrespective of causality. Included are all AEs and those considered temporally associated with the Hizentra infusion, i.e., occurring during or within 72 hours after the end of an infusion. Local reactions were the most frequent AEs observed, with injection-site reactions (i.e., swelling, redness, heat, pain, and itching at the site of injection) comprising 98% of local reactions.
Table 2: Incidence of Subjects With Adverse Events (AEs)* (Experienced by 4 or More Subjects) and Rate per Infusion, Irrespective of Causality (ITT Population)

<table>
<thead>
<tr>
<th>AE (≥4 Subjects)</th>
<th>All AEs*</th>
<th>AEs* Occurring During or Within 72 Hours of Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%) of AEs of Subjects (n=49)</td>
<td>Number (%) of AEs (n=2264 Infusions)</td>
<td>Number (%) of Subjects (n=49)</td>
</tr>
<tr>
<td>Local reactions*</td>
<td>49 (100)</td>
<td>1340 (0.592)</td>
</tr>
<tr>
<td>Other AEs:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Headache | 13 (26.5) | 40 (0.18) | 12 (24.5) | 32 (0.14)
| Cough | 8 (16.3) | 9 (0.04) | 5 (10.2) | 6 (0.03)
| Diarrhea | 7 (14.3) | 8 (0.04) | 5 (10.2) | 6 (0.03)
| Fatigue | 6 (12.2) | 6 (0.03) | 4 (8.2) | 5 (0.02)
| Back pain | 5 (10.2) | 11 (0.05) | 4 (8.2) | 5 (0.02)
| Nausea | 5 (10.2) | 5 (0.02) | 4 (8.2) | 4 (0.02)
| Abdominal pain, upper | 5 (10.2) | 5 (0.02) | 3 (6.1) | 3 (0.01)
| Rash | 5 (10.2) | 7 (0.03) | 2 (4.1) | 3 (0.01)
| Pain in extremity | 4 (8.2) | 7 (0.03) | 4 (8.2) | 6 (0.03)
| Migraine | 4 (8.2) | 5 (0.02) | 3 (6.1) | 4 (0.02)
| Pain | 4 (8.2) | 5 (0.02) | 3 (6.1) | 4 (0.02)
| Epistaxis | 4 (8.2) | 6 (0.03) | 2 (4.1) | 3 (0.01)
| Pharyngolaryngeal pain | 4 (8.2) | 6 (0.03) | 2 (4.1) | 2 (<0.01)
| Arthralgia | 4 (8.2) | 5 (0.02) | 2 (4.1) | 3 (0.01)

* Excluding infections.
† Rate of AEs per infusion.
‡ Includes injection-site reactions as well as bruising, scabbing, pain, irritation, cysts, eczema, and nodules at the injection site.

The ratio of infusions with temporally associated AEs, including local reactions, to all infusions was 1338 to 2264 (59.1%; upper 95% confidence limit of 62.4%). Excluding local reactions, the corresponding ratio was 173 to 2264 (7.6%; upper 95% confidence limit of 8.9%).

Table 3 summarizes the most frequent ARs (i.e., those AEs considered by the investigators to be *at least possibly related* to Hizentra administration) experienced by at least 2 subjects.

Table 3: Incidence of Subjects With Adverse Reactions (Experienced by 2 or More Subjects) to Hizentra and Rate per Infusion (ITT Population)

<table>
<thead>
<tr>
<th>Adverse Reaction (≥2 Subjects)</th>
<th>Number (%) of Subjects (n=49)</th>
<th>Number (%) of Adverse Reactions (n=2264 Infusions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local reactions†</td>
<td>49 (100)</td>
<td>1338 (0.591)</td>
</tr>
<tr>
<td>Other AEs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>12 (24.5)</td>
<td>36 (0.016)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3 (6.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Pain</td>
<td>3 (6.1)</td>
<td>4 (0.002)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3 (6.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Confusion</td>
<td>2 (4.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Back pain</td>
<td>2 (4.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Migraine</td>
<td>2 (4.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
<tr>
<td>Abdominal pain, upper</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
<tr>
<td>Nausea</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
<tr>
<td>Rash</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
</tbody>
</table>

† Rate of AEs per infusion.
‡ Includes injection-site reactions as well as bruising, scabbing, pain, irritation, cysts, eczema, and nodules at the injection site.

Table 4 summarizes injection-site reactions based on investigator assessments 15 to 45 minutes after the end of the 683 infusions administered during regularly scheduled visits (every 4 weeks).

Table 4: Investigator Assessments* of Injection-Site Reactions by Infusion

<table>
<thead>
<tr>
<th>Injection-Site Reaction</th>
<th>Number† (Rate‡) of Reactions (n=683 Infusions§)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edema/induration</td>
<td>467 (0.68)</td>
</tr>
<tr>
<td>Erythema</td>
<td>346 (0.50)</td>
</tr>
<tr>
<td>Local heat</td>
<td>108 (0.16)</td>
</tr>
<tr>
<td>Local pain</td>
<td>88 (0.13)</td>
</tr>
<tr>
<td>Itching</td>
<td>64 (0.09)</td>
</tr>
</tbody>
</table>

† 15 to 45 minutes after the end of infusions administered at regularly scheduled visits (every 4 weeks).
‡ For multiple injection sites, every site was judged, but only the site with the strongest reaction was recorded.
§ Rate of injection-site reactions per infusion.
§ Number of infusions administered during regularly scheduled visits.

Most local reactions were either mild (93.4%) or moderate (6.3%) in intensity.

6.2 Postmarketing Experience

Because postmarketing reporting of adverse reactions is voluntary and from a population of uncertain size, it is not always possible to reliably estimate the frequency of these reactions or establish a causal relationship to product exposure.

The following adverse reactions have been identified and reported during the postmarketing use of IGIV products:

- **Infusion reactions:** Hypersensitivity (e.g., anaphylaxis), headache, diaphoria, tachycardia, fever, fatigue, dizziness, malaise, chills, flushing, urticaria or other skin reactions, wheezing or other chest discomfort, nausea, vomiting, agitation, back pain, myalgia, arthralgia, and changes in blood pressure
- **Renal:** Acute renal dysfunction/Failure, osmotic nephropathy
- **Respiratory:** Apnea, Acute Respiratory Distress Syndrome (ARDS), TRALI, cyanosis, hypoxemia, pulmonary edema, dyspnea, bronchospasm
- **Cardiovascular:** Cardiac arrest, thromboembolism, vascular collapse, hypotension
- **Neurological:** Coma, loss of consciousness, seizures, tremor, aseptic meningitis syndrome
- **Integumentary:** Stevens-Johnson syndrome, epidermolysis, erythema multiforme, dermatitis (e.g., bullous dermatitis)
- **Hematologic:** Pancytopenia, leukopenia, hemolysis, positive direct antiglobulin (Coombs') test
- **Gastrointestinal:** Hepatic dysfunction, abdominal pain
- **General/Body as a Whole:** Pyrexia, rigors

To report SUSPECTED ADVERSE REACTIONS, contact CSL Behring Pharmacovigilance at 1-866-915-6958 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

7 DRUG INTERACTIONS

7.1 Live Virus Vaccines

The passive transfer of antibodies with immunoglobulin administration may interfere with the response to live virus vaccines such as measles, mumps, rubella, and varicella (see Patient Counseling Information [17]).

7.2 Serological Testing

Various passively transferred antibodies in immunoglobulin preparations may lead to misinterpretation of the results of serological testing.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted with Hizentra. It is not known whether Hizentra can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Hizentra should be given to pregnant women only if clearly needed.

8.3 Nursing Mothers

Hizentra has not been evaluated in nursing mothers.

8.4 Pediatric Use

The safety and effectiveness of Hizentra have been established in the pediatric age groups 2 to 16, as supported by evidence from adequate and well-controlled studies. Hizentra was evaluated in 10 pediatric subjects with PI (3 children and 7 adolescents) in a study conducted in the US (see Clinical Studies [14]) and in 23 pediatric subjects with PI (18 children and 5 adolescents) in Europe. There were no differences in the safety and efficacy profiles as compared with adult subjects. No pediatric-specific dose requirements were necessary to achieve the desired serum IgG levels.

Safety and effectiveness of Hizentra in pediatric patients below the age of 2 have not been established.

8.5 Geriatric Use

Of the 49 subjects evaluated in the clinical study of Hizentra, 6 subjects were 65 years of age or older. No overall differences in safety or efficacy were observed between these subjects and younger subjects.
If you live with primary immunodeficiency disease (PIDD)...

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The Sub-Q Ig therapy that fits your life

Hizentra is a subcutaneous immune globulin (Sub-Q Ig) therapy that was deliberately designed to give you freedom and flexibility with your Ig treatment.

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• Always ready for immediate use

*Based on an equivalent dose in grams.

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Ask your doctor about Hizentra today.

Important Safety Information

Hizentra is indicated for the treatment of various forms of primary immunodeficiency (PI).

If you have a history of anaphylactic or severe systemic response to immune globulin preparations or selective immunoglobulin A deficiency, check with your physician, as Hizentra should not be used.

Hizentra is to be infused under your skin only; do not inject into a blood vessel.

Hypersensitivity reactions may occur with Hizentra. If your physician suspects you are having a negative reaction or are going into shock, treatment will be discontinued. Because Hizentra contains proline, you cannot be treated with Hizentra if you have hyperprolinemia (a high level of proline in your blood).

Hizentra is derived from human plasma. The risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated.

The most common drug-related adverse reactions (seen in 5% or more of subjects in the clinical trial) were local reactions (swelling, redness, heat, pain, and itching at the injection site), headache, vomiting, pain, and fatigue.

Your physician will monitor for potentially serious reactions associated with intravenous immunoglobulin treatment that might also occur with Hizentra, including renal dysfunction/failure, osmotic nephropathy, thrombotic events, aseptic meningitis syndrome (AMS), hemolysis, and transfusion-related acute lung injury (TRALI).

Ig administration may impair the effect of virus vaccines, such as measles, mumps and rubella. Before getting any vaccination, inform your doctor that you are using Hizentra.

Please see brief summary of full prescribing information for Hizentra on previous pages.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.
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