Lifelong Need for IG?
Weighing the Pros and Cons

Diagnosing PIDD: Problems & Solutions

Employment Screening: What’s Legal, What’s Not

Understanding SCID | IG Success Stories
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 immobolization 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).


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.

Evidence based. Patient proven.
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.
- Hyperproteinaemia, with resultant changes in serum viscosity and electrolyte imbalances may 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 (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.
- Passive transfer of antibodies may confound serologic testing.

---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.
A bout IG Livin g is the only m agazine dedicated to bringing comprehensive healthcare inform ation, imm une globulin inform ation, com m unity and reim bursem ent new s, and resources for successful living directly to imm une globulin consum ers and their healthcare providers.

IG Livin g, (ISSN 1949-4548), published bim onthly, is a com m unity service provided by FFF Enterprises, 41093 County Center Drive, Temecula, CA 92591, (800) 843-7477 x1362, fax (951) 699-9655.

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IG Living is the only magazine dedicated to bringing comprehensive healthcare information, immune globulin information, community and reimbursement news, and resources for successful living directly to immune globulin consumers and their healthcare providers.

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LEMS Syndrome 101
“It’s good to be living in the 21st century. This is especially true for those with chronic illness who rely on immune globulin to survive.”

Employment Screening: What’s Legal, What’s Not
“Hiring cases are difficult to win, but if a person doesn’t get the job and really feels their interviewer was in the wrong, there are options.”

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IG Living isn’t just a magazine; it’s an interactive community of people with interesting stories.
Our blog: www.igliving.com/blogengine
Our Facebook page: www.Facebook.com/IGLivingMagazine

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 kmcfalls@IGLiving.com or calling (888) 433-3888, ext. 1349.
Undiagnosed Consequences

One of my favorite TV shows is “House.” Each episode, Dr. Gregory House and his staff of expert physicians solve a medical puzzle to save the life of their patient. Theories and tests fail to reveal the patient’s true illness, until minutes before the show ends something triggers Dr. House’s brilliance and he makes a diagnosis. Too bad diagnoses don’t happen that quickly in real life!

Primary immunodeficiency (PIDD) is one of the most perplexing of medical puzzles. According to the Immune Deficiency Foundation (IDF), it takes, on average, 12.4 years for a PIDD patient to be diagnosed. And, while more Americans are diagnosed with PIDD every year, thousands more go undiagnosed.

The consequences of undiagnosed PIDD are many and hefty, including poor quality of life, permanent physical damage and more costly healthcare and other payments. According to a 2005 IDF survey, many patients have serious and/or chronic health conditions prior to diagnosis and are frequently too sick to perform normal activities. Thirty-seven percent of patients have permanent damage to their bodies by the time they are diagnosed. And, the cost to treat PIDD patients with intravenous immune globulin is a minimum of $25,300 cheaper per patient than it is to treat patients who go undiagnosed. Savings would be even higher for patients who didn’t suffer permanent organ damage prior to diagnosis. Add to all of this the cost of disability payments for those who suffer from permanent damage due to a late diagnosis.

Why does it take so long for a diagnosis? That’s the question Kris McFalls, IG Living’s patient advocate, explores in this issue’s article Diagnosing PIDD: Problems and Solutions. Lack of immunology training among physicians, no family history of PIDD among patients, and the economic climate that puts undue pressure on healthcare providers are major stumbling blocks. But, this situation is slowly improving with greater awareness among physicians about the signs of PIDD and new laws enacted to assist in earlier diagnosis for some PIDD disease states.

One of these disease states is severe combined immunodeficiency (SCID). In our article, Understanding SCID, or Bubble Boy Disease, we take a look at the seriousness of an early diagnosis for infants with SCID — so serious that those undiagnosed before 1 year of age typically die. Many states now have laws that require newborn screening for SCID, and many other states are following suit.

Knowing that early diagnosis and treatment leads to better outcomes, in 2008, a group of scientists analyzed PIDD disorder practice and awareness data among physicians and the public. They found that, overall, only 32 percent of physicians had diagnosed, treated or referred a patient with PIDD in the last five years. In the general population, only 49 percent of people surveyed were aware of PIDD. The scientists’ recommendation: Additional PIDD educational efforts targeting both physicians and the public is needed to lead to earlier diagnosis and less morbidity and mortality. 

Ronale Tucker Rhodes, MS, Editor
IG Living Fans Learn From and Inspire Each Other

I enjoy the questions IG Living poses on Facebook, and I enjoy reading others’ comments as well. It gives a sense of community for sure. Just as important, we (the IG Living “fans”) can learn from and inspire each other through our comments.

I also enjoy the magazine. The articles have been quite helpful at times. For example, I was having a bad flare-up with gastrointestinal (GI) issues. My gastroenterologist did not know much, if anything, about primary immune deficiency diseases (PIDDs) and how common GI complications are among us with PIDD (especially those with common variable immune deficiency [CVID]). During that time, I received an issue of IG Living in the mail and there was a short but helpful article regarding the common connection between CVID and GI problems. If nothing else, it helped me to understand (or more accurately, remind me) that the immune system is systemic and plays a role in all of our body’s systems. It was encouraging, as I was going through yet another struggle of receiving a proper “diagnosis” and useful treatment. I am glad to say that since that time, a diagnosis was made and the treatment for my chronic GI complications seems to be working well.

“Hope” is huge [and] way-too-often underappreciated; it is something that we (humans) cannot survive without.

— Charlene M. Woodley
Bloomsburg, Pa.

[IG Living] is very helpful, and I … show it to patients on intravenous immune globulin (IVIG) at the hospital.… The articles are great. It’s comforting (poor choice of words) to see others who have similar issues and [to hear] their stories and how they are coping with their illness.… It’s always nice to see someone you know stand up and write about their dealings with specific issues.… It’s like a family of us out here, knowing others around the country/world are dealing with these issues.… The magazine brings a name with a face [of] someone we’ve talked with and possibly met at one of the [industry] meetings. That’s [also] why I believe the IG Living reader teleconference calls are so important. [The information] I hear has taught me a lot, and I’m sure you will hear the same from others.… Knowledge is power.… There is so much to learn and, no doubt, as more drugs are developed, we’ll continue to learn as long as we have people like Kris McFalls [IG Living’s patient advocate] and IG Living to keep us informed.

Since I have Medicare and a secondary (Medigap) policy, I don’t have insurance issues, but in the beginning I did. Fortunately, I could call Kris McFalls for help.… IG Living has helped me and others in the past and, quite possibly, in the future. It’s a place to research issues, see what others did and find out if that is an answer for you. It can be lonely out here believing you’re the only one, but with the staff at IG Living, NuFACTOR [and] any pharmaceutical company that cares enough, answers can be gotten and a person can feel that they’re not the only one in this situation.

I praise all of you and thank you for the job you’re doing [to help] us understand our illness, how to cope and the ramifications of the insurance, the drug companies and the government, which many times have [become] stumbling blocks that we, as involved, self-absorbed patients, can’t see the answers [to] clearly. I would not have come this far if it were not for people willing to help and make it more than a job!

— Raye Corey
Arizona patient
Faces of IG Living

If you could give your disease(s) a color, what would it be and why?

Valerie Jordan
Clear. Color is alive and happy or it brings whatever emotion. For me, this disease clears out what I used to know as my “self.” I choose no color at all.

Debbie Spencer
Gray, because it makes you feel so foggy. It doesn’t make itself clear and it isn’t to the point of killing me yet. Gray says it all; people look at you and know you’re not quite right, but can’t figure out exactly what’s wrong with you. Doctors don’t really understand it and can’t explain it or cure it.

Carolyn Cate Shular
Yellow, like the warm sunshine. I am feeling so much better with IG Living; it has made all the difference in the world!

How critical is it to learn how to navigate the insurance system? What tips do you have for someone who is new to this?

Cathy Chappell Edminster
Find someone who has waded through it and knows it forward and backward. Preferably someone who is, or has a family member, dealing with the same chronic illness. Each diagnosis and treatment requires a new twist to what you know about your coverage. Also, once you know your plan, really know your plan, don’t hesitate to challenge the insurance if they process something wrong; it happens. You usually have to go up the chain of command to get someone who can think “off script” and understand[s] what you’re telling them! Also, don’t hesitate to clue your doc(s) in on your coverage. Don’t assume that they know, they usually don’t. And how they write the orders can make the difference of whether or not your plan covers the procedure or prescription.

Mary McDole
Most insurance companies will give you an advocate who will help you navigate the insurance system, but remember, they do work for the insurance company. It also helps to have someone in your doctor’s office who will help you. Learn your rights and know your health insurance plan well. Keep records of who you talk to, what they said and when it was. Don’t be afraid to be the squeaky wheel. Persistence will eventually win out.

Laura Guenther
Familiarize yourself with your plan (deductible, out-of-pocket max, exclusions, process for authorization). Ask for a nurse case manager; most insurers provide them upon request and they can help move things along for authorization and help coordinate care between your medical team and insurance company. Review all of your EOBs that come in; make sure everything that was covered was supposed to be. Don’t take any denial at face value; most of the time, with enough calls and advocacy, you can get it paid for. Don’t wait for your providers to appeal or inquire on your behalf, as oftentimes you can get the process started and prevent being erroneously billed for something that should have been covered. Finally, take a deep breath and relax between insurance calls!

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Did You Know?

Understanding SCID, or Bubble Boy Disease

By Ronale Tucker Rhodes, MS

IN 1976, THE world learned about a rare genetic disease, commonly referred to as the “bubble boy disease,” when the made-for-television movie “The Boy in the Plastic Bubble” (starring John Travolta) portrayed the story of David Vetter. David lived his entire life in a plastic, germ-free bubble and died in 1984 at the age of 12 from the disease, the medical term for which is severe combined immunodeficiency (SCID). Now, 35 years later, people are still familiar with the term bubble boy disease, but few really understand what it is, why it strikes and how it is diagnosed and treated.

What Is SCID?

SCID, a deficiency of the immune system, occurs in about one in every 500,000 births. Babies born with SCID lack antibodies and T cells that protect against infection. These babies typically acquire serious and even life-threatening infections, such as pneumonia, meningitis and bloodstream infections, in the first few months of life.

There are five types of SCID, each caused by a different genetic defect. X-linked SCID is the most common type, caused by a genetic flaw that damages molecules that allow T cells and B cells to receive signals from crucial growth factors. David suffered from X-linked SCID, which occurs only in males. This is because females have two X chromosomes; if they have a mutation on one X chromosome, they have a spare X that can help compensate. Males, however, with only one X chromosome and one Y chromosome, do not have a spare X chromosome to help them compensate for a mutation. The sons who inherit the mutant X chromosome will have X-linked SCID, and the daughters who inherit the mutant X chromosome will be carriers like their mother.

The other types of SCID are inherited in an autosomal recessive pattern (AR-SCID) and affect males and females equally. AR-SCID occurs if two abnormal genes, one from each parent, are present in the patient. In this case, each parent carries an abnormal gene but does not have any physical symptoms of the disorder itself.

Diagnosing SCID

Babies with SCID will normally begin showing symptoms by the time they are 3 months old. Symptoms usually include persistent thrush, extensive diaper rash, chronic diarrhea and a lack of growth or weight gain. Some children have a sharp, persistent cough with pneumocystis pneumonia, blood disorders or chronic hepatitis.

Tests to measure immune function are necessary for a diagnosis. And, because ongoing infections can interfere with results, tests may have to be repeated several times. Those who have SCID usually have a very low number of white blood cells, or lymphocytes, as well as few or no B cells and T cells. The few cells they do have often do not function properly. SCID patients also have very low levels of IgG, IgA and IgM antibodies.

Jennifer Puck, MD, professor of pediatrics at the University of California, San Francisco, has developed a method for identifying presymptomatic children with SCID using the dried blood spots already obtained from all babies for newborn screening. DNA is extracted and the polymerase chain reaction (PCR) is used to determine the number of T cell receptor excision circles (TRECs) versus a copy number of a control genomic DNA segment. Patients who lack TRECs may have SCID or other disorders with very low T cells. Pilot screening of newborns using this method is currently ongoing in Wisconsin, Massachusetts and Navajo Indian populations, where SCID incidence is high. The tests cost between $6 and $10 per sample to perform.
According to Puck, performing inexpensive quantitative PCR assays may help avert expensive and ineffective later-stage treatments for children with SCID. Currently, about 80 percent of infants with SCID go unrecognized until they develop infectious complications due to their immune deficiency.

But, an early diagnosis of SCID has traditionally been rare because doctors don’t routinely perform a test in newborns to count white blood cells. And, since babies with SCID typically appear healthy, parents and healthcare providers are unaware that these children are susceptible to life-threatening diseases. What’s more, the Centers for Disease Control and Prevention (CDC) recommends starting the first dose of vaccines when an infant is 2 months old, some of which can be contraindicated for babies with SCID. Last June, the CDC announced the addition of SCID to the list of contraindications for the two live rotavirus vaccines after several documented cases of vaccine-acquired rotavirus in infants who were undiagnosed with SCID at the time the vaccine was given.

Fortunately, screening newborns for SCID is now occurring in many states. In January 2010, the Advisory Committee on Heritable Disorders in Newborns and Children voted unanimously to add screening for SCID to the core panel for universal screening of all newborns in the U.S. Then, in May 2010, Kathleen Sebelius, secretary of the Department of Health and Human Services, announced the addition of SCID to the core panel of 29 genetic disorders as part of her recommendation to adopt the national Recommended Uniform Screening Panel. SCID is the first nominated condition to be added to the core panel of disorders. In 2008, Wisconsin became the first state to screen babies for SCID. Since then, five other states and one territory have added SCID to their panels: California, Louisiana, Massachusetts, New York, Puerto Rico and, most recently, Florida. In addition, seven other states have voted to recommend the addition of SCID to their newborn screening panels, but screening has not yet begun. These include Colorado, Delaware, Iowa, Michigan, Minnesota, North Carolina and Rhode Island.

**Babies with SCID will normally begin showing symptoms by the time they are 3 months old.**

**Treating SCID**

The most effective treatment for SCID is transplanting bone marrow from a healthy sibling whose tissue type closely matches the patient’s. If a matched sibling is not available, a donor as closely matched as possible can be used. The earlier the diagnosis, the better chances of survival after a bone marrow transplant. The Medical College of Wisconsin recently instituted universal newborn screening, and researchers there noted that among 46 children in whom SCID was diagnosed before 3.5 months of age, 96 percent survived 26 years post transplantation, compared with 66 percent of 116 children who did not receive an early diagnosis.

Until the transplant takes effect (in one to three years), intravenous immunoglobulin (IVIG) is given to normalize antibody levels. SCID patients with adenosine deaminase (ADA) deficiency have been treated successfully with enzyme replacement therapy called PEG-ADA, a long-circulating form of ADA that almost completely corrects metabolic abnormalities, allowing the recovery of a variable degree of immune function sufficient to protect against opportunistic and life-threatening infections.

Gene therapy for correction of both forms of SCID also is under investigation. In one study, reported on in the July 22, 2010, issue of the *New England Journal of Medicine*, eight of nine male infants born with SCID were still alive and well nine years after they underwent gene therapy. The nine boys in the study, who had a median age of 7 months at the time they received the corrected gene (between 1999 and 2002), had normal T cell levels and were able to lead normal lives up to 11 years after the therapy. And, their weight and height were not stunted, as is usually the case with SCID. However, almost half of the participants in the study developed acute leukemia after the therapy. Three survived and one died.

In another study, performed in Italy and Israel and reported on in the Jan. 28, 2009, issue of the *New England Journal of Medicine*, gene therapy cured eight of 10 children with SCID. Following the patients’ progress for four years after treatment, the eight patients were no longer on medication, while the other two patients needed further treatment, and none showed signs of leukemia or other health problems from the therapy.
In October, GlaxoSmithKline reported it had licensed an experimental gene therapy from two Italian institutions (Fondazione Telethon and Fondazione San Raffaele) that aims to fix the stem cells in the patient’s own bone marrow. Stem cells are removed and a healthy gene is inserted before the cells are returned to the body. The therapy has demonstrated “potential” in Phase I and II studies, according to the company.

Renewed Hope

As awareness of SCID increases and research progresses to improve diagnoses and treatments, there is renewed hope for this once-fatal disease. SCID patients no longer have to live in a bubble, such as the fate of David Vetter. Instead, they are living longer, healthier and normal lives.

RONALE TUCKER RHODES, MS, is the editor of IG Living magazine.

Sources


Correction

3,000 People in the U.S., Not 30,000, Live with MMN

In the article Diagnosing and Treating MMN, in IG Living’s February-March issue, page 26, we incorrectly reported that there are 30,000 people in the U.S. living with multifocal motor neuropathy (MMN). The article should have read: “With upwards of 30,000 people in the United States living with amyotrophic lateral sclerosis (ALS) and just 3,000 with MMN, Marsalisi’s experience of delayed and misdiagnosis is not unique.”

Research

Study Helps to Explain IG Distribution in the Body

CSL Behring has developed a pharmacokinetic (PK) model that shows how the body absorbs, distributes, metabolizes and eliminates immunoglobulin (IG) following subcutaneous (SC) administration. The PK model provides a new means of simulating the mechanism by which SCIG is transported after it is injected into the subcutaneous tissue, which could affect the volume and frequency of IG dosing for primary immunodeficiency (PI) patients.

Currently, little is understood about the clinical implications of SC versus intravenous (IV) dosing of IG in PI patients, or about where SCIG travels within the body after it is administered and how long it remains there. This new model, which describes a complex system of continuous interactions between extravascular (tissue) and intravascular (blood) compartments that help determine the location and level of SCIG in different parts of the body after injection, shows that fluctuations in serum IgG after IVIG dosing were lower in the first half of the 30-day dosing cycle and higher in the second half of the cycle than would be anticipated. This, then, supports the theory that IgG distribution from the intravascular to the extravascular compartment occurs early in the dosing cycle, with the reverse occurring later in the dosing cycle.

“Clearly, a need exists to better understand the highly complex pharmacokinetic interactions that take place after an infusion of IgG, especially SCIG, in areas of the body that are not traditionally monitored by clinicians,” said Stephen Jolles, MD, University Hospital of Wales, Cardiff, U.K. “This new PK model represents a major step toward filling this need, especially for clinicians who measure serum IgG as a means of determining overall levels of IgG, and provides valuable insight into movement of IgG around the body with implications for improving PI patient dosing and treatment.”

Research

COPD Patients Have Higher Risk of Shingles

Patients with chronic obstructive pulmonary disease (COPD) are at greater risk of shingles compared with the general population, according to a study published in the Canadian Medical Association Journal. And, the risk is greatest for patients taking oral steroids to treat COPD.

The study, which used data from the Taiwan Longitudinal Health Insurance Database, included 8,846 patients with COPD and 33,944 subjects from the comparison cohort. Of the total 42,430 patients, 1,080 had an incident of shingles (or herpes zoster, which is a reactivation of the chickenpox virus) during the follow-up period. Of those, there were 321 cases of shingles identified among COPD patients, which is 16.4 cases per 1,000 person years, and 759 cases in the comparison cohort, which is 8.8 per 1,000 person years.

Because there is increasing evidence that COPD is an autoimmune disease and other autoimmune diseases, such as “rheumatoid arthritis and inflammatory bowel disease, have been reported to be associated with an increase of herpes zoster, it is reasonable to hypothesize that immune dysregulation found in COPD may put patients at higher risk of developing herpes zoster,” says Dr. Hui-Wen Lin of the Taipei Medical University.
**Product Recall**
**Povidine Iodine Prep Pads Are Voluntarily Recalled**

On March 16, H&P Industries Inc., the parent company of the Triad Group of Hartland, Wis., voluntarily recalled all lots of povidine iodine prep pads. The recalled products all were distributed in the United States and include those pads made by H&P Industries and packaged under the names Cardinal Health, Medical Specialties, VHA, Triad, Triad Plus, North Safety and Total Resources. According to the recall notice, the pads may be contaminated with Elizabethkingia meningoseptica, an organism that has caused rare but serious infections in humans, including meningitis in newborn infants, pneumonia in patients on ventilators and necrotizing fasciitis, more commonly known as flesh-eating bacteria disease. However, there have been no reported illnesses from the contaminated pads as of this writing.

This recall comes more than two months after H&P Industries issued a global recall of hundreds of millions of contaminated alcohol prep pads and wipes because of potential contamination with a rare bacteria called Bacillus cereus. This contamination was found after children in Colorado came down with bloodstream infections caused by the organism and a Colorado hospital cultured the pads and found the potentially life-threatening bacteria. A 2-year-old boy in Houston died from bacterial meningitis after becoming infected with the bacteria.

Specific customers distributing povidine iodine prep pads and selling them at the wholesale and hospital level are being notified by certified mail with instructions on how to return the product. Consumers who have any of these types of products in their possession should not use the product and should return it to the place it was purchased for a full refund. Or, they can call customer service at H&P Industries Inc. from Monday through Friday between the hours of 8:30 a.m. and 4 p.m. central time at (262) 538-2900 to be issued a return authorization number and return arrangements.

Adverse reactions or quality problems experienced with the use of this product may be reported to the FDA’s MedWatch Adverse Event Reporting Program at www.fda.gov/medwatch/report.htm or by calling (800) 323-0178.

**FDA Approval**
**FDA Extends Shelf Life of Hizentra to 30 Months**

The U.S. Food and Drug Administration has approved a supplemental Biologics License Application to extend the shelf life of Hizentra, Immune Globulin Subcutaneous (Human), 20% Liquid, from 24 months to 30 months. Stabilized with L-proline, a naturally occurring amino acid, Hizentra can be stored at room temperature (up to 25 degrees Celsius or 77 degrees Fahrenheit) for up to 30 months, and because no refrigeration is necessary, it can be ready to use without warning, offering patients and physicians convenience and portability.

Hizentra is the first and only 20 percent subcutaneous immune globulin approved in the U.S. It is indicated for the treatment of primary humoral immunodeficiency, a group of disorders that result from a dysfunctional immune system that prevent patients from fighting off infections caused by common germs.

**Research**
**‘Master Switch’ Identified in Inflammatory Diseases**

Imperial College London scientists have identified a protein, called IRF5, that acts as a “master switch” in certain white blood cells that either stimulate or suppress inflammation. The findings suggest that blocking the production of IRF5 may help treat autoimmune diseases, such as rheumatoid arthritis, inflammatory bowel disease, lupus and multiple sclerosis. In addition, boosting IRF5 levels might help to treat people whose immune systems are compromised. The study was reported on in the journal *Nature Immunology.*
There is some debate among immunologists as to whether IG therapy prescribed to treat adults diagnosed with immune deficiencies should be temporarily halted to determine its necessity. Here, two experts present their sides of the issue.

Patients and doctors have reported that many insurance companies have adopted a policy to require all patients diagnosed with hypogammaglobulinemia, subclass deficiency or selective antibody deficiency to trial off of immunoglobulin (IG) therapy after a year of treatment in order to reassess its necessity. There is some research to support this policy. For instance, studies show that the immune systems of pediatric patients may need time to mature and, therefore, trialing these patients off IG to reassess their innate immune systems may be reasonable. Likewise, it has been reported that some patients who have dealt with a long-term disease may simply need to rest their immune system to give it a chance to heal and repair itself. Similar to the support of a crutch for a broken limb, the body uses the passive immunity provided by IG so that the immune system can rest and repair itself.

Lifelong Need for IG?
Weighing the Pros and Cons
Regardless, even expert clinical immunologists have a difference of opinion on the subject. Therefore, having a one-size-fits-all approach may not be in the best interest of the patient.

For this article, we invited two expert immunologists to present their analyses, pro versus con, on the issue of whether adults diagnosed with these immunodeficiency diseases should trial off IG after a period of therapy.

**Argument in Favor of Lifelong IG**

By Francisco A. Bonilla, MD

Many clinical immunologists stipulate that following a correct diagnosis of antibody deficiency (or combined immunodeficiency) in adults, IgG replacement therapy should be lifelong. The reason for this is that these forms of immune deficiency are 1) genetically determined and unlikely to resolve spontaneously, 2) usually have a constant or gradually worsening clinical course over time, and 3) there is usually unequivocal evidence through experience regarding the benefit of IgG replacement for improving the course of the disease.

The most prevalent form of antibody deficiency in adults is common variable immunodeficiency (CVID), which may have its onset at any age. CVID is properly diagnosed when it is found that patients have a reduced number of two or more antibody classes (must include IgG with low IgA and/or IgM) and a clear impairment of antibody formation in response to vaccination, infection or both. In CVID patients, there are no well-described cases of resolution of the disease, and there is abundant evidence of the effectiveness of IgG therapy for reducing infections and improving other manifestations. Even after a period of relative clinical wellness, in properly diagnosed patients, it is expected that cessation of IgG therapy will result in a rapid waning of IgG levels, and a markedly increased risk of infection or worsening of chronic lung disease, etc. These complications may lead to an irreversible worsening of function that never would have occurred if therapy had not been temporarily halted, and does not return to baseline with its resumption.

Other antibody deficiency disorders in adults include X-linked agammaglobulinemia and various forms of hyper-IgM syndrome. Combined deficiencies include Wiskott-Aldrich syndrome, and additional forms of hyper-IgM syndromes, as well as others. These diseases almost always are diagnosed in childhood, but many individuals will survive into adulthood with appropriate therapy, including IgG. Some patients may receive bone marrow transplantation in infancy for immunodeficiency. Many may fail to properly reconstitute B cell function and have persistent antibody deficiency. In all of these situations, spontaneous improvement in the course of the disease is not expected, and IgG therapy must be lifelong. Inappropriate cessation of therapy would expose these patients to the same risks described above.

Milder forms of antibody deficiency have been described in adults. These include hypogammaglobulinemia that does not meet criteria for CVID, IgG subclass deficiency with or without associated IgA deficiency and/or defects of specific antibody production, and defects of specific antibody production with normal immunoglobulins. These remain controversial as diagnoses of “true” immunodeficiency, and the natural histories of these “disorders” are less well-understood, and the role of IgG therapy in their management is less well-substantiated. For these reasons, many clinicians argue that IgG replacement is not indicated for these patients at all, and it should never be used. That being the case, then, IgG therapy is to be used only for those diseases described above for which therapy is expected to be lifelong, and for which interruption of therapy could be expected to have dire adverse consequences.

Thus, IgG replacement in properly diagnosed immunodeficient adults should never be discontinued.
Before discussing situations in which IG therapy may be discontinued, it is important to first consider the initial indications for IgG replacement therapy. These are largely based on the immunodeficiency with which each patient is diagnosed. If the immunodeficiency involves a deep decrease in IgG concentrations, as in agammaglobulinemia, hyper-IgM syndrome and in many patients with common variable immunodeficiency (CVID), there is little doubt that IG therapy is indicated and that there are no reasons to ever discontinue IG treatment.

Second, it is important to consider the clinical severity, which refers mostly to the severity and frequency of infections. Clinical severity may vary even for some patients with agammaglobulinemia and CVID. And, an occasional X-linked agammaglobulinemic patient may have a very mild clinical course, and therefore, they may not be diagnosed until adulthood. Still, the need for treatment is rarely questioned if the patient came to clinical attention due to unusual or recurrent infections. However, some patients with CVID and many patients with immunologically milder forms of hypogammaglobulinemia need a clear assessment of their infection history as the need for IG therapy is considered.

If infections have already led to comorbidities like bronchiectasis or severe chronic sinus disease, these complications may become the strongest indication for long-term treatment, even if the immunologic severity is mild (e.g., mild hypogammaglobulinemia, IgG subclass deficiency with normal total IgG concentrations, or specific antibody deficiencies with normal immunoglobulins). Again, in these situations, IG therapy should be indicated and not discontinued.

So, when is a trial discontinuation of IG therapy warranted? There are several situations when this may be appropriate.

First, the need to continue treatment may no longer be present in patients who may have started therapy early in life. This is because the transient nature of an immune deficiency is not apparent at the time of initiation of therapy, despite a diagnosis of hypogammaglobulinemia stemming from significant infections that are affecting quality of life and the cost of medical care. Some of these patients could retrospectively be diagnosed with a transient hypogammaglobulinemia of infancy. In patients treated for hypogammaglobulinemia in the first years of life that do not have very low B lymphocytes, such as in an agammaglobulinemic patient, it is important to monitor IgM and IgA concentrations during IG therapy. Ideally, IgG trough levels also should be carefully monitored by keeping the dose of IgG per kilo and the interval of infusion constant. If the patient has improved clinically and the concentrations of immunoglobulins increase over time, a trial discontinuation of IG therapy should be considered.

There also are antibody and combined immunodeficiencies in which a limited period of IG therapy should be considered as part of the initial therapeutic plan. This includes some patients with IgG subclass deficiency and most patients with specific antibody deficiencies and normal immunoglobulin concentrations. In these patients, a limited period of IG therapy of one to two years should be planned from the start. This is recommended not so much to see if IG therapy works, since a well-designed treatment with appropriate concomitant management of infections will almost always be effective. Discontinuation of therapy is indicated because there is a reasonable expectation that, after a period of time, IgG replacement may no longer be needed.

An indication of IG therapy for a limited period of time also is almost always appropriate when IG is used as concomitant treatment for patients receiving a stem cell transplant or gene therapy. In many cases, these treatments offer a permanent cure for a primary immunodeficiency, enabling the patient to produce their own antibodies.

Another situation in which discontinuation of IG therapy should be considered is if there is an unclear indication for IG therapy when it is initiated at any age. For instance, patients may have been prescribed IG therapy without...
solid evidence of an immunodeficiency or without a sufficiently documented history of infections. In these cases, patients may be re-evaluated, in some cases as a result of a request for a second opinion about the need to continue lifelong IG therapy. However, before discontinuing treatment, it would be appropriate to measure mature B lymphocytes and memory B lymphocytes by flow cytometry. If they are clearly below normal numbers, it is very likely patients will suffer from a recurrence of infections after discontinuing IG treatment. If treatment is discontinued, careful observation is advisable to avoid infections that may cause secondary damage.

In all of these situations, infections need to be monitored during IG therapy to ensure successful treatment. However, since the absence of infections is the main goal of IG therapy, this fact alone should not be an indication for discontinuation of therapy. Discontinuing IG therapy should be considered only if patients have had a sufficiently long period of well-being on IG therapy. This usually requires at least one and up to two years of treatment to allow mucosal surfaces to heal and normal clearing functions altered by recurrent or severe infections to be restored.

If no clinical improvement occurs with IG treatment, it is necessary to examine why this generally very effective therapy has failed. If failure to improve is due to an inappropriate indication for IG therapy, then it should be discontinued.

The decision to discontinue IG therapy should be made by the treating or consulting immunologist in agreement with the patient. And, each time IG therapy is discontinued, there should be a period of at least four months prior to re-evaluating the need to restart it. The decision to restart IG therapy should be based more on the return of well-documented infections than on the depth of the immunological abnormality. This is because the presence of infections that improve on IG therapy and that return upon discontinuation of therapy is an indirect but very strong proof of a functional antibody deficiency.

The decision to discontinue IG therapy should be made by the treating or consulting immunologist in agreement with the patient.

When there is a justifiable reason to stop IG therapy, it can be stopped at once, because the long IgG half-life will actually provide for a slow decrease in available circulating IgG over several months. Tapering off IG therapy by giving smaller doses of IgG or prolonging the interval between infusions is usually not done. It is recommended by many clinicians to discontinue IG therapy in the spring, when many patients experience a decreased number of infections even without treatment.

A Debate Among Shades of Gray

As these two experts so expressly convey in their analyses, this issue of lifelong need for IG is far from black and white. Instead, whether pro or con, the grays in their lines of thinking come across explicitly: Determining when to treat primary immunodeficiency patients with IG must be based upon a proper diagnosis, severity of infections, patient response and the doctors’ expertise.

No doubt, this debate represents just one of many differences of opinion that patients and immunologists will have concerning treatment with IG therapy. In the relatively young field of study of primary immunodeficiencies, the understanding of how and why IG treatment is and is not effective will continue to evolve.

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Editor’s note: This article refers to both IG and IgG. To clarify: IG is used when referring to the immune globulin therapy (the drug used to treat an immune deficiency). IgG is used when referring to the specific antibody found in the body that immune deficient patients are lacking.
When college student Tyler Sutton started his job hunt, he was confident. The exceptional student was in a top-rated program at a private university, where big firms recruit prospective employees before they graduate. He was practically guaranteed a job. But Sutton started to worry when the offers weren’t coming in. “I would be interviewing for some of the same positions as someone else; I’d have a higher grade point average than they would, have better social skills than they would and they’d give them a job offer,” he says. “No matter how well the job interview went, I wouldn’t get asked for a second interview. I went back to one of the recruiters to find out what the interviewer had to say as to why I didn’t get the job. The only feedback I got was to speak up louder.”

Although Sutton couldn’t pinpoint why he failed to get past the initial interview, he later found out that the companies do Internet searches on job candidates before the second interview. I went back to one of the recruiters to find out what the interviewer had to say as to why I didn’t get the job. The only feedback I got was to speak up louder.”

People with chronic illness often feel they are being unfairly discriminated against because of their disease. But, there are laws in place to protect against this, guidelines that patients can follow and even recourse they can seek.

By Jennifer Kester

Title I of the Americans with Disabilities Act restricts the questions that prospective employers can ask about a disability before making a job offer, like how a person handles stress or whether they work well under pressure. “The stereotypical red flags for sickness-[related] or disability-related discrimination that could be proxies for finding out [about] people’s health are: How active are you? Do you enjoy outdoor activities?” says Wakefield. He adds that questions of attendance from previous jobs should be ones to answer carefully as well: “Those could be very innocuous questions, but they could not be. It puts you on notice that they are paying attention to those things.”

Another red flag is if the interviewer asks whether candidates have a physical condition that would interfere with their ability to do the job, says Jennifer C. Jaff, attorney and founder of Advocacy for Patients with Chronic Illness Inc. But even if they feel the question is inappropriate, calling out the interviewer on it may not be the best option. “If
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someone asked me if I had a physical condition that would interfere with my job, if the answer is no, I would just say no,” says Jaff. “My philosophy about a lot of this stuff is you could fight about it, but if you want a job, a lawsuit won’t do you any good.” Another problem, Jaff points out, is how the interviewee’s reaction will read with the interviewer. “If you don’t answer the question or assert you won’t answer the question, you won’t get the job, not because you’re disabled but because you’re argumentative. People are looking to hire individuals who are going to get along with others in the workplace,” she says. “So if there’s a way to answer the question without making a big deal out of it, I’d do it.”

There is a stipulation in Title I that says it applies only to employers with 15 or more employees in 20 nonconsecutive workweeks, which basically gives small-business owners more leeway in asking questions during an interview. “The fact that you can’t sue someone for something doesn’t mean they shouldn’t do it,” says Jaff. “I would still consider those questions inappropriate, and it might be a place you don’t want to work.”

To Tell or Not to Tell

Jaff says people don’t have to disclose any illnesses to an interviewer. “You’re not legally obligated to tell, unless it prevented you from doing your job,” she says. “Or unless it’s a safety hazard for them and other employees. If you have a problem that poses a safety hazard and don’t tell anyone about it, you’re liable.” And if an individual gets a job, she advises keeping any illness under wraps, at least for a while. “At work, I pretty much showed people I’m a workaholic and then told, so that the employer never had a question that I was not

What Can and Cannot Be Asked During an Employment Interview

Many laws exist to protect people from being discriminated against during employment interviews. For the chronically ill, these laws can be especially important for patients to understand. The U.S. Equal Employment Opportunity Commission (EEOC) has specific guidelines for disability and medical questions and exams on its website. According to the U.S. EEOC:

- Under the law, employers generally cannot ask disability-related questions or require medical examinations until after an applicant has been given a conditional job offer. This is because, in the past, this information was frequently used to exclude applicants with disabilities before their ability to perform a job was evaluated.
- Employers are permitted to ask limited questions about reasonable accommodation if they reasonably believe that the applicant may need accommodation because of an obvious or voluntarily disclosed disability, or where the applicant has disclosed a need for accommodation.
- Employers may ask if the applicant will need an accommodation to perform a specific job duty, and if the answer is yes, the employer may then ask what the accommodation would be.
- The employer may not ask any questions about the nature or severity of the disability.

The U.S. EEOC also lists the American with Disabilities Act (ADA) restrictions on employers when it comes to asking job applicants to answer medical questions, take a medical exam or identify a disability:

- An employer may not ask a job applicant, for example, if he or she has a disability (or about the nature of an obvious disability). An employer also may not ask a job applicant to answer medical questions or take a medical exam before making a job offer.
- An employer may ask a job applicant whether they can perform the job and how they would perform the job. The law allows an employer to condition a job offer on the applicant answering certain medical questions or successfully passing a medical exam, but only if all new employees in the same job have to answer the questions or take the exam.
- Once a person is hired and has started work, an employer generally can only ask medical questions or require a medical exam if the employer needs medical documentation to support an employee’s request for an accommodation or if the employer has reason to believe an employee would not be able to perform a job successfully or safely because of a medical condition.
- The ADA also requires that the employers keep all medical records and information confidential and in separate medical files.

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<td>How many sick days did you take last year?</td>
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<td>Or, do you have family members with health concerns?</td>
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going to be reliable, be absent, that I wasn’t going to work hard, that type of thing,” says Jaff, who has Crohn’s disease.

Wakefield also had to face telling his employers about his chronic illness. He felt guilty after the law firm was told that someone in the group had a condition that was very expensive. “I assumed it was me. Ultimately, this was costing my partners money and that was troubling to me, so I went to one of them eventually,” he says. “I didn’t want to be the insurance burden, but they said, ‘Absolutely not, this is what it is to be a human being.’ So I stayed on, but I was faced with a decision of where I was going to work based on my condition. One has to be really, really careful.”

But coming clean to employers about a health issue doesn’t always end well. On IG Living’s Facebook page, Lisa E. Hadden Smith revealed she had problems in her workplace. She wrote: “New boss told me people like me are a burden on companies. She asked why I would keep working.” But while Hadden Smith missed only four days of work in a year, she said she felt targeted and that her boss might look for a way to fire her. It seemed timely, since her doctors had been talking about her leaving work due to her CVID and T cell failure. “I decided rather than fight the issue, it was time to leave the workplace,” she wrote.

Submitting to Testing

Another gray area concerns health exams. Some employers are giving conditional job offers that depend upon the passage of a health exam, or even hair or urine samples to test for drugs. Although companies aren’t allowed to misuse that information, it can be discourteous to be forced to submit to these tests if a person has a chronic illness. “Those kinds of things are usually for law enforcement, people who have to operate heavy machinery or places where safety is an issue,” says Jaff. However, she says, if candidates do find themselves with a rescinded job offer after something turns up on their health exam, and the finding has no relation to their future duties, they can file a complaint. Sutton does research before submitting to any tests. “I look into it to see if it’s not on the company record and make sure it’s not going to be in my employee file or anything of that nature,” she says.

Beware of an Online Presence

The media poses another workplace problem for people with chronic illnesses. Patients regularly use social media forums, such as Facebook, as well as other websites, such as IGLiving.com, as resources. But as Sutton’s case proves, it can backfire, and future employers can use the information against people. However, Sutton doesn’t regret being interviewed for stories and participating in the online community for those with immune deficiencies. “I am more passionate that it gets out there and people can hear about it,” Sutton says. “It’s something I keep in mind now, but it doesn’t stop me from doing what I want to do.”

Jaff says there are ways to protect personal online identity to ensure they have privacy. “First off, never use your work computer. People should know that anything you do on your work computer belongs to your employer. Anything you do on that computer, they own,” she says. “People use fictitious names, some people only talk about illness on websites that require registration.” The general rule of thumb for anything that is put on the Internet applies here. “You just have to be very careful about how you maintain your online presence,” says Wakefield. “If you don’t want there to be a possibility that someone will do something improper with your health information, you have to be careful [about] how you share it.”

Is There Recourse?

Hiring cases are difficult to win, but if a person doesn’t get the job and really feels that their interviewer was in the wrong, there are options. Wakefield recommends taking careful notes right after the interview and writing down verbatim what was said. He adds that consulting a human resources attorney, who can tell them if there’s a potential for discrimination, is an option. “Usually they’ll do a free consultation or a low-cost consultation and you’ll get a pretty quick sense if the lawyer thinks there’s something there or not,” says Wakefield. Jaff adds that people can seek help at the National Health Law Program, a public interest law firm that protects the healthcare rights of low-income or underserved people, or her own organization, Advocacy for Patients with Chronic Illness Inc., which provides free information, advice and advocacy services to those with chronic illnesses.

Never Give Up

But job-seekers with chronic illnesses needn’t lose hope. Sutton is set to graduate this spring and has a government job lined up. He offers this advice: “You have to keep applying. You just have to keep on working it. If you let yourself be a victim of these issues, then it never gets solved.”

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

Sources:
Diagnosing PIDD: Problems and Solutions

The words *defiant* and *truant* often are used to describe children, but they very easily can be used to describe difficult-to-diagnose diseases, especially primary immunodeficiency disease (PIDD).

By Kris McFalls

Primary immunodeficiency disease (PIDD) is a very broad term for more than 140 diseases, all of which occur when an individual’s immune system fails to function properly. A specific and early diagnosis of a PIDD is the key to getting proper treatment and minimizing permanent tissue damage. However, since the discovery of PIDD, diagnosis has proved difficult and lengthy. A study commissioned in 2007 by the Immune Deficiency Foundation (IDF) showed that, on average, it takes 12.4 years from the onset of symptoms for a patient to be diagnosed with PIDD. But, there may be hope for the
future. The same study showed that diagnoses since the year 2000 have been occurring at a faster rate: an average of 5.5 years since the onset of symptoms.

How long a diagnosis takes depends upon the specific PIDD disease state. Those with more severe PIDs, such as severe combined immune deficiency (SCID), are more likely to be diagnosed more quickly. For example, the study reports that it takes, on average, 3.1 years to diagnose SCID. That being said, the more severe the disease state, the more serious a late diagnosis will be. For each month after birth an SCID baby goes undiagnosed, the chances of survival decrease dramatically. Going undiagnosed for a year is almost always fatal.

Why is it so hard to diagnose PIDD? Unlike a broken limb, PIDD is not well understood and cannot be diagnosed from something as simple and as routine as an X-ray. And, most PIDs cannot be diagnosed with a routine blood test. In fact, a PIDD diagnosis is so complicated that it often can be made only by specialty physicians who have the expertise and knowledge not commonly found in the skill-set of primary care physicians (PCPs) and/or pediatricians who are on the front lines of patient care. Many other obstacles also make for a difficult diagnosis, such as poor communication, lack of collaboration between PCPs and specialists, and the current economic environment.

**Obstacles to Diagnosing PIDD**

According to Dr. Troy Torgerson, co-director of the Immunology Diagnostic Laboratory Center for Immunity and Immunotherapies at Seattle Children’s Research Institute, “Immunology is not well-taught in most medical schools, if it is taught at all.” He explains that some medical schools don’t even have an immunology department, making teaching medical students about immunology even more difficult. And, because PIDD is a bit esoteric, diagnosing patients without any immunology training is difficult at best.

For the majority of PIDD patients, there is no one cardinal sign or symptom that would lead doctors to automatically suspect PIDD. While doctors are trained in medical school to consider family history when investigating a patient’s complaints and symptoms, few PIDD patients report a family history of PIDD. In the 2007 IDF survey, only 17 percent of patients reported having a family history of PIDD prior to their diagnosis.

Therefore, doctors understandably turn to the tools they know best, such as routine blood work, to help guide them in one direction or another. Routine blood work, such as a complete blood count (CBC), can and should immediately set off alarm bells for a small number of severe forms of PIDD. For instance, babies born with SCID typically have a severely low lymphocyte count, or lymphopenia. However, SCID and other diseases that have obvious hallmark signs make up a very small portion of PIDs. Therefore, routine blood work may be the start of a workup for the majority of PIDS, but not much in the routine blood work will lead directly to a PIDD diagnosis.

In addition to blood work, PIDD patients have few tell-tale physical signs that would lead a doctor inexperienced in immunology to consider PIDD. Only some of the more severe PIDs have hallmark signs that should raise a red flag for PCPs. For instance, patients with X-linked agammaglobulinemia (XLA) have no tonsils. Seeing a patient with no tonsil tissue should raise a red flag and prompt further evaluation. And, about 20 percent of common variable immune deficiency (CVID) patients have an enlarged spleen, which also should prompt further evaluation.

Symptoms typically thought of as classic signs of infection, such as a fever, also can be misleading. A fever is often an indicator of infection, but an infection also can be present without a fever, and that infection may be wrongly discounted by PCPs when no fever accompanies it. In fact, many PIDD patients feel the lack of running a fever, despite long-term infections, is a red flag for PIDD that many PCPs miss or poorly understand. Indeed, patients often hear from these physicians that they couldn’t be that sick or they would be running a fever.

Dr. Terry Harville, consultant and medical director of the Special Immunology Laboratory at the University of Arkansas, further explains that the lack of ability to mount a fever is not really an indicator of immune disease or even
infection for that matter. Immune deficiency is the result of a dys-
function of adaptive immunity (T and B cells). The ability to run a
fever is a function of innate immu-
nity, which includes white blood
cells. Therefore, a person with a
low white blood cell count or an
impaired ability to produce white
blood cells also may have trouble
mounting a fever, but that does
not mean they have a PIDD.
Consequently, Dr. Harville states,
“We tend not to rely on the febrile
response as the main indicator
that an infection is present.”

Further complicating the picture
are the kinds of infections PIDD
patients most often get. Probably
the most common complaint
among PIDD patients is sinusitis
brought on by sinus infections.
But, sinusitis does not always
mean there is a bacterial-caused
sinus infection present. Sinusitis is
a very common complaint among
the normal population, which
means PCPs see people with
sinusitis every day and consider
the cause allergies or a virus. And, because sinusitis is
treated as an acute care problem, the patient and doctor
are allotted very little time together. Consequently, undi-
agnosed PIDD patients with chronic sinusitis brought on
by bacterial infection as their chief complaint tend to
linger in primary care much longer than they should.

The bigger problem for PIDD patients occurs when they
present with recurrent infections, but their PCP still does
not connect the dots that paint the bigger picture. The
PCP may see one hard-to-treat infection, when instead
that infection might actually be a series of infections being
under-treated. Again, this underscores the importance for
doctors and patients to have enough time to spend
together to understand the patient’s health history.

In addition to a lack of immunology training, the current
economic climate adds undue pressure on all healthcare
providers. PCPs in particular are under increasing pressure
by employers and payers to cut costs, increase efficiency
and take more responsibility for chronic care patients who

The results of all of these factors is
that PIDD patients go undiagnosed
and suffer much longer than neces-
sary, which ultimately leads to
decreased health outcomes.

Where Do We Go From Here?
It is hoped that the evolution of
electronic medical records (EMRs) will
help with many of the problems
caused by our current healthcare
system. Having access to all of a
patient’s healthcare records should
help all doctors involved with that
patient to see the bigger picture. Dr.
Torgerson feels that programs such as
Microsoft’s Health Vault are a step in
the right direction, but he cautions
that all EMRs need to be accessible to
both patients and doctors. In the
meantime, he highly recommends
patients come prepared with either a

health binder or flash drive containing their medical history,
current medications and a health log that details their symp-
toms and responses to treatment regimens.

Even with the advent of improved recordkeeping, raising
awareness and funds for research is still the main key to
early PIDD diagnosis and treatment. Nonprofit organiza-
tions, such as the Jeffrey Modell Foundation (JMF) and IDF,
have committed a lot of resources toward public aware-
ness, campaigns, research and advocacy.

JMF has been the driving force behind the establish-
ment of immunology centers of excellence around the world.
Seattle Children’s Immunology Diagnostic Laboratory
Center for Immunity and Immunotherapies is an important
part of the Jeffrey Modell Centers Network (JMCN), which
contains several Jeffrey Modell (JM) diagnostic and
research centers and JM referral centers throughout the
world. Currently, there are more than 100 centers in the
JMCN. The next center is planned at Johns Hopkins
Medical Center in Baltimore, Md.
IDF is a major player in bringing PIDD patients and immunologists together at regional and national meetings, including its national conference to be held June 23 through 25 in Phoenix, Ariz. In addition, IDF is a staunch supporter of patient rights, frequently lobbying on the behalf of PIDD patients in Washington, D.C., to ensure they retain access to immune globulin treatment.

IDF, JMF, SCID Angels for Life Foundation and SCID.net have been instrumental in raising awareness of the need for newborn screening for SCID. Newborn screening is the best way to diagnose babies born with SCID, who when treated at birth have a 95 percent survival rate (see the related story on page 9). Additionally, JMF collaborated on and funded the first statewide screening program in 2008 in Wisconsin. Since that time, the United States Department of Health and Human Services has recommended that all states add SCID to the core screening panel for newborns. Now it is up to each state to adopt the recommendations. For updates on state activities, go to http://idfscidnewbornscreening.org.

Professional organizations also are doing their part to raise awareness about PIDD in the medical community. The Clinical Immunology Society for several years has conducted a summer immunology school to teach interested doctors more about immunology. When instructing PCPs, Dr. Torgerson tries to help them spot PIDD with three simple things to look for:

1) Too many or difficult-to-treat infections. This would include patients who require too many antibiotics, unusual antibiotics and recurrent antibiotics.

2) Odd infections. Dr. Torgerson terms this the “Huh?” factor. For example, a nail fungal infection in a young child is never normal. When a PCP finds himself thinking, “Huh, that’s strange, why does this patient have that?” the doctor needs to be encouraged to take the next step and refer that child for further testing.

3) Lymphopenia in neonates (children under 1). This is never normal, and counts below 2,500 could indicate SCID. Low lymphocyte counts in a neonate should always be evaluated with no delay.

What Does the Future Hold?
No matter which PIDD patients have, they all want to know two things: Where did the disease come from? And, when is there going to be a cure? We already can identify the genes for several PIDDs carried on the X gene, such as SCID and XLA. And, now, several researchers are focusing on CVID to identify the gene(s) involved.

Finding the genes that cause the diseases can make curing the diseases much more likely. Dr. Torgerson believes we are getting closer. “I would predict in five years, maybe 10 years, we are going to be doing whole genome sequencing. We are not going to identify every gene that causes immune deficiency, but we are going to identify a whole lot more,” he says. “I would predict that we are going to have an answer for at least a handful of the CVID patients.” But, as Dr. Torgerson cautions, the problem with CVID is that it might be multi-factorial, which will make the most common PIDD also the most difficult disease to figure out.

As the field of immunology continues to progress with more doctors specializing in this area, more research being conducted and more organizations advocating for and taking action to find solutions for an easier and faster PIDD diagnosis, the future can only look better for the growing number of PIDD patients.

KRIS MCFALLS is IG Living’s full-time patient advocate.
Introducing

Flebogamma® 10% DIF
Immune Globulin Intravenous (Human)

Shaping the future

Highly purified IGIV
- Trace amounts of IgA: <0.006 mg/mL \(^1\)
  (specification value: <0.1 mg/mL)
- Very low sodium content
- Sorbitol stabilized

Demonstrated benefits in replacement therapy
- In the pre-approval clinical trial: \(^2\)
  - 0.025 serious bacterial infections/patient/year
  - Well tolerated: Does not put patients at increased risk
    for any adverse events other than those that could be
    reasonably expected in primary immune deficiency
    patients who are receiving an infusion of intravenous
    immune globulin

Broad pathogen safety margin
- Seven validated pathogen elimination steps including:
  - 20 nm nanofiltration
  - Dual specific inactivation:
    pasteurization and solvent detergent
- Highly effective process:
  - 15.0 log reduction of PPV (PVB19 model)
  - ≥ 13.3 log reduction of EMCV (HAV model)
  - ≥ 6.2 log reduction through 4% PEG precipitation
    and ≥ 5.5 log reduction through 20 nm nanofiltration
    of an experimental agent considered a model for the
    vCJD and CJD agents \(^3\)

Please see reverse for Important Safety Information and Black Box Warning.

---

\(^1\) Data on file, Instituto Grifols, S. A.
For your convenience

- Liquid
- Room temperature storage 2-25°C (36-77°F) for the entire 2-year shelf life
- Three presentations: 5, 10 and 20 gram vials

Enhancing our commitment to you

- Every vial is laser etched with its own unique identifier number*, which helps to deter tampering and counterfeiting
- PediGri® On Line, unique to Grifols, offers full traceability from donation to the final product at www.pedigri.grifols.com

Important Safety Information

Flebogamma® 10% DIF is a human immune globulin intravenous (IGIV) that is indicated for the treatment of primary immune deficiency (PI), including the humoral immune defect in common variable immunodeficiency, x-linked agammaglobulinemia, severe combined immunodeficiency, and Wiskott-Aldrich syndrome.

**WARNING: ACUTE RENAL DYSFUNCTION AND ACUTE RENAL FAILURE**

- Use of immune globulin intravenous (IGIV) products, particularly those containing sucrose, has been reported to be associated with renal dysfunction, acute renal failure, osmotic nephropathy, and death (1). 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, paraproteinemia, or those receiving known nephrotoxic drugs (see Warnings and Precautions [5.2]). Flebogamma® 10% DIF does not contain sucrose.
- For patients at risk of renal dysfunction or failure, administer Flebogamma® 10% DIF at the minimum infusion rate practicable (see Dosage and Administration [2.3], Warnings and Precautions [5.2]).

Flebogamma® 10% DIF is contraindicated in patients who have had a history of anaphylactic or severe systemic reactions to the administration of human immune globulin and in IgA deficient patients with antibodies to IgA and a history of hypersensitivity. In case of hypersensitivity, discontinue Flebogamma® 10% DIF infusion immediately and institute appropriate treatment. Medications such as epinephrine should be available for immediate treatment of acute hypersensitivity reactions.

In patients at risk for developing acute renal failure, monitor renal function, including blood urea nitrogen, serum creatinine, and urine output.

Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving Flebogamma® 10% DIF therapy.

Thrombotic events may occur during or following treatment with Flebogamma® 10% DIF. Monitor patients at risk for thrombotic events, including those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, coagulation disorders, prolonged periods of immobilization, and known or suspected hyperviscosity.

Aseptic meningitis syndrome (AMS) may occur infrequently with Flebogamma® 10% DIF treatment. AMS may occur more frequently following high doses and/or rapid infusion of IGIV.

Flebogamma® 10% DIF may contain blood group antibodies that can act as hemolysins and induce in vivo coating of red blood cells (RBCs) with immunoglobulin, causing a positive direct antiglobulin reaction and hemolysis.

Non-cardiogenic pulmonary edema [Transfusion-Related Acute Lung Injury (TRALI)] may occur in patients following Flebogamma® 10% DIF treatment. If TRALI is suspected, perform appropriate tests for the presence of antineutrophil antibodies and anti-HLA antibodies in both the product and patient serum.

All patients, but especially individuals receiving Flebogamma® 10% DIF for the first time or being restarted on the product after a treatment hiatus of more than 8 weeks, may be at a higher risk for the development of fever, chills, nausea, and vomiting. Careful monitoring of recipients and adherence to recommendations regarding dosage and administration may reduce the risk of these types of events.

Because Flebogamma® 10% DIF is made from human plasma, it may carry a risk of transmitting infectious agents, e.g., viruses, and theoretically, the Creutzfeldt-Jakob (CJD) agent. No cases of transmission of viral diseases or CJD have ever been identified for Flebogamma® 10% DIF.

The most common adverse reactions (reported in ≥ 5% of clinical trial subjects) occurring during or within 72 hours of the end of an infusion were headache, chills, fever, shaking, fatigue, malaise, anxiety, back pain, muscle cramps, abdominal cramps, blood pressure changes, chest tightness, palpitations, tachycardia, nausea, vomiting, cutaneous reactions, wheezing, rash, arthralgia, and edema. The most serious adverse reactions observed with Flebogamma® 10% DIF were back pain, chest discomfort, and headache (2 patients); and chest pain, maculopathy, rirors, tachycardia, bacterial pneumonia, and vasovagal syncope (1 patient).

Please refer to enclosed Flebogamma® 10% DIF full prescribing information for full prescribing details, including comprehensive adverse event profile and black box warning.

See the difference today
Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving Flebogamma® 10% DIF at the minimum infusion rate practicable, and maximum rate of 0.08 mL/kg/minute (8 mg/kg/minute). Ensure that patients with pre-existing renal insufficiency are not volume depleted. For patients judged to be at risk for renal dysfunction or thrombotic events, administer Flebogamma® 10% DIF at the minimum infusion rate practicable, and consider discontinuation of administration if renal function deteriorates.

CONTRAINdications

Flebogamma® 10% DIF is contraindicated in patients who have had a history of anaphylactic or severe systemic reactions to the administration of human immune globulin and in IgA deficient patients with antibodies to IgA and a history of hypersensitivity.

WARNINGS AND PRECAUTIONS

WARNING: ACUTE RENAL DYSFUNCTION AND ACUTE RENAL FAILURE

• Use of immune globulin intravenous (IGIV) products, particularly those containing sucrose, has been reported to be associated with renal dysfunction, acute renal failure, osmotic nephropathy, and death (1). 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, paraproteinemia, or those receiving known nephrotoxic drugs (see Warnings and Precautions [5.2]). Flebogamma® 10% DIF does not contain sucrose.

• For patients at risk of renal dysfunction or failure, administer Flebogamma® 10% DIF at the minimum infusion rate practicable (see Dosage and Administration [2.3], Warnings and Precautions [5.2]).

• Weigh the potential risks and benefits of Flebogamma® 10% DIF against those of alternative therapies in all patients for whom Flebogamma® 10% DIF is being considered.
• Before prescribing Flebogamma® 10% DIF, the physician should discuss risks and benefits of its use with patients.

Hypersensitivity

Severe hypersensitivity reactions may occur. In case of hypersensitivity, discontinue Flebogamma® 10% DIF infusion immediately and institute appropriate treatment. Medications such as epinephrine should be available for immediate treatment of acute hypersensitivity reactions.

Renal Dysfunction/Failure

Periodic monitoring of renal function and urine output is particularly important in patients judged to be at increased risk of developing acute renal failure. Assess renal function, including measurement of blood urea nitrogen (BUN) and serum creatinine, before the initial infusion of Flebogamma® 10% DIF and at appropriate intervals thereafter. If renal function deteriorates, consider discontinue use of Flebogamma® 10% DIF.

In patients who are at risk of developing renal dysfunction because of pre-existing renal insufficiency or predisposition to acute renal failure, administer Flebogamma® 10% DIF at the minimum rate of infusion practicable.

Hyperproteinemia

Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving Flebogamma® 10% DIF therapy. It is clinically critical to distinguish true hyponatremia from a pseudo-hyponatremia that is temporarily or causally related to hyperproteinemia with concomitant decreased calculated serum osmolarity or elevated osmolar gap, because treatment aimed at decreasing serum free water in patients with pseudohyponatremia may lead to volume depletion, a further increase in serum viscosity and a higher risk of thrombotic events.

Thrombotic events may occur during or following treatment with Flebogamma® 10% DIF. Monitor patients at risk for thrombotic events, including those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, coagulation disorders, prolonged periods of immobilization, and known or suspected hypersensitivity.

Consider baseline assessment of blood viscosity in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/high triacylglycerols (triglycerides), or monoclonal gammapathies, because of the potentially increased risk of thrombosis.

If signs and/or symptoms of hyperviscosity are present after an infusion of Flebogamma® 10% DIF, perform laboratory testing for confirmation.

If TRALI is suspected, perform appropriate tests for the presence of anti-neutrophil antibodies and anti-HLA antibodies in both the product and patient serum.

Dose Titration

In patients who are at risk of developing renal dysfunction or failure because of pre-existing renal insufficiency or predisposition to acute renal failure, administer Flebogamma® 10% DIF at the minimum rate of infusion practicable.

Monitoring: Laboratory Tests

• Periodic monitoring of renal function and urine output is particularly important in patients judged to be at increased risk of developing acute renal failure. Assess renal function, including measurement of BUN and serum creatinine, before the initial infusion of Flebogamma® 10% DIF and at appropriate intervals thereafter.

• Consider baseline assessment of blood viscosity in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/high triacylglycerols (triglycerides), or monoclonal gammapathies, because of the potentially increased risk of thrombosis.

• If signs and/or symptoms of hyperviscosity are present after an infusion of Flebogamma® 10% DIF, perform appropriate laboratory testing for confirmation.

Adverse Reactions

The most common adverse reactions (reported in a ≥5% of clinical trial subjects) occurring during or within 72 hours of the end of an infusion were headache, chills, fever, shaking, fatigue, malaise, anxiety, back pain, muscle cramps, abdominal cramps, blood pressure changes, chest tightness, palpitations, tachycardia, nausea, vomiting, cutaneous reactions, wheezing, rash, arthralgia, and edema. The most serious adverse reactions observed with Flebogamma® 10% DIF were back pain, chest discomfort, and headache (2 patients); and chest pain, maculopathy, rashes, tachycardia, bacterial pneumonia, and vasovagal syncope (1 patient).

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

In a multicenter, open-label, non-randomized, historically controlled clinical study, 46 individuals with primary humoral immunodeficiency received infusion doses of Flebogamma® 10% DIF at 300 to 600 mg/kg body weight every 3 weeks (mean dose 469 mg/kg) or 4 weeks (mean dose 457 mg/kg) for up to 12 months (see Clinical Studies [14.1]). Routine pre-medication was not allowed. Of the 61 infusions administered, 130 infusions (22%) in 21 (47%) subjects were given pre-medications (antihistropic, antihistamine, or antiemetic agent) because of experience with consecutive infusion-related adverse reactions.

One subject experienced four serious adverse events (AEs) (bacterial pneumonia, subcutaneous abscess and two episodes of cellulitis) and withdrew from the study. Two other subjects who participated in the study discontinued prematurely due to AEs (back pain/chest pain/headache; and chills/febrile). Three subjects experienced four serious non-related AEs (drug abuse/depression; hernia; and sinusitis).

Forty-five (98%) subjects experienced at least 1 AE irrespective of the relationship with the product, and these subjects reported a total of 723 AEs. Thirty-eight subjects (83%) had an adverse reaction at some time during the study that was considered product-related. Of the 21 subjects receiving pre-medications, 12 (57%) subjects reported adverse reactions during or within 72 hours after the infusion of AEs in 48 of the 130 pre-medicated infusions (37%).

Table 2. Treatment-related Adverse Events Occurring in ≥5% of Subjects with PI during a Flebogamma® 10% DIF infusion or within 72 Hours after the End of an infusion

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Subjects (%)</th>
<th>Infusions (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=46)</td>
<td>(N=681)</td>
</tr>
<tr>
<td>Headache</td>
<td>24 (52%)</td>
<td>67 (11%)</td>
</tr>
<tr>
<td>Rigors</td>
<td>17 (37%)</td>
<td>37 (6%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>15 (33%)</td>
<td>27 (5%)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>10 (22%)</td>
<td>18 (3%)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>9 (20%)</td>
<td>11 (2%)</td>
</tr>
</tbody>
</table>
known nephrotoxic drugs with any degree of pre-existing renal insufficiency, diabetes mellitus, advanced age
Precautions [5.2]).
the minimum infusion rate practicable
If there are no adverse drug reactions, the infusion rate for subsequent infusions can be slowly increased to the
(
intervals thereafter.
gammopathies, because of the potentially increased risk of thrombosis.
HLA antibodies in both the product and patient's serum.

### Post-marketing Experience
Because adverse reactions are reported voluntarily post-approval from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to product exposure. The following adverse reactions have been identified during post approval use of intravenous immune globulins, including Flebogamma 5% (see References [15]).

#### Infusion reactions
Hypersensitivity (e.g., anaphylaxis), headache, diaphoresis, fever, fatigue, diziness, malaise, chills, flushing, urticaria or other skin reactions, wheezing or other chest discomfort, nausea, vomiting, rigors, back pain, myalgia, arthralgia, and changes in blood pressure

#### Renal
Acute renal failure/insufficiency, eosinophilia

#### Respiratory
Acute Lung Injury (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, hemolytic, positive direct antiglobulin (Coombs) test

#### Musculoskeletal
Back pain

#### Gastrointestinal
Hepatic dysfunction, abdominal pain

#### General/Body as a Whole
Pyrexia, rigors

### DRUG INTERACTIONS
Possible transfer of antibodies may transiently impair the immune response to live attenuated virus vaccines such as measles, mumps, and rubella. Inform the immunizing physician of recent therapy with Flebogamma® 10% DIF so that appropriate measures may be taken (see Patient Counseling Information [17]).

### USE IN SPECIFIC POPULATIONS
#### Pregnancy
Pregnancy Category C. Animal reproduction studies have not been performed with Flebogamma® 10% DIF. It is also not known whether Flebogamma® 10% DIF can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Flebogamma® 10% DIF should be given to a pregnant woman only if clearly needed. Immunoglobulins cross the placenta from maternal circulation increasingly after 30 weeks of gestation.

#### Nursing Mothers
Use of Flebogamma® 10% DIF has not been evaluated in nursing mothers.

#### Pediatric Use
Three (3) pediatric patients with primary humoral immunodeficiency (two between the ages of 6 and 10, and one 16 year old) were included in the clinical evaluation of Flebogamma® 10% DIF. This number of subjects is too small to establish safety and efficacy in the pediatric population (see Clinical Studies [14]).

#### Geriatric Use
Use caution when administering Flebogamma® 10% DIF to patients over 65 years of age who are judged to be at increased risk for developing certain adverse reactions such as thromboembolic events and acute renal failure (see Boxed Warning, Warnings and Precautions [5.2]). Do not exceed the recommended dose, and infuse Flebogamma® 10% DIF at the minimum infusion rate practicable.

One (1) patient with primary humoral immunodeficiency at or over the age of 65 was included within the clinical evaluation of Flebogamma® 10% DIF. This number of geriatric patients was too small for separate evaluation from the younger patients for safety or efficacy (see Clinical Studies [14]).

### HOW SUPPLIED/STORAGE AND HANDLING
Flebogamma® 10% DIF is supplied in single-use, individually laser etched vials containing the labeled amount of functionally active IgG.

The following presentations of Flebogamma® 10% DIF are available:

<table>
<thead>
<tr>
<th>NDC Number</th>
<th>Fill Size</th>
<th>Grams Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>61953-0005-1</td>
<td>50 mL</td>
<td>5g</td>
</tr>
<tr>
<td>61953-0005-2</td>
<td>100 mL</td>
<td>10g</td>
</tr>
<tr>
<td>61953-0005-3</td>
<td>200 mL</td>
<td>20g</td>
</tr>
</tbody>
</table>

Each vial has an integral suspension band and a label with two peel-off strips showing the product name and lot number.

#### DO NOT FREEZE.
When stored at room temperature (up to 25 °C (77 °F)), Flebogamma® 10% DIF is stable for up to 24 months, as indicated by the expiration date printed on the outer carton and container label.

Keep Flebogamma® 10% DIF in its original carton to protect it from light.

Manufactured by INSTITUTO GRIFOLS, S.A.
Barcelona - Spain
U.S. License No. 1181
Distributed by GRIFOLS BIOLOGICALS Inc.
Los Angeles - CA 90032
Phone: 888-GRIFOLS (888-474-3657)
Madlynn: I am doing well with infusions for my primary immune deficiency disease (PIDD), and I want to start exercising. The problem is, there is no one who knows about my illness who can put together an appropriate exercise plan. I have looked online and asked doctors, physical therapists, nutritionists and personal trainers. Do you have any suggestions or guidance?

Kris: I am so glad to hear you are doing well and are ready to take the next step. I am not surprised healthcare workers such as physical therapists and nutritionists have not heard of your disease. The trick is to find one you like and ask them if they would be willing to research your disease in order to better guide you.

Patients with PIDD are perfectly capable of participating in a physical activity program. However, some of the symptoms of PIDD and other diseases that immune deficiency patients often suffer from, such as decreased stamina, asthma and arthralgia, may require special precautions.

I would recommend starting with a physical therapist before working with a personal trainer. Many physical therapists will have expertise in the symptoms associated with your disease. One who does can help you modify exercises to fit your needs and help you learn how to progress your program without overexerting yourself. Once you are on an established program, a personal trainer can be helpful. Many people find having a personal trainer helps them stick to a regular exercise program. However, keep in mind that many states do not regulate personal trainers. Therefore, they may have little or no medical training or the expertise needed to understand the complex nature of immune diseases and how they affect the body.

Most physical therapists will require a prescription from your doctor before beginning a physical therapy program. While several states allow physical therapists to see patients without a prescription, insurance companies in those states generally still require a prescription in order for patients to obtain coverage. Therefore, the best place to start is with your primary care provider. A good primary care provider should be able to recommend a physical therapist whom they already know. In addition, your primary care provider should explain to your physical therapist your basic medical history, as well as a list of possible precautions. The goal of physical therapy is to get on a program that you will be able to perform independently and that is successful for you.

Many physical therapists now work with personal trainers to help transition patients to a more independent, but still monitored program. A good website to assist in your search is http://www.apta.org/AM/Template.cfm?Section=Find_a_PT&Template=/APTAAPPS/FindAPT/findaptsearch.cfm.

Your primary care provider should also be able to direct you to a dietitian he or she has worked with. Quite often, local hospitals also will have nutrition classes that are reasonably priced. Another good source to find a registered dietitian is http://www.eatright.org. Again, few dietitians will know about your disease, but a good one should be able to understand the symptoms commonly associated with your disease.

In the December-January 2011 issue of IG Living, we published an in-depth article on arthritis and exercise. I think you will find it very applicable to your situation. I am so glad that you are anxious to get started. As a former physical therapist assistant, I can tell you this is a great decision. Please keep in mind, though, that progress can sometimes be slow. However, as long as you are making progress, you are doing great! I would highly recommend keeping a diary listing your goals and your progress so you can reflect on where you started, where you want to go and how you are doing. Stay positive and stay focused.
I have a new diagnosis to add to my list: fibromyalgia. I guess this would explain the chronic pain I have been feeling for the last six years.

Yet another invisible illness. Not that I am complaining. Invisible is fine with me, although it can be very confusing and frustrating for those around me.

Maybe I contribute to the confusion. Since I am a positive person by nature, my frown muscles don’t work, and I like wearing pretty clothes. I also love to have fun, laugh and be around people. This image portrays the shell of a “healthy looking” person. But, I am not healthy; I am in pain all the time, even though people can’t see my pain. Sometimes I say: “You should see my insides!” When I tell people I’m chronically ill, they look at me in disbelief. What am I to do? Keep a list of lab results in my wallet?

I don’t always let people know about my illnesses. Sometimes, I want those who are around me often to know. And not just to know, but to understand (not an easy task). But then, there are times when I think: “No one needs to know. No one needs to have an excuse not to do business with me, or not to call me too early in the morning, or not to ask me for a favor.”

I realize that “understanding” a chronic illness can be challenging for people. And I try to put myself in their shoes. If they were trying to explain their illness to me, would I understand? Would I say, “Well, you don’t look sick”? Probably not, but that’s because I am already so educated and sensitive about chronic illness — not to mention I live with it!

Deciding not to communicate about a chronic illness makes for a lonely existence. It’s no different, really, than being around someone who absolutely does not understand it. In either of these circumstances, I feel alienated and alone. I feel like I’m different. I wonder if people think that being chronically ill is like having the flu. Do they think they are going to catch it? Do they think they will get a sore throat? A cough? A runny, chapped, red nose? Or, maybe it’s just more comfortable for them to not know? I wish I could take my body off like a coat and let someone else try it on — just to see their face when they begin to feel what I feel. Then, maybe, they could relate. And, afterward, they could just hang the coat up and go on with their healthy lives.

I was doing business with a woman earlier this year, and during our first meeting, she asked me how I got started. (I have a business designing hair accessories, and she wanted to carry them in her store.) I told her that it all started with a terrible haircut because my hair was falling out. Her eyes got so wide, and she asked, “But why was your hair falling out?” I told her that I was on high doses of steroids to treat a lung disease and it made my hair fall out. When I looked up at her, I thought I saw her hovering over the ground. I believe that if she could have, she would have run out of her own store. But, she asked! What was I supposed to say? It was then that I knew that if I wanted this business relationship to work, I was going to have to be a little more superficial. Everything since then has been great. We talk about clothes and shoes, and I bring her cookies.

Nothing is easy, but it can be easier to keep my personal illness to myself at times. I have learned that most people don’t have room in their hearts for empathy for everyone they encounter. Living with a chronic illness can be a blessing and a burden. Through it all, I have grown as a person, and it has helped me to set boundaries. Don’t judge a book by its cover, right? Well, if only they could see my pages. Then, they would know how special I am.

Ever Fecske was diagnosed with CVID and interstitial lung disease in 2004. She is a fashion design student, loves spending time with her fiancé, family and bulldog, Dunkin, and can’t get enough of writing, cake decorating and anything that sparkles!
“DOES THAT STUFF really happen to you guys?” That’s the question I regularly field in response to my columns. My patent answer: “Ninety-nine percent. The leftover percent is humor.” And this, my friend, is why humor is so hard to communicate. Humor is personal. It is as unique to each person as the human thumbprint; a funny bone is rarely tickled the same way for everybody.

For example, I don’t think the 1970s watermelon-mutilating comedian is funny. His routine is very stressful to me because, instead of laughing, I’m thinking about how in the heck I am going to get the red stains out of my juice-soaked socks. However, and to keep the food theme going, I think the recent table-flipping, ripped-off Italian mobesque episode on the reality show “The Real Housewives of New Jersey” is sidesplitting good stuff. If I was to psychoanalyze the hair-raising, plate-crashing and manicotti-flying scene, the diagnosis would explain that I’m frankly relieved that my family isn’t the reason the catty cable mischief started in the first place! And maybe I feel a tinge of relief while watching reality TV, knowing my family isn’t the medical freak show it seems to portray. As most of you know, living with chronic illness isn’t that funny, but for me it has the potential to lend itself nicely to hilarious opportunities!

The writing process for me has to start with someone doing something silly, foolish or downright column-worthy (table flipping is good). Then, as with a good steak, I let the incident marinate for a while and voila: An uplifting story (I hope) is born! But these last few months haven’t been publish worthy! As my deadline crept closer and closer, the healthier my family became! (Note to self: Isn’t this what gamma globulin is supposed to do — keep us healthy?) I mean, no one attracted some horrific parasite or needed repeat sinus surgery. Every day, I waited at the door for my brood to come home from school having either green goop dripping or the sudden urge to puke. In fact, because of my looming deadline, I was the only one who was nauseated. “You guys are healthy at the wrong time of the month and that’s not fair!” I’d admonish the immune deficient.

A glimmer of hope came when the weekend before this column was due, I landed in the hospital with an infection that needed intravenous (IV) antibiotics. I thought to myself: This is your big chance! The emergency room is always news worthy! But, no. Everything went like clockwork. In fact, I ended up sleeping through
most of whatever was going on around me. Can a nap be funny, I pondered? I didn’t even manage a goofballish dream!

OK, well, the only slightly funny thing that happened was the minute I plopped on the gurney, I announced to the orderly, “It really smells in here!”

“Yeah, we had some guy blow through here a bit ago who smelled so bad his odor seems to have penetrated the whole place!”

“I guess I should’ve brought a candle,” I continued, as the orderly ignored my suggestion.

I looked around and whispered to myself, “There has got to be something in here for me to go off on!” A magazine cover. A funny-looking tool. A conversation I was listening in on. Nothing.

“Well, this oughta help,” the orderly announced as he plopped a filter with fresh coffee grounds on the counter.

Surprisingly, the coffee did seem to help dissipate the offensive odor. But I’m not writing a column for Better Homes and Gardens, I argued with the air.

Out of sheer desperation, while my nurse was “shushing up” the IV pump, I asked her: “Did anything good happen while I was napping? I have an article to write, and I need something good.”

She looked at me as if I had horns.

I was discharged, insanely disappointed in my hospital stay.

A couple of days later and waiting at my doctor’s office with my laptop open and ready, I kept my senses at high alert. The first person to do even the smallest bit of funny was going to become column fodder. Humor is life exaggerated. But, once again, I found myself more exasperated as the clock kept ticking away, along with the potentially ridiculous.

“Cheryl,” my rheumatologist’s nurse called and interrupted my search and rescue op. “C’mon, fall down or something, would ya?” I secretly wished upon my very sweet nurse, Sally. We passed the weigh-in station. No, there is absolutely nothing funny about that. We passed the infusion suite and went into the examination room. Still nothing.

I closed my laptop in defeat and hung my head in shame. Moments later, my rheumatologist, Dr. Dagene, knocked softly on the door, making her way into my sad state of human humor horror.

I knew I wasn’t going to get anything out of Dr. Dagene. She is eloquent, classic, charming and all-around a good egg. How our small city found such a diplomatic and attention-getting physician is short of miraculous. Dr. Dagene is so kind to me. Even if she did manage to pull off good material, I’d never print anything about her. And she knows it! She loves IG Living, and she has told me how proud her husband is that she has never been written about in my column.

“How you doing?” Dr. Dagene asked, but this time without flashing her notorious white smile.

“Great,” I mumbled. I looked into Dr. Dagene’s face and noticed something missing: her perfectly coiffed hair and painted face. She looked, well, absolutely awful.

“You OK?” I asked carefully.

“I’ll be all right. Something I ate for lunch didn’t agree with me,” she managed, while scrubbing down the wrong date. It also was not even quite 10 o’clock in the morning!

Dr. Dagene’s ashen face slowly started to tint lime green as her expression became unintelligible. She covered her mouth with her hand as she scrambled for the sink. And there is where she tasted “lunch” for the second time today.

I twiddled my thumbs in the waiting room, doing anything to keep my fingers from writing about what just happened. It was the perfect scenario, but I kind of pinky-swore to myself I’d never write about Dr. Dagene.

“Cheryl?” Sally called. “Dr. Dagene is going to be out for the rest of the day, but she wanted me to give you this note. Don’t go anywhere; we’re going to try to fit you in with another provider.”

“Oh, uh, thank you, Sally,” I said, sputtering.

I opened the note and it read: Cheryl, Sorry about the mess. I guess the tables are turned, as I am the patient now. And yes, I’d love to see what kind of creative license you will muster up. I give you full permission to write about me. Can’t wait. Signed, Dr. Dagene.

I sped home after my second but more official appointment and wrote this article as fast as my motherboard could handle.

But, have you ever heard the saying, “Be careful what you wish for?”

When I opened the door to let my three primary immune deficient kids in, one was doubled-over chewing into the neighbor’s boxwoods and another wiped her green sinus slime down her sweater sleeve. The third asked, “So, have you finished your article yet?”

Well, at least I don’t have to worry about next month’s column.

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.
Many who rely on immune globulin (IG) treatments to sustain them physically also have discovered the power of support groups to sustain them emotionally. Recently, I had the opportunity to speak with Steven Smith, an IG Living subscriber who is a co-leader for a Manhattan-based neuropathy support group. Steven, who has chronic inflammatory demyelinating polyneuropathy (CIDP), provides his group members with inspiration, encouragement and connection. Whether members are depressed from a recent diagnosis or are seasoned attendees, Steven points them to the tools and resources they need to live life to the fullest.

Carla: Since your diagnosis with CIDP, what challenges have you overcome?

Steven: At first, it took some time to get past the depression and denial that I was sick. Every day has new physical challenges, and you have to learn to handle them. I use my AAA thought process to help me cope with my illness: Accept (the disease), adjust (your lifestyle) and adapt (to day-to-day challenges).

Carla: Why did you become a neuropathy support group leader?

Steven: The diagnosis of a chronic illness is often accompanied by feelings of loneliness and isolation. I didn’t want to feel alone. When I decided to do some research on my illness, I discovered that there are over 20 million neuropathy patients just like me who must deal with this disease. It never ceases to amaze me how I can have a two-hour conversation with another neuropathy patient — a complete stranger — and have so much in common.

Carla: Tell me about how you became a support group leader.

Steven: While I was having my IVIG infusion at the treatment center, a fellow patient and I were talking about the importance of support groups. Both of us were surprised that a large city like New York doesn’t have a group for patients to attend. Another patient who overheard our conversation mentioned that if one ever got started, he would like to donate a conference room for the meetings.

Carla: How are you helping neuropathy patients who attend your support group sessions?

Steven: When new members attend my meetings, they are given a lot of educational information. I make sure to ask them what it is that brought them to the meeting, and what they would like to get out of it. I also speak to them privately to get an understanding of where they are, both physically and mentally. With established members, I try to address any concerns or problems they may have.

Carla: How do you encourage patients to take charge of their own health?
Steven: We discuss health issues and concerns, like maintaining a healthy diet and staying as active as possible. Physical therapy is also very important, as long as the therapist understands that you have a neurological disorder, not an injury. I also remind my members that their mind is a powerful tool, so having a positive outlook on life will go a long way toward helping them to feel better.

Carla: What do you want people to take away from support group meetings?

Steven: If members of my support group walk away learning or understanding one new aspect about neuropathy each month, then it was a successful meeting. Sometimes people just need to vent or share their experiences; a support group meeting is the perfect venue. Members are surrounded by friends and peers who can relate to what they are going through.

“Sometimes people just need to vent or share their experiences; a support group meeting is the perfect venue.”

Carla: How do you structure your support group sessions so that everyone benefits?

Steven: I usually lead the group in a discussion, but every once in a while we have the opportunity to invite a guest speaker. Sometimes a member will express an interest in a particular subject, so I’ll research it and then present the information the following month. With new members, I ask if they care to share their story. And there is always a member who will offer advice.

Carla: How do you encourage a patient who is struggling with their neuropathy?

Steven: If I see that a person is struggling, I take them under my wing and give them extra attention. That may take several phone calls and even visits to their residence. When I first became sick, I tripped and fell, but I was able to find my way out of the forest. Now, I take others by the hand; we may trip and fall together, but I promise I’ll get them out of the forest. And I do, so they can go on with their lives. They have the strength, but if they’re having a particularly bad day and they stumble, they know that I’ll be there to pick them up.

Carla: What encouragement can you give to someone who was recently diagnosed with neuropathy?

Steven: At first, it may be scary, frustrating and demoralizing. From time to time, you may have setbacks, but remember, you are not alone! There are many “tricks of the trade” to make your life as meaningful, enjoyable and productive as possible.

Carla: What would you say to someone who is considering joining a support group?

Steven: It is very important to join a support group. You will pick up ideas on how to manage different aspects of living with neuropathy, including learning how you can successfully navigate through daily challenges. You may hear about different medications, nutritional supplements, alternative therapies and even some home remedies that can help you deal with the pain and fatigue.

Carla: Finish this sentence: “The strength of a support group is…”

Steven: Being with others who understand exactly what we live with, from the physical to the emotional. We are all in this fight together.

Carla Schick is a staff writer for IG Living magazine.
LifeStyle

Transitions
By Ronale Tucker Rhodes, MS

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.

Adversity Leads to Giving Back

Tiffani Pekkala, who suffers from PIDD, held her third annual personally sponsored blood drive with the help of her family and friends.

NOTHING CAN FORCE a child to grow up faster than when faced with serious adversity. Raised by her grandmother, Bette-Jo, 16-year-old Tiffani Pekkala never got to have much of a childhood. Her story is similar to that of other chronically ill children. But, it is also unique. She has turned her lifetime of sickness into a mission of giving back.

A Long Road to Diagnosis
According to Bette-Jo, Tiffani had been sick since she was 2 weeks old. She had sinus infections, pneumonia and asthma that required the use of a nebulizer, and she was hospitalized a few times. Bette-Jo knew that there was something very wrong, and when she gained custody of Tiffani at age 9, she took her to see an allergist for testing. Tiffani tested positive for everything. “He said, ‘That’s impossible,’“ says Bette-Jo. “So, he ran some blood tests and he called and said, ‘She has primary immune deficiency disease’ (PIDD). I didn’t even know what that was.’”

Tiffani was then sent to an immunologist who discovered she had low subclasses of IgG. Because the immunologist believed in home treatment, Tiffani was treated immediately with subcutaneous immune globulin (SCIG). “She didn’t even offer us IVIG [intravenous IG],“ explains Bette-Jo. “Her philosophy was ‘treat at home.’”

Tiffani was started on weekly SCIG treatments, but she continued to have sinus infections every month. “Two days before weekly infusions, she’d be slumping down and sick,” says Bette-Jo. So, her dosage was increased and they decided to infuse twice-weekly. “Now, it’s been working pretty good,” says Bette-Jo, although their insurance company has now forced them to change products for the third time, and they’re worried there may be new side effects.

Growing Up All Too Fast
As if being sick since birth wasn’t enough, Tiffani’s continued challenges
As if being sick since birth wasn’t enough, Tiffani’s continued challenges due to her PIDD diagnosis have made her grow up all too fast.

due to her PIDD diagnosis have made her grow up all too fast. When she was in fifth grade, she had the first of four major reconstructive surgeries, waiting six months between each. She was flatfooted and her ankles collapsed under her feet, causing her knees to turn in. To correct her condition, bone was removed from her hips to make new ankle bones and lengthen her legs. While this may sound scary for a child, it was even more so for Bette-Jo, because finding a doctor to perform the surgery on a chronically ill child proved very difficult.

On top of all of this, Tiffani was facing challenges in school. Because she infuses twice a week, she has to miss school every Wednesday. “In middle school, it wasn’t good,” says Tiffani. “The teachers I had were helpful, but they didn’t quite get it. They didn’t understand what it was.”

But, Tiffani and Bette-Jo weren’t giving up. They got through the surgeries, and they went to bat for Tiffani at school. “When people look at these kids, they don’t look sick,” explains Bette-Jo. So, they had her education plan changed from a 504 Plan to an Individual Education Plan. Now, says Tiffani, “they have bent over backward to make sure I have all the work I need and that I’m not docked anything for having late work because I’m sick.”

Now a thriving student, Tiffani is active on the student council. She’s on the mural project, which is funded by a grant that allows students to design and paint a mural every year. And, she is a member of the prom committee. She also speaks to classrooms of fellow students to explain to the teens about her disease. “Some students, I’m sure, still don’t quite get it, but most are just welcoming,” says Tiffani. “They see me in the hall and I look perfectly fine. I don’t go around acting like I’m sick all the time. Some ask what they can do to help. Some just walk away. And, a couple of them cried. They say they love me because I love them back, and that they’ll be here for me no matter what, even after they graduate.”

Turning Adversity Into Action

Outside of school, Tiffani is an inspiration. She has been on the Immune Deficiency Foundation’s (IDF) Teen Council for the past year, which she joined shortly after she attended IDF’s Teen Escape. “That was the first time I met anybody that even closely resembled having what I have,” says Tiffani. “Meeting people who have what I have was life-changing.”

In April 2009, in recognition of national PIDD month, she and Bette-Jo decided to do something to make people aware of Tiffani’s disease in their community of Camas, Wash. They decided on a blood drive. “Tiff and I went everywhere, talking to businesses and organizations and handing out fliers,” says Bette-Jo. “Our first drive had 80 donors, and we had to turn people away.” And, the drives keep on growing. This April was their third blood drive, which is the largest personally sponsored blood drive in Clark County.

They accomplish these drives with the help of their family, friends and students, and this year, Tiffani’s principal helped. “The Red Cross says it’s the weirdest thing they’ve ever been to,” explains Bette-Jo. At most blood drives, people come, donate blood and leave. “Not at our blood drive,” says Bette-Jo. “We have people who come and stay for hours, visiting with other people who are there. It’s like a big community get-together.”
This year, Tiffani organized her first blood drive at Hayes Freedom High School. “I did that all by myself, and I had over 40 donors, which was over our quota,” says Tiffani. “It was really cool for our school of only 120 students.” At the drives, Tiffani often offers reassurance to donors. “Like some of the big tough guys,” explains Tiffani. “They’ll have me hold their hands because they’re scared of the needles.” She also visits the local Red Cross to thank donors.

In 2010, Tiffani was chosen as the Red Cross Hero for blood products. “They’ve never had that category in Clark County,” says Bette-Jo. “They call her their blood hero. They’re amazed that she’s so sick and she takes the time to give back to everyone else.” A Hero Breakfast and Reception was held for her and other award recipients, and each person was videotaped during an interview. The video is on the IDF website at www.youtube.com/user/idfcommonground?feature=mhum.

“She’s really driven,” says Bette-Jo. “Her place here on earth is to educate people about this disease.” Tiffani says the Red Cross Hero award has inspired her “to keep to help, donate blood, and you save three people.”

A Future of Giving Back

Tiffani knows she’s going to college, but hasn’t decided on a major. “But, I’m definitely a people person, so I’ll end up doing something like that,” says Tiffani. Giving back to people is something that she learned from a lifetime of adversity. And, it’s something she learned from Bette-Jo, who long, I’ve backed off and let her lead whatever life she can. She knows her limits now. She’s free to do what she wants. She has accomplished so much. You have to let these kids live as normal as they can. If your child is going to get sick, she’s going to get sick. They have to get out in the real world.”

Tiffani has. She’s got a boyfriend who protects her and who has been there for her infusions, and he knows he can’t be around her when he’s sick. Tiffani does her own infusions, and she’ll be ready to go to college when it’s time. Her advice to other kids with PIDD: “It’s not the end of the world. It seems like it for a while, but life adjusts. With anything, you get used to it. You can’t let it control your life. You still have to be you, no matter what.”

RONALE TUCKER RHODES, MS, is the editor of IG Living magazine.

In 2010, Tiffani was chosen as the Red Cross Hero for blood products.
IG Success Stories: Maintenance Miracles and Mom Theories

The true miracle of IVIG can only be appreciated by hearing the stories of those whose lives have flourished with the help of this life-saving therapy.

By Mark T. Haggard

TWENTY-FIVE YEARS ago, my appendix burst and I spent a week in a hospital with a hose suctioning peritonitis out of my innards. I was fortunate, a doctor reminded me. Had this happened 20 years earlier, I might not have survived.

It’s good to be living in the 21st century. Medicine continues to progress, allowing us and our children to enjoy longer, healthier lives. This is especially true for those with chronic illnesses who rely on immune globulin (IG) to survive.

My own experience with IG began when my wife and I sought relief for my son’s constant ear, sinus, lung and skin infections; he started intravenous IG (IVIG) at age 4 in 2003 and has lived a full life ever since. His sister started IVIG at age 3 in 2004 and has lived just as fully. Had my son and daughter been born with common variable immune deficiency (CVID) 20 years earlier, they might not have survived.

My children are not the only ones whose lives have been saved with IVIG. Here are a few of many IG success stories. With the help of IVIG:

- Jordan Leventhal attended private high school away from home and played goalkeeper on the school’s soccer team. He is now at Georgetown Medical School preparing for a career in pediatric immunology. He also is a popular speaker at immune deficiency conferences.
- Branson Worthen achieved his lifelong goal of being a missionary, recently finishing the first year of his mission in Raleigh, N.C.

But, perhaps the two most profound IVIG success stories that I have come across are those of Rhett and Zach Riggins and Cathryn Achilles.

Rhett and Zach Riggins

When Rhett Riggins was born in 1990, there were no living adults with adenosine deaminase deficiency, also called ADA-SCID (severe combined immunodeficiency). Doctors tested Rhett for ADA-SCID after his body showed signs of an immune deficiency. But they assured his parents, Rich and Lori, that the disease was so rare (one in a million) that it was highly unlikely he had it. Tests came back positive.

ADA-SCID left Rhett with virtually no immune system and susceptible to any bacteria, virus or fungi with which he came into contact. Doctors prescribed the combination of PEG-ADA (Adagen), an enzyme replacement, and IVIG. Miraculously for the Rigginses, the U.S. Food and Drug Administration had just approved PEG-ADA for ADA-SCID a mere four months before Rhett’s diagnosis, which allowed him to live life outside a bubble.

When Lori became pregnant two years later with Rhett’s brother Zach, ADA-SCID left Rhett with virtually no immune system and susceptible to any bacteria, virus or fungi in which he came into contact.

When Lori became pregnant two years later with Rhett’s brother Zach,
The results of treatment were astounding. The boys suffered from few sicknesses growing up. Rhett was hospitalized once with chickenpox, and Zach had to be hospitalized a couple of times with chickenpox and shingles. Rhatt also had a bout of whooping cough when he was taken off IVIG for a short time. But other than those viruses, there were no chronic illnesses and no respiratory issues, and many people were shocked that they never had anything as simple as an ear infection.

Rich Riggins calls IVIG a “maintenance miracle.” “People told us what to expect: recurring sicknesses, continual trips to the hospital,” says Rich, and then he pauses and shakes his head. “Didn’t happen.”

For the Rigginses, there was a choice between “maintenance” and the “cure”: a bone marrow transplant. But Rich believed that it was too risky for his kids. “Why go there if you don’t have to?” he asks. “IVIG works for them. Let them live their lives.”

So the boys grew into young men. In high school, Rhett was part of his high school’s chapter of Future Farmers of America and acquired a love of fishing — two activities certain to top most immunologists’ “do not do” list — but there was never a second thought in Rhett’s mind. Zach was on the drumline of the high school band and ran cross-country. Both took up golf with their grandfather. Neither could have engaged in these activities without IVIG.

Rhett is now 20 years old and works as an assistant to a computer programmer in an online business. He has switched to subcutaneous IG (SCIG), which he receives once a week. He wants to go on to college, but he isn’t sure what degree he will pursue. Brother Zach is 18 and just graduated from high school. He receives IVIG once a month. His favorite activity now is writing science-fiction stories online, but he plans to go to college and study either medical research or city planning. Both of the brothers love computers. “We could see Zach writing a book and Rhett illustrating it,” says Lori.

“We have benefited from the experience of the pioneers,” says Rich, summing up his experience with his sons’ “maintenance miracle.” “We hope that our experience benefits those who follow us.”

Cathryn Achilles

For the first seven years of Cathryn Achilles’ life, doctors were puzzled by her failure to thrive. Finally, in May 2000, she was diagnosed with ataxia telangiectasia (A-T), a degenerative genetic disorder characterized by the gradual loss of voluntary motor skills and a severely compromised immune system. This immune defect means that there is a one-in-three chance of developing cancer, usually leukemia or lymphoma. Radiation is ineffective as a treatment for A-T patients, since their DNA does not repair properly. Doctors told her parents, Jim and Deanna, that there was no cure for A-T and that most patients do not live past their teens.

In the summer of 2007, at a Joni
Cathryn Achilles was diagnosed with A-T at age 9, and her “mom’s theory” is that IVIG has prevented her from getting cancer.

and Friends Disabilities Conference, Cathryn was a beautiful 16-year-old young lady with fair skin, piercing blue eyes and lovely blond hair flowing from underneath a broad-brimmed hat. Her effervescent personality bubbled throughout the campsite and her face was continually colored with a smile.

Cathryn will turn 20 on July 1, 2011, outliving the original prognosis. Her mother credits her monthly infusions of IVIG. Before starting infusions, Cathryn was sick many times a year. Since starting infusions in 2004, on average, Cathryn has been sick only once a year; in fact, her brother has been sick more often than she has been. “I am very grateful for IVIG,” muses Cathryn, “since I don’t like going to the hospital.”

More important than infection, though, is the risk of cancer. Cathryn’s blood is checked yearly, and there have been no signs of leukemia or lymphoma. “It’s a mom theory,” says Deanna. “Although the doctors don’t believe it, IVIG will prevent cancer.” She theorizes that Cathryn’s overall health is the direct result of her IVIG treatments.

In 2009, Cathryn graduated from high school. Deanna did most of the teaching, but was aided by an educator named Sharon Hensley, who helped find adaptive material for Cathryn to use. “I couldn’t have done it without her!” states Deanna. Because A-T hampers fine motor skills, Cathryn dictated and Deanna typed. Cathryn met all the requirements to graduate in the state of California, which includes core classes like algebra and economics, and her favorite subject, literature. She now meets the academic requirements to go on to most colleges, but she says that’s not for her: “I would rather spend my time doing what I want.”

What Cathryn is doing now is fundraising. She enjoys quilting, and her creations are being sold as fundraisers for A-T, orphans, disadvantaged children and the local crisis pregnancy center. Her favorite organization is Joni and Friends, an outreach for people with disabilities started by Joni Eareckson Tada. “Joni is my hero,” states Cathryn.

Cathryn is a hero to others. Cathryn’s father was running marathons for A-T awareness when he met ultra-runner Tim Borland. After running the Walt Disney World Marathon together, Borland started running for A-T.

“When I first met Cathryn,” says Borland, “I thought to myself, here is a teenage girl living with a terrible disease that has no cure. Her peers are out driving, playing sports and dating, yet Cathryn is as happy a human being as you will find. That inspired me to do something.” That something culminated in 63 marathons in 63 days during the fall of 2007 in an effort to raise money and awareness for A-T.

Thanks to Past and Future Pioneers

What if these diseases had struck Rhett, Zach and Cathryn 20 years earlier? We can only be grateful for those pioneers who have gone before us and, now, to a new wave of pioneers like the Rigginses and the Achilleses.

For Rhett and Cathryn, who have both celebrated their 20th birthday, IVIG has helped them exceed their life expectancies. With more research, perhaps one day soon, timelines will disappear forever. In the 11 years since Cathryn’s original diagnosis, doctors have raised the expected lifespan of A-T patients to 30 years. “We have hope,” Deanna said, “but when God calls her name, we are ready for it.”

With the success of IVIG, that may not be anytime soon.

For more information on Joni and Friends Disabilities Ministry, go to www.joninandfriends.org.

To view the video of Tim Borland’s 63 marathons in 63 days, go to www.featmovie.com.

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.
EVEN THE SMALLEST of needles can scare the largest of men. While many of us may get a chuckle out of knowing that a supersized man can be brought to his knees at the mere sight of a needle, doctors know that needle anxiety is a real problem with potentially life-altering consequences.

The problem is simple: Needles poked into the skin cause pain, and most humans try to avoid pain. However, many medications require the use of a needle for administration, and patients who cannot overcome their fear of needles often tend to forgo treatment. But, patients who rely on immune globulin have no choice but to deal with the pain and anxiety a needle can bring. And, while a certain amount of pain is unavoidable, there are products and techniques that patients can use to distract them from, desensitize them to and minimize the discomfort.

Distraction
Research has shown that a pain signal can be perceived as stronger or weaker depending on where the brain is focused. If the brain is solely focused on the pain, the brain will focus all of its energy on that pain. If the brain is actively engaged in a distracting activity at the time of pain, it has a decreased ability to focus on that pain. Because the perception of pain requires attention, providing a distraction from the infusion process can decrease the pain caused by needle insertion. Using devices such as virtual reality glasses or videos can be useful tools of distraction.

Desensitization
Young children in particular can be overwhelmed with the amount of uncontrollable and unexpected intrusion medical procedures have on their lives. In addition, just the sight of the supplies and equipment needed for infusions can be intimidating. Many child life experts have used therapeutic play to help desensitize children and alleviate some of the anxiety surrounding medical procedures. During therapeutic play, children, in essence, play doctor by utilizing much of the same equipment used on them to give their dolls and stuffed animals the same treatment they receive.

Similarly, adults can desensitize themselves to needle anxiety. While they may not want to play with a stuffed animal, they can use some of the infusion supplies, such as alcohol wipes, to simulate an infusion experience. Talking with a partner about what to expect at an infusion also can be helpful.

Minimization
Changes in the medical regimen also can help patients have a more comfortable experience. Minimizing the size of the needle helps bring the anxiety level down. Naturally, if the first thing a patient sees is a needle the size of a garden hose coming at them, their immediate response will be to tighten their muscles in anticipation of the poke. Veins are much easier to access if the muscles surrounding them are relaxed. Research shows that using the smallest needle possible that will still get the job done will minimize not only anxiety but scar tissue buildup in the veins. So, using a small needle will make the process less intimidating and will help to ease the process for all.

Numbing cream made of lidocaine and prilocaine also can help minimize discomfort. Applied as directed before an infusion, this cream can numb the skin so that the poke is less painful. Having numb skin also helps the patient to relax, thereby making the vein easier to access.

Ask About Possible Solutions
Patients need not be embarrassed or avoid treatment because of needle anxiety. Healthcare professionals are experienced at helping with this, so patients should talk with them about possible solutions. ■

KRIS MCFALLS is the full-time patient advocate for IG Living magazine.
EMLA Cream (lidocaine 2.5% and prilocaine 2.5%) is a eutectic mixture of lidocaine and prilocaine available without a prescription. It is indicated for dermal anesthesia, and is packaged in 5- and 30-gram tubes.

MMJ Labs LLC

Buzzy is a portable, reusable plastic bee that gives natural pain relief through cold and vibration. Designed for individuals 4 years and older, the bee vibrates and a specially prepared ice pack fits underneath. A pilot study in adults for IV starts in the October 2009 Clinical Journal of Pain found that Buzzy significantly decreased pain. And, the more needle anxiety subjects had, the better Buzzy worked, with a significant reduction for each centimeter of increased anxiety on a 10-centimeter scale. Also available for kids are Bee-Stractor cards with age-specific questions that help them focus away from medical procedures.

CSL Behring

The Hizentra Child Therapy Kit is a Hizentra starter kit for caregivers of children with primary immune deficiency disease. It includes a travel bag to hold supplies, an infusion placemat, a 52-week therapy journal, a therapeutic play pack and an “Our Immune System” storybook.

Eloquest Healthcare

L.M.X.4 is a 4% lidocaine topical anesthetic cream available without a prescription. It is intended for adults and children 2 years and older, and comes in 5-, 15- and 30-gram tubes.

i-O Display Systems

The i-glasses 920HR virtual reality glasses are a 920,000 pixel high-resolution head-mounted display. Weighing only 2.4 ounces, they feature a virtual image size of 80 inches as seen from 5 feet, with the capability of viewing 3D-formatted programming in true stereoscopic 3D. It connects to any standard video source (DVD, VCR, MP4 Player) via the included cables, and has adjustable brightness and contrast features.

Sources

Directory of Infusion Anxiety Products

AstraZeneca

(800) 236-9933; www1.astrazeneca-us.com/pi/EMLA.pdf

Eloquest Healthcare

(877) 433-7626; www.eloquesthealthcare.com

i-O Display Systems

800-339-5287; www.i-glassesstore.com
Sources

For a more comprehensive list of resources, visit the Resources page at www.IGLiving.com.

**General Resources**

**Other Organization Websites**

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
- Alliance for Plasma Therapies (fair access to plasma therapies): www.plasmaalliance.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 Institutes of Health:
- 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

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

**IG Manufacturer Websites**

- Baxter: www.baxter.com
- CSL Behring: www.cslbehring.com
- Grifols: www.grifolsusa.com
- Octapharma: www.octapharma.com
- Talecris: www.talecris.com
- 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
Sources

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
• International Myositis Assessment and Clinical Studies Group: http://www.niehs.nih.gov/research/resources/collab/imacs/main.cfm

Online Peer Support
• Juvenile Myositis Family Support Network: www.curejm.com/family_support/index.htm
• Myositis Association Community Forum: www.myositis.org
• Myositis Support Group: www.myositissupportgroup.org

Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus (PANDAS)
Websites
• P.A.N.D.A.S. Network: pandasnetwork.org
• Behavioural Neurotherapy Clinic – Australia: www.adhd.com.au/PANDAS.htm

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

Peripheral Neuropathy (PN)
Websites
• 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 for persons with primary immunodeficiency diseases through advocacy, education and research. (800) 296-4433

• 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

Online Peer Support
• American Academy of Allergy, Asthma & Immunology: www.aaaai.org
• International Patient Organization for Primary Immunodeficiencies (IPPOI): www.ipopi.org
• Michigan Immunodeficiency Foundation: www.midf.org

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

The Cure JM Foundation
www.curejm.com
(760) 487-1079
• 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

• Rainbow Allergy-Immunology: www.uhhospitals.org/tabid/132/Default.aspx

• 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

Other Resources
Education and Disability Resources
• Americans with Disabilities Act of 1990: www.ada.gov

- Provides protection for people with disabilities from certain types of discrimination, and requires employers to provide some accommodations of the disability.


• DisabilityInfo.gov: http://www.disability.gov/

- U.S. Federal government’s disability-related information and resources.

• 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 Carimune NF: http://www.cslbehring-us.com/s1/cs/enus/1151517250474/Web_Product_C/1151517249408/ProductDetail.htm

• IVIG Flebogamma: www.grifolsusa.com/pdfs/flebo_14Jun05.pdf

• IVIG Gammagard Liquid: www.gammagardliquid.com

• IVIG Gammagard S/D: www.immunedisease.com

• IVIG Gamunex: www.gamunexconnexions.com

• IVIG Octagam: www.octapharma.com

• IVIG Privigen: www.privigen.com

• SCIG Hizentra: www.hizentra.com

• SCIG Vivaglobin: www.vivaglobin.com

Pump and Infusion Sets Websites
• EMED 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.norfolkmedical.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.
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 Reactions Reported to Occur With IGIV Treatment**

The following reactions have been reported to occur with IGIV treatment and may occur with IGIV 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 cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammapathies. For patients judged to be at risk of developing thrombotic events, administer Hizentra at the minimum rate practicable.

**Aseptic Meningitis Syndrome (AMS)**

AMS may occur with use of human immune globulin products. The syndrome usually begins within several hours to 2 days following IGIV treatment. AMS is characterized by signs and symptoms including 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, with 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 IGIV.

Conduct a thorough neurological examination, including CSF studies, to rule out other causes of meningitis in patients exhibiting signs and symptoms of AMS. Discontinuation of IGIV treatment has resulted in remission of AMS within several days without sequelae.

**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.

**5.3 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.

**5.4 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 ≥25% of 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 Subjects (n=49)</td>
<td>Number (Rate) of AEs (n=2264 Infusions)</td>
<td>Number (%) of Subjects (n=49)</td>
</tr>
<tr>
<td>Local reactions1</td>
<td>49 (100)</td>
<td>1340 (0.592)</td>
</tr>
</tbody>
</table>
Table 2: (Continued)

<table>
<thead>
<tr>
<th>AE (&lt; = Subjects)</th>
<th>All AEs*</th>
<th>AEs* Occurring During or Within 72 Hours of Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number (%) of Subjects (n=49)</td>
<td>Number (Rate) of AEs (n=2264 Infusions)</td>
</tr>
<tr>
<td>Other AEs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>13 (26.5)</td>
<td>40 (0.018)</td>
</tr>
<tr>
<td>Cough</td>
<td>8 (16.3)</td>
<td>9 (0.004)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7 (14.3)</td>
<td>8 (0.004)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6 (12.2)</td>
<td>6 (0.003)</td>
</tr>
<tr>
<td>Back pain</td>
<td>5 (10.2)</td>
<td>11 (0.005)</td>
</tr>
<tr>
<td>Nausea</td>
<td>5 (10.2)</td>
<td>5 (0.002)</td>
</tr>
<tr>
<td>Abdominal pain, upper</td>
<td>5 (10.2)</td>
<td>5 (0.002)</td>
</tr>
<tr>
<td>Rash</td>
<td>5 (10.2)</td>
<td>7 (0.003)</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>4 (8.2)</td>
<td>7 (0.003)</td>
</tr>
<tr>
<td>Migraine</td>
<td>4 (8.2)</td>
<td>5 (0.002)</td>
</tr>
<tr>
<td>Pain</td>
<td>4 (8.2)</td>
<td>5 (0.002)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>4 (8.2)</td>
<td>6 (0.003)</td>
</tr>
<tr>
<td>Pharyngolyngeal pain</td>
<td>4 (8.2)</td>
<td>6 (0.003)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>4 (8.2)</td>
<td>5 (0.002)</td>
</tr>
</tbody>
</table>

* Excluding infections.
† 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)

<p>| Table 3: Incidence of Subjects With Adverse Reactions (Experienced by 2 or More Subjects) to Hizentra and Rate per Infusion (ITT Population) |</p>
<table>
<thead>
<tr>
<th>ADVERSE REACTION (≥2 SUBJECTS)</th>
<th>Number (%) of Subjects (n=49)</th>
<th>Number (Rate) 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>Contusion</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>3 (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.

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

- **Infusion 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 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.

8.2 Women of Reproductive Potential

Hizentra is not intended for use in females who are 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

Hizentra was evaluated in 10 pediatric subjects (3 children and 7 adolescents) with PI. No pediatric-specific dose requirements were necessary to achieve the desired serum IgG levels.

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.

15 REFERENCES


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Distributed by: CSL Behring LLC Kankakee, IL 60901 USA
Based on March 2010 version
Vivaglobin®

Immunoglobulin Subcutaneous (Human) 16% Liquid

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

1 INDICATIONS AND USAGE

Vivaglobin is an Immune Globulin Subcutaneous (Human) (IGSC), 16% Liquid indicated as replacement therapy for primary humoral immunodeficiency (PI). This includes, but is not limited to, the primary immunodeficiency in common variable immunodeficiency (CVID), X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies.

4 CONTRAINDICATIONS

Vivaglobin is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of Immune Globulin (Human).

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

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Severe hypersensitivity reactions may occur (see Patient Counseling Information [17.2]). In case of hypersensitivity, discontinue the Vivaglobin infusion immediately and institute appropriate treatment. Epinephrine should be immediately available to treat any acute severe hypersensitivity reactions.

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. Vivaglobin contains ≤1.7 mg/mL IgA (see Description [11]). The minimum concentration of IgA that will provoke a hypersensitivity reaction is not known; therefore all IgG preparations carry the risk of inducing an anaphylactic reaction to IgA.

5.2 Aseptic Meningitis Syndrome (AMS)

AMS has been reported to occur infrequently with IGIV treatment3 and with Vivaglobin treatment. The syndrome usually begins within several hours to 2 days following IGIV treatment. AMS is characterized by signs and symptoms including 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 with 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 IGIV.

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

5.3 Reactions Reported 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 Vivaglobin and at appropriate intervals thereafter.

Periodic monitoring of renal function and urine output is particularly important in patients who have a history of renal disease or other risk factors, such as advanced age, impaired cardiac output, hypercoagulable disorders, prolonged periods of immobilization, or those who are on dialysis or anticoagulants. Patients who are at risk for acute renal failure should be monitored closely, and renal function should be tested before initiating IGIV treatment.

Thrombotic Events

Thrombotic events may occur with use of human immune globulin products. Patients at 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 hypercoagulability. Because of the potentially increased risk of thrombosis, consider baseline assessment of blood viscosity in patients at risk for hypercoagulability, including those with cryoglobulins, fasting chylomicronemia/markedly high triglycerides (triglycerides), or monoclonal gammapathies. For patients at risk, consider prophylactic anticoagulation therapy, such as low-molecular-weight heparin, aspirin, or clopidogrel, to reduce the risk of thrombosis. Individuals at risk should also be counseled on lifestyle modifications, such as smoking cessation, weight loss, and regular physical activity.
Table 3: Incidence of Subjects With Adverse Events (AEs) (Experienced by >5% of Subjects) and Rate* per Infusion, Irrespective of Causality, in the US-Canada Study

<table>
<thead>
<tr>
<th>AEs* (&gt;5% of Subjects)</th>
<th>Number (%) of Subjects (n=65)</th>
<th>Number (Rate1) of AEs per Infusion (n=3656)</th>
<th>Number (%) of Subjects (n=65)</th>
<th>Number (Rate1) of AEs Per Infusion (n=3656)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs at the injection site*</td>
<td>60 (92%)</td>
<td>1789 (0.49)</td>
<td>60 (92%)</td>
<td>1767 (0.4848)</td>
</tr>
<tr>
<td>Other AEs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>31 (48%)</td>
<td>159 (0.04)</td>
<td>30 (46%)</td>
<td>104 (0.033)</td>
</tr>
<tr>
<td>Gastrointestinal disorder</td>
<td>24 (37%)</td>
<td>35 (0.01)</td>
<td>18 (28%)</td>
<td>24 (0.007)</td>
</tr>
<tr>
<td>Fever</td>
<td>16 (25%)</td>
<td>28 (0.008)</td>
<td>12 (18%)</td>
<td>20 (0.005)</td>
</tr>
<tr>
<td>Nausea</td>
<td>12 (18%)</td>
<td>18 (0.005)</td>
<td>11 (17%)</td>
<td>15 (0.004)</td>
</tr>
<tr>
<td>Rash</td>
<td>11 (17%)</td>
<td>22 (0.006)</td>
<td>10 (15%)</td>
<td>16 (0.004)</td>
</tr>
<tr>
<td>Sore throat</td>
<td>10 (15%)</td>
<td>17 (0.005)</td>
<td>8 (12%)</td>
<td>11 (0.003)</td>
</tr>
<tr>
<td>Allergic reaction</td>
<td>7 (11%)</td>
<td>8 (0.002)</td>
<td>5 (8%)</td>
<td>5 (0.001)</td>
</tr>
<tr>
<td>Pain</td>
<td>6 (9%)</td>
<td>8 (0.002)</td>
<td>4 (6%)</td>
<td>4 (0.001)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>6 (9%)</td>
<td>6 (0.002)</td>
<td>5 (8%)</td>
<td>5 (0.001)</td>
</tr>
<tr>
<td>Cough increased</td>
<td>6 (9%)</td>
<td>6 (0.002)</td>
<td>5 (8%)</td>
<td>5 (0.001)</td>
</tr>
<tr>
<td>Gastrointestinal pain</td>
<td>5 (8%)</td>
<td>6 (0.002)</td>
<td>4 (6%)</td>
<td>5 (0.001)</td>
</tr>
<tr>
<td>Migraine</td>
<td>5 (8%)</td>
<td>5 (0.001)</td>
<td>2 (3%)</td>
<td>2 (0.001)</td>
</tr>
<tr>
<td>Skin disorder</td>
<td>5 (8%)</td>
<td>7 (0.002)</td>
<td>3 (5%)</td>
<td>5 (0.001)</td>
</tr>
<tr>
<td>Asthma</td>
<td>5 (8%)</td>
<td>8 (0.002)</td>
<td>3 (5%)</td>
<td>5 (0.001)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>4 (6%)</td>
<td>4 (0.001)</td>
<td>3 (5%)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Asthenia</td>
<td>4 (6%)</td>
<td>4 (0.001)</td>
<td>2 (3%)</td>
<td>2 (0.001)</td>
</tr>
<tr>
<td>Malaise</td>
<td>4 (6%)</td>
<td>5 (0.001)</td>
<td>2 (3%)</td>
<td>2 (0.001)</td>
</tr>
</tbody>
</table>

* Excluding infections. 1 Rate, number of AEs per infusion. 2 Includes injection-site inflammation.

The total number of AEs, irrespective of causality, including injection-site reactions, that began during or within 72 hours after the end of an infusion was 2262 (a rate of 0.62 AEs per infusion); excluding injection-site reactions, the rate of AEs per infusion was 0.14.

Table 4 summarizes the severity of local AEs by infusion, irrespective of causality.

Table 4: Severity of Local Adverse Events (AEs) by Infusion, Irrespective of Causality, in the US-Canada Study

<table>
<thead>
<tr>
<th>AEs at the injection site</th>
<th>Number (%) of AEs (n=3656)</th>
<th>Number (Rate1) of AEs per Infusion (n=3656)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>21 (32%)</td>
<td>59 (0.016)</td>
</tr>
<tr>
<td>Nausea</td>
<td>7 (11%)</td>
<td>9 (0.002)</td>
</tr>
<tr>
<td>Rash</td>
<td>4 (6%)</td>
<td>9 (0.002)</td>
</tr>
<tr>
<td>Asthenia</td>
<td>3 (5%)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Gastrointestinal disorder</td>
<td>3 (5%)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Fever</td>
<td>2 (3%)</td>
<td>2 (0.001)</td>
</tr>
<tr>
<td>Skin disorder</td>
<td>2 (3%)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>2 (3%)</td>
<td>2 (0.001)</td>
</tr>
<tr>
<td>Urine abnormality</td>
<td>2 (3%)</td>
<td>3 (0.001)</td>
</tr>
</tbody>
</table>

* Rate, number of adverse reactions per infusion. 1 Includes injection-site inflammation.

Europe-Brazil Study

In a clinical study conducted in Europe and Brazil, the efficacy and safety of Vivaglobin were evaluated for 10 months in 60 subjects with PI. Subjects were treated weekly with Vivaglobin at a mean dose of 89 mg/kg body weight (range: 51 to 147 mg/kg), which was 101% of their previous weekly IGIV or IGSC dose (see Clinical Studies [14.2]). Study subjects received a total of 2,297 infusions of Vivaglobin.

The AEs and their rates reported in this study were similar to those reported in the US-Canada study, with two exceptions: no episodes of headache were reported; and 18 (a rate of 0.008 per infusion) episodes of fever were judged to be related to the administration of Vivaglobin. One subject discontinued due to repeated local reactions of moderate severity.

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.

Vivaglobin

Adverse reactions identified during worldwide postmarketing use of Vivaglobin for treatment of PI are allergic-anaphylactic reactions (including dyspnea, pruritus, urticaria, rash, edema and other cutaneous reactions, wheezing, syncope, hypotension, and throat swelling), generalized reactions (including flu-like symptoms, myalgia, chills, fever, tachycardia, arthralgia, nausea and vomiting, diarrhea, gastrointestinal cramping, stomach pain, back pain, headache, headache possibly caused by increased blood pressure, and chest tightness), migraine, and injection-site reactions.

General

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

- 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, bullous dermatitis
- Hematologic: Pancreatitis, leukopenia, hemolysis, positive direct antithrombin (Coombs') test
- General/Body as a Whole: Pyrexia, rigors
- Musculoskeletal: Back pain
- Gastrointestinal: Hepatic dysfunction, abdominal pain

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 [17.2]).

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 Vivaglobin. It is also not known whether Vivaglobin can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Vivaglobin should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers

Vivaglobin has not been evaluated in nursing mothers.

8.4 Pediatric Use

- In the US-Canada study, Vivaglobin was evaluated in 6 children (ages 5 through 11) and 4 adolescents (ages 13 through 16). In the Europe-Brazil study, Vivaglobin was evaluated in 16 children (ages 3 through 11) and 6 adolescents (ages 13 through 16).
- The safety and efficacy of Vivaglobin were not studied in pediatric subjects under 2 years of age.
- There were no differences in the safety and efficacy profiles as compared with adult subjects.
- No pediatric-specific dosing requirements were necessary to achieve the desired serum IgG levels.
- For recommendations on the number of simultaneous injection sites for pediatric patients who weigh less than 45 kg (99 pounds), see Administration (2.4).

8.5 Geriatric Use

The clinical studies of Vivaglobin did not include sufficient numbers of subjects 65 years of age and older to determine whether they respond differently from younger subjects. For recommendations on the number of simultaneous injection sites for geriatric patients, see Administration (2.4).

Manufactured by: CSL Behring GmbH
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Based on April 2010 Revision.
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Important Safety Information
Hizentra and Vivaglobin are 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 you should not use Hizentra or Vivaglobin.

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

Hypersensitivity reactions may occur with Hizentra or Vivaglobin. If you have antibodies to IgA, you face a greater risk of developing severe hypersensitivity or going into shock. 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 and Vivaglobin are 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.

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The most common drug-related adverse reactions with Hizentra (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. The most common drug-related adverse reactions with Vivaglobin (seen in 5% or more of subjects in the clinical trial) were injection-site reactions (eg, swelling, redness, and itching), headache, nausea, rash, reduced strength and energy, and gastrointestinal disorders.

Your physician will monitor for potentially serious reactions associated with intravenous immunoglobulin treatment that might also occur with Hizentra or Vivaglobin, including aseptic meningitis syndrome (AMS), renal dysfunction/failure, osmotic nephropathy, thrombotic events, 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 or Vivaglobin.

Please see brief summary of full Prescribing Information for Hizentra and Vivaglobin, including the Patient Product Information for each, on previous pages.

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