IG Dosing
Not One-Size-Fits-All

Weight Loss for the Mobility Impaired

Diagnosing and Treating MMN

Understanding Antibody Class-Switch

Coping Strategies for PIDD Preteens
Important Safety Information for GAMUNEX

Gamunex, Immune Globulin Intravenous (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).

Immune Globulin Intravenous (Human) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis and death. Patients predisposed to acute renal failure include patients with any degree of pre-existing renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Especially in such patients, IGIV products should be administered at the minimum concentration available and the minimum rate of infusion practicable. While these reports of renal dysfunction and acute renal failure have been associated with the use of many of the licensed IGIV products, those containing sucrose as a stabilizer accounted for a disproportionate share of the total number. Gamunex does not contain sucrose. Glycine, a natural amino acid, is used as a stabilizer.

Gamunex 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.

There have been reports of noncardiogenic pulmonary edema (Transfusion-Related Lung Injury (TRALI)), hemolytic anemia, and aseptic meningitis in patients administered with IGIV. 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, and/or known or suspected hyperviscosity. Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving IGIV therapy.

Gamunex 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.

In clinical studies, the most common adverse reactions with Gamunex were headache, fever, chills, hypertension, rash, nausea, and asthenia (in CIDP); headache, cough, injection site reaction, nausea, pharyngitis, and urticaria (in PI); and headache, vomiting, fever, nausea, back pain, and rash (in ITP). The most serious adverse reactions were pulmonary embolism (PE) in one subject with a history of PE (in CIDP), an exacerbation of autoimmune pure red cell aplasia in one subject (in PI), and myocarditis in one subject that occurred 50 days post-study drug infusion and was not considered drug related (in ITP).

*CIDP=chronic inflammatory demyelinating polyneuropathy; PI=primary immunodeficiency; ITP=idiopathic thrombocytopenic purpura.


You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088. Please see adjacent page for brief summary of GAMUNEX full Prescribing Information.

Evidence based. Patient proven.
HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use GAMUNEX®, Immune Globulin Intravenous (Human), 10% Caprylate/Chromatography Purified, safely and effectively. See full prescribing information for GAMUNEX.

GAMUNEX (Immune Globulin Intravenous [Human], 10% Caprylate/Chromatography Purified) 10% Liquid Preparation

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 be associated with Immune Globulin Intravenous (Human) (IGIV) products in predisposed patients.
■ Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. GAMUNEX does not contain sucrose.
■ Administer IGIV products at the minimum concentration available and the minimum infusion rate practicable.

INDICATIONS AND USAGE

GAMUNEX is an immune globulin intravenous (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. Epinephrine should be 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.

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

ADVERSE REACTIONS

■ PI – Most common drug related adverse reactions during clinical trials were headache and cough.
■ ITP – Most common drug related adverse reactions during clinical trials were headache, vomiting, fever, and nausea.
■ CIDP – Most common drug related adverse reactions during clinical trials were headache and fever.

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

USE IN SPECIFIC POPULATIONS

■ In patients over age 65 or in any patient at risk of developing renal insufficiency, do not exceed the recommended dose, and infuse GAMUNEX at the minimum infusion rate practicable.
■ Pregnancy: no human or animal data. Use only if clearly needed.
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About IG Living
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.

IG Living, (ISSN 1949-4548), published bimonthly, is a community service provided by FFF Enterprises, 41093 County Center Drive, Temecula, CA 92591, (800) 843-7477 x1362, fax (951) 699-9655.

Subscriptions to IG Living are free, and readers may subscribe at www.IGLiving.com or by calling (800) 843-7477 x1351.

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About IG Living

All manuscripts should be submitted in MS Word, in Arial font. Manuscripts should be between 650 and 1,300 words in length, with unjustified margins and without any other formatting. Submission guidelines are available for download from the Contact Us page on www.IGLiving.com. Email manuscripts to editor@IGLiving.com. IG Living retains the right to edit submissions. The contents of each submission and their accuracy are the responsibility of the author(s) and must be original work that has not been, nor will be, published elsewhere, without the written permission of IG Living. A copyright agreement attesting to this and transferring copyright to FFF Enterprises will be required. Acceptance of advertising for products and services in IG Living in no way constitutes endorsement by FFF Enterprises. ©2011 FFF Enterprises Inc.

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Coping Strategies for PIDD Preteens
“In a world where popular is cool and cool is popular, it’s hard for PIDD kids to fit in when they appear to have something strange.”

Understanding and Treating Multifocal Motor Neuropathy
“Early treatment of MMN usually leads to enough of a reduction, if not a resolution, of symptoms so that permanent disability is avoided.”

Understanding Antibody Class-Switch
“The process of changing from IgM production to IgG production (and also to IgA and IgE production) is called ‘class-switch.’”

IG Dosing Strategies
“Clinical trials and scientific studies help to establish standard maximum and minimum IG dosing standards.”

Weight-Loss Strategies for the Mobility Impaired
“A healthful way to balance your diet is to make two-thirds or more of your food vegetables, fruits, whole grains and beans and only one-third or less animal protein.”

Be a Part of IG Living’s Blog and Facebook Discussions!
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 Teleforsums!
IGL’s Readers Group Teleforsums 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 teleforsums.
- IG Living will send you invitations to let you know when the two-per-month, hosted, toll-free teleforsums 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 Teleforsums now by emailing kmcfalls@IGLiving.com or calling (888) 433-3888, ext. 1349.
Our mission is to support the IG community through education, communication and advocacy

As I begin my third year as editor of IG Living magazine, I am reflecting on all the articles we have published that shed light on how truly miraculous immune globulin is — as evidenced by the stories about your illnesses, treatments and struggles to regain your health, and the physicians and caregivers who work so diligently to help you.

Immune globulin is perhaps the most unique therapy ever discovered. The number of diseases it treats and the intricate issues associated with treatment far exceed any other medication available today. So little is known by the general population about this unique medicine, yet for the intimate community that is enmeshed in the IG world, we are all too familiar with and intrigued by how much is yet to be discovered about this drug’s potential.

One of the most hotly debated topics right now is how much and how often IG should be prescribed. In our article, An Overview of Immune Globulin Dosing, Kris McFalls aptly describes IG as “not a one-size-fits-all drug.” Even with each drug manufacturer’s dosing recommendations, industry standards and FDA on- and off-label approvals, physicians still must assess each patient individually to determine an appropriate dosing regimen, which often results from trial and error.

Many scientists are looking at industry standards about appropriate dosing recommendations. In 2009, scientists in Canada reported on a study conducted over a 22-year period to determine the optimal dose and target trough IgG levels of individual patients to prevent infection. They found that despite clinical data that is typically used to prescribe dosing regimens, infections were best prevented in those patients when a customized IG dose was prescribed to maintain their own optimal trough IgG level. We hope to report more in-depth on this study in a future issue of IG Living.

So many serious concerns are at the heart of living with IG therapy. Insurance is perhaps one of the most discussed. In this issue, we provide a detailed step-by-step look at how to apply for Social Security Disability Insurance (SSDI). If you think you are eligible for SSDI, this article should dispel any doubts you may have, guide you through the application procedure, and let you know what to expect after applying.

Second to, but no less important than, insurance is lifestyle. Our feature titled Weight-Loss Strategies for the Mobility Impaired will no doubt strike a chord for many of you. We provide you with some simple steps to change your daily habits that can make a significant impact on your weight-loss or weight-management goals.

And, as always, our entire LifeStyle section features personal accounts from those who rely on IG to survive. What’s unique in this issue, however, is one account of a young man transformed by IG, but unlike most of you, he doesn’t rely on IG to survive; instead, he was cured by the therapy. We hope that our Transitions interview with Nicholas Burrus will show you just how miraculous IG truly is.

To your health,

Ronale Tucker Rhodes, MS, Editor
Best Exercise Advice for Neuropathy

Matthew Hansen’s article “Exercise for CIDP” (August-September 2010) is the best article I have ever read on this subject. From my experience as a patient and professional working with neuropathy patients, this brilliant article should be given the broadest circulation among physical therapists and patient advocates. As a CIDP/autonomic neuropathy patient for 43 years due to exposure to Agent Orange during the Vietnam War in 1968, I have been to the experts who still thought that “working through the pain” was appropriate [for] neuropathy patients. My nightmare from those who thought they knew resulted in many horror experiences, not the least of which was the increase of extreme fatigue, along with the frightening experience of my legs from the waist down turning into numb cement when I was told to “push through the pain.” For the record: The pain did not go away with regular exercise.

The greatest words [in this article] are “appropriate exercise” for neuropathy and the FITT principle (frequency, intensity, time and type of activity), which I have written about and that have been confirmed a million times in my experience over the years. Yet, just recently, in a neuropathy newsletter, I read the words, “If patients adhere to a regular exercise regimen, over time, they notice that their overall pain levels go down. And the difficulty for most peripheral neuropathy (PN) patients is to overcome the initial increase in pain that comes with exercise.” I would never advise any PN patient to listen to such advice, as the issues [concerning] exercise for the neuropathy patient, whether CIDP or other causes, [are] more complex than this would suggest.

Exercise is very important, but if the professional does not understand the many causes of neuropathy that will influence the physical therapy approach, while listening to the patient, and [also] apply the words “appropriate” and the FITT principle, they will do a great disservice to the neuropathy patient. Thanks, Matthew, for your brilliant article.

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

Exercise for CIDP

The Editor replies:

Thanks for your feedback. The article, “Exercise for CIDP,” is but one of many articles we have written about exercise for various disease states. We have more planned in the future.

Kids Get Sick

Cough, cough, sniffle, sniffle
Kids get sick they say.
Sore throat and bellyaches
Are just an average day.
Now 3 and he’s in the hospital
There has to be something they’ve missed,
It can’t be normal for a kid to keep getting sick like this.
Sores on the skin, tons of medicines
Why can’t they figure this out?
Then, finally, some hope of healing to discover
An immune deficiency is what it is about.

— Roni M. Ray
(dedicated to son Brandon)

Your feedback, opinions, suggestions and anything else you’d like to share are important! Email us at editor@IGLiving.com or visit www.IGLiving.com and go to the Be Heard/Feedback page to send your comments.
Faces of IG Living

There are many faces in the IG Living community, representing hundreds of immune-mediated diseases and countless medical and lifestyle issues. IG Living’s magazine, website, Facebook page and blog are the ways in which our community can connect with one another. Be a part of the community by interacting with us. Your comments could lead you to others who share similar issues, and vice versa. Monday through Friday, we pose a new question on the IG Living Facebook page. Here is what some of our faces of IG Living are saying in response.

Tammee Frye Ryan
Vitamin D. And it did help. Those of us who live in long-winter states often are vitamin-D deficient. It helps my son! You had a great article on the very subject last month!

Joanna Tierno
I am leery of many supplements since so many make false promises and claims, but I did try one once that my doctor suggested. I can’t tell for certain if it was helpful or not, but I stopped using it because supplements aren’t covered by insurance and the cost was high for something I couldn’t really prove was beneficial. I just take all my medicines and infusions as prescribed, eat a healthy diet and stay active. You can’t go wrong with that!

Cheryl Fournier
My five-year anniversary of chronic inflammatory demyelinating polyneuropathy (CIDP) was just the other day. A very good friend and I got tattoos. Mine is a five-pointed star to remind me when I have a bad day that I have been worse and I will be better and to keep my head up, my feet on the ground and reach for the stars!

IG Living
How do you explain your illness to people without offering “too much information”?

Joanna Tierno
I mention David Vetter, the bubble boy, because it’s the only story most people are familiar with. But, I also sometimes explain that it is like diabetes in that I need to get antibodies put in that my body can’t make for itself, just like diabetics need insulin that they no longer make.

Carla Beatley
The nickname for my IVIG is “globs.” Everyone in my workplace knows when it is “glob day,” and it has caught on to many of my fellow infusion buddies. I often just say my body quit making antibodies and I need a monthly infusion to help me survive. I think what most people don’t understand is that we are constantly fighting infection and most of us struggle with being tired a great deal.

Debbie Spencer
I can’t even walk a mile in my shoes, why would I expect someone else to?
Immunology 101: Understanding Antibody Class-Switch

By Terry O. Harville, MD, PhD

LAST MONTH’S COLUMN ended with a discussion of the somatic (or acquired) mutation of immunoglobulin genes to produce an antibody that can have a stronger affinity for an antigen and, therefore, stronger protection against a pathogen. We also discussed that the initial antibody, IgM, is typically “switched” to IgG production. All of this occurs to increase the affinity and specificity of the antibody.

The Process of “Class-Switch”

The process of changing from IgM production to IgG production (and also to IgA and IgE production) is called “class-switch.” This occurs based on the linear arrangement of the immunoglobulin heavy chain gene components on chromosome 14. Although we tend to speak only of IgG, there actually are four subclasses of immunoglobulin G: IgG1, IgG2, IgG3 and IgG4. Additionally, there are two subclasses of IgA: IgA1 and IgA2. IgG proteins (as a result of the gene positions and arrangements) can be broadly apportioned into two parts — 1) the “variable” (V) region and 2) the “constant” (C) region — which when brought together make the functional antibody. The V region arises from specific gene recombination events (to be discussed in detail later). Each new V region defines the antibody specificity, of which many millions can be generated, but our bodies ultimately select 15 million or so to be our antibody repertoire.

The immunoglobulin heavy chain genes reside on chromosome 14 in this order: variable (V) genes — IgM constant gene — IgD constant gene — IgG3 constant gene — IgG1 constant gene — IgA1 constant gene — IgG2 constant gene — IgG4 constant gene — IgE constant gene — IgA2 constant gene. During B lymphocyte development, the recombined V gene will be transcribed with the IgM constant gene or IgD constant gene and will be expressed as IgM or IgD proteins, respectively, on the surface of the developing B lymphocyte. Subsequently, IgM will be secreted into the blood. If a specific antigen can be recognized by this B lymphocyte and its specific IgM antibody, and T lymphocyte stimulation occurs, then the B lymphocyte can be stimulated. With stimulation, and depending on the type of antigen being responded to, the DNA between the V gene and a specific C gene will be removed, and class-switch will occur.

For example, tetanus toxoid protein antigen tends to elicit an IgG1 antibody response. After the B lymphocyte has received appropriate stimulation, the intervening DNA between the tetanus toxoid-responsive V region gene and IgG1 C region gene (IgM constant gene — IgD constant gene — IgG3 constant gene) is removed from chromosome 14, bringing about class-switch. Another example is: If an IgE antibody is to be produced, the intervening DNA containing the IgM constant gene — IgD constant gene — IgG3 constant gene — IgG1 constant gene — IgA1 constant gene — IgG2 constant gene — IgG4 constant gene will be removed, again bringing about class-switch to IgE production. After class-switch, the process cannot go backward. In other words, if there has been a switch to IgE production, there can never be a return back to IgG1, IgG2, IgG3, IgG4 or IgA1 antibody production.

Antibody Classes and Subclasses

At this point, it should be recognized that we have the capacity to produce nine different classes and subclasses of antibodies: IgM, IgD, IgG1, IgG2, IgG3, IgG4, IgA1, IgA2 and IgE. Each has a specific role for which it is best suited.

For instance, IgD has an important role during B lymphocyte development. And, it may have a role in subsequent activation of B lymphocytes, but not a major antigen recognition role. Because IgD is typically not found in the blood stream, deficiency of IgD is not recognized as causing adversity (immunodeficiency). Alternatively, elevation of IgD in the blood is found in the autoimmune disorder known as hyper-IgD syndrome (HIDS), which is a periodic fever syndrome. These patients may have bouts of unexplained fevers and rashes at periodic intervals, severe mouth ulcers, abdominal pain, joint and muscle discomfort. HIDS patients don’t, however, experience recurrent infections.

Next month, we will continue defining the roles of the specific classes and subclasses of immunoglobulin.
**Research Funding**

Cure JM Wins $250,000 Grant

Cure JM, the nonprofit organization founded in October 2003 to raise awareness of juvenile myositis (JM), competed and won first place out of 1,200 organizations for one of the two top 2010 Pepsi Refresh Project grants of $250,000. The project is an “initiative designed to fund good ideas, big and small, that help refresh our world.” A total of 32 grants were awarded to the top vote-getters in six categories. Cure JM plans to commit $169,000 of the grant to support the JM Center of Excellence, $11,000 to conduct a pilot study of cardiovascular risk factors in patients with juvenile dermatomyositis (JDM), and $70,000 to conduct a genome study.

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**Medicine**

First Oral Drug Approved to Treat MS

The Food and Drug Administration (FDA) has approved Gilenya (fingolimod), the first oral drug to treat relapsing multiple sclerosis (MS), the most common form of the autoimmune disease. Gilenya, manufactured by Novartis, works differently than other drugs used to treat MS by preventing the entry of certain types of blood cells into the brain and spinal cord, reducing the severity of the disease. This is an improvement for MS patients who have received many injections to treat the disease thought to be influenced by genetic and environmental factors. Side effects include a decrease in heart rate when first taking the drug, headache, flu-like symptoms, diarrhea and back pain. The approval is based on the largest-ever clinical trial program submitted to the FDA for a new MS drug, and the company is working to get the drug approved throughout the rest of the world.

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**Research**

GSK Licenses New Gene Therapy for ADA-SCID

Following the formation of a new stand-alone unit specializing in the development and commercialization of medicines for rare diseases, GlaxoSmithKline (GSK) is licensing a gene therapy for ADA severe combined immune deficiency (ADA-SCID), in which kids cannot make a crucial enzyme called adenosine deaminase (ADA) that is needed to create immune system cells. It is licensing the method from the Italian charity Fondazione Telethon and Fondazione San Raffaele.

While ADA-SCID is similar to severe combined immune deficiency, the techniques used in this gene therapy treatment are different. According to an article published on Patent Docs (www.patentdocs.org): “In this ex vivo stem cell therapy, the patient's hematopoietic stem cells are harvested from the body, functional copies of the gene are inserted into the stem cells using a modified viral vector, and the cells are re-introduced to the patient. Because the technique uses the patient's own cells, there is much less risk of immune rejection compared to a bone marrow transplant, which is currently the best treatment option available. Most importantly, the ex vivo technique appears to be extremely safe.” The San Raffaele Institute published results of its study on the gene therapy in the July 22, 2010, issue of the New England Journal of Medicine, which showed “successful treatment in eight out of 10 children without substantial side effects, including no leukemia cases observed after four years.”

GSK also plans to work with the Italian researchers to develop ex vivo stem cell therapy for six other rare diseases, with the potential to treat a range of rare disorders.
Influenza

Flu Vaccine Safe for People with Egg Allergy

According to a new paper published by the American Academy of Allergy, Asthma & Immunology (AAAAI), recent studies show that most egg-allergic individuals can receive the flu vaccine safely under the care of their allergist/immunologist. “In the past, persons with egg allergy were told not to get the influenza vaccine because the vaccine contained egg protein and could trigger an allergic reaction,” says James T. Li, MD, PhD, FAAAAI, co-author of the paper. But, “research in the past year now shows that influenza vaccines contain only tiny amounts of egg protein. Clinical studies proved that the vast majority of persons with egg allergy did not experience a reaction when immunized with the influenza vaccine.” Yet, while the authors no longer recommend the practice of skin testing to the seasonal trivalent influenza vaccine (TIV), they do say it may be useful as an extra level of caution in cases where the patient has a documented history of a past allergic reaction to the vaccine.

Medicine

Subcutaneous Ofatumumab Studied for Autoimmune Disease

GlaxoSmithKline (GSK) and Genmab are collaborating to refocus the development of ofatumumab from intravenous delivery to subcutaneous delivery to treat autoimmune diseases. The decision is based on positive results from a Phase II trial evaluating infused ofatumumab in multiple sclerosis (MS) patients.

The Phase II study was a double-blind, dose-escalation, safety and pharmacokinetics trial that evaluated ofatumumab in 38 patients with relapsing-remitting MS. Patients were randomized to receive two infusions of 100 mg, 300 mg or 700 mg of ofatumumab or placebo. After 24 weeks, the patients randomized to placebo were treated with ofatumumab, and those patients initially treated with ofatumumab were switched to a placebo. All patients were then followed for an additional 24 weeks. Repeated MRI scans showed a sustained reduction in the number of brain lesions up to week 48 in patients who were initially treated with ofatumumab, and patients who were initially treated with a placebo showed similar results at 24 weeks.

GSK now plans to start a Phase IIb dose-ranging MS trial using subcutaneously administered ofatumumab in 2011. And, further work on subcutaneously delivered ofatumumab for rheumatoid arthritis (RA) therapy is separately under review. “Although the intravenous delivery of ofatumumab has previously demonstrated positive results in MS and RA studies, the autoimmune program is being refocused on the subcutaneous delivery of ofatumumab because GSK believes this route of administration has the potential to offer added convenience and improved tolerability,” says Ian Tomlinson, senior VP of biopharmaceuticals R&D at GSK.

Research

Researchers Find New Immune Cell

Researchers from the Dana-Farber Cancer Institute in Boston have identified a new type of cell that weakens the immune system and protects the body’s cells from immune system attack. In most studies, scientists focus on regulatory CD4+ T cells, known as CD4+ Treg, to find cells that calm down the immune response. However, a new team of researchers funded by the Lupus Research Institute found that besides the CD4+ T cells, there also are CD8+ T cells that have a positive effect on the “overreacted” response of the immune system. These new cells don’t reduce inflammation like CD4 cells do; instead, they prevent the immune system from producing antibodies that would attack normal cells. The discovery of this new cell will help to explore new therapies that could control the extreme immune system that lupus and other autoimmune patients have.
How to Apply for Social Security Disability Insurance

By Ronale Tucker Rhodes, MS

As of June 2010, there were a little more than eight million disabled workers receiving Social Security Disability Insurance (SSDI) benefits, according to the Social Security Administration’s website. Of these, it is estimated by the Immune Deficiency Foundation (IDF) that approximately 4,000 beneficiaries are those who have been diagnosed with a primary immune deficiency disease (PIDD), and there are likely thousands more who suffer from autoimmune diseases who receive SSDI benefits. But, with approximately 250,000 PIDD patients in the U.S. and unknown hundreds of thousands more who suffer from autoimmune diseases, it is likely that many more of these individuals could be receiving SSDI and are not. These guidelines can help those who think they are eligible for SSDI to apply.

What Is SSDI?

According to federal law, individuals who reside in the U.S. or one of its territories/commonwealths who are unable to work because of a medical condition that is expected to last at least one year or that may result in death are eligible to receive SSDI if they meet certain criteria. Beneficiaries qualify for SSDI benefits if they meet two earnings tests: 1) a recent work test based on the age at which they became disabled, and 2) a duration of work test based on age that shows a long enough work history during which they have paid into the Social Security system. In both instances, the older the individual is, the longer they will have had to work to qualify. For specific rules, log on to www.ssa.gov/pubs/10029.html#part2.

Deciding to Apply

Unfortunately, many people often associate a stigma with SSDI. But, worrying about others’ perceptions is the last thing immune-mediated patients should think about when faced with the inability or reduced ability to work and mounting bills. Even if individuals are able to work part time, they still may be eligible for SSDI if their earnings average less than the amount set by annual federal guidelines. While this amount changes each year, in 2010, individuals had to earn less than $1,000 per month to qualify for SSDI benefits.

As soon as individuals become disabled, they should apply for SSDI, especially since it takes, on average, three to five months for the government to process each application. In fact, delay in applying means the amount of benefits for which they are eligible could be less than they are entitled to.

How to Apply

Individuals who are 18 and older can apply online for SSDI at www.socialsecurity.gov/applyfordisability. There are many advantages to applying online, including starting a claim immediately, applying from the convenience of home and/or any computer, and avoiding trips to the Social Security Administration offices. However, individuals who would rather apply in person can call (800) 772-1213 (for the hearing) or (800) 325-0778 (for the deaf or hard of hearing) to make an appointment at an office near them.

Before applying, applicants need to gather the following information: Social Security number; birth certificate; names, addresses and phone numbers of doctors, caseworkers, hospitals and clinics the patient went to, as well as dates of visits; names and dosages of medicines being taken; medical records from doctors, therapists, hospitals, etc., in the patient’s possession; lab and test results; a work history; and a copy of the most recent W-2 Form or federal tax return for the past year (if self-employed). Two other forms also will need to be filled out: One collects information about the patient’s medical condition and how it affects their ability to work; the other gives healthcare professionals who have treated the patient permission to send the government information about the patient’s medical condition.

A recent article in Patient Service Inc.’s (PSI) publication, Advocate, also recommended that patients take some other preliminary steps prior to applying for SSDI. The first is to consult with
Did You Know?

their physician to assess their need for benefits. In addition, patients should ask their physicians to document their work restrictions in detail and provide appropriate supporting clinical data. Patients receiving intravenous immune globulin (IVIG) treatments should document how often they receive treatments, how long it takes to administer them, any side effects and their duration after being infused, and the fatigue they experience the week leading up to their next infusion. Last, they should document the frequency, severity and duration of infections that continue to occur, despite compliance with prescribed therapy, and how often those infections and their infusions cause them to miss work. A statement from their physician concerning their problem with maintaining regular work attendance also is helpful.

As soon as individuals become disabled, they should apply for SSDI, especially since it takes, on average, three to five months for the government to process each application.

After the Application

Government doctors and disability experts will consider all the information submitted in an application to make a decision to grant or deny SSDI benefits. To decide, a five-step process is used in which the following questions are answered: 1) Is the individual working? 2) Is the medical condition “severe”? 3) Is the medical condition on the list of impairments that describes those conditions that are so severe that an individual is deemed automatically disabled as defined by law? 4) Can the individual work as they did before? 5) Can the individual do any other type of work? In some instances, the Social Security Administration will determine it needs more medical information. In that case, it will ask the individual to go for a special examination either with their own or another doctor, and the agency will pay for both the exam and related travel costs.

If the application is approved, the individual will receive a letter that shows the amount of the benefit. SSDI benefits begin in the sixth full month after approval. For instance, if approved on January 15, the patient’s first payment will be for the month of July, but that won’t actually be paid until August, since benefits are paid the month following the month for which they can work and still receive benefits for any month their earnings do not exceed the federal guideline.

It is not unusual for an initial application to be denied, and many are later approved, according to the article by PSI. If the application is denied, a letter will be sent explaining why and how to appeal the decision. An appeal must be filed within 60 days of the date the disapproval letter was received.

It’s There for a Reason

Nobody expects to have to file for disability; instead, most people expect to be able to work until retirement. However, if they become disabled, they have earned the right to apply for SSDI benefits since all workers pay into the Social Security system. All that is required is that they meet the requirements that deem them eligible and follow the appropriate steps to apply.

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

Sources

An Overview of Immune Globulin Dosing

How much IG to prescribe differs for each individual based on a variety of clinical and non-clinical factors, as well as physician discretion.

By Kris McFalls
Immune globulin (IG) is not a one-size-fits-all drug. Prescribing the proper dose to administer can be difficult and is dependent on several factors, the most important of which is a clinical assessment. However, other non-clinical variables also are important. Understanding all of the factors that determine proper IG dosing will ensure the patient is being prescribed the amount of the drug that will provide them with the most effective treatment.

**Considering the Disease**

When prescribing IG, the first clinical consideration is the patient’s disease. IG was initially prescribed to treat primary immune deficiency diseases (PIDD) and immune thrombocytopenic purpura (ITP). Over time, IG also has proven to be an effective treatment for numerous inflammatory and immune-mediated diseases affecting the neuromuscular system. Current IG products collectively carry Food and Drug Administration (FDA)-approved indications for PIDD, ITP, Kawasaki disease (KD), chronic inflammatory demyelinating polyneuropathy (CIDP) and chronic B-cell lymphocytic leukemia (CLL). Although there are other FDA-approved indications for intravenous IG (IVIG), the products used to treat those indications are no longer on the market.

Dosing recommendations for FDA-approved indications for each IG product are included in its package insert (PI). These recommendations are based on the results of individual clinical trials, and they change only when a new clinical trial is conducted that results in positive outcomes for new dosing guidelines. Yet, as physicians learn more about diseases and patients’ responses to treatment, the amount of IG prescribed does vary from patient to patient and can differ from manufacturer PI recommendations. In addition, physicians also can prescribe IG for off-label indications, but by law, dosing guidelines for off-label indications cannot be included on the PI. Instead, physicians must use peer-reviewed literature, clinical observations and their best judgment when deciding on the proper dose to prescribe for off-label indications. Having so many dynamic variables makes it easy to see why there may be some confusion and inconsistencies in IG treatments.

**Empirically Measuring Effectiveness**

PIDD associated with hypogammaglobulinemia (low immunoglobulin [IgG] levels) is an example of how IG replacement therapy and dosing have changed over time. It was first treated with intramuscular injections of IG, which were not only extremely painful for patients, but also proved difficult to achieve high enough serum IgG levels to adequately prevent infections. As a result, IVIG became the preferred route of administration in the early 1980s.

When prescribing IG, the first clinical consideration is the patient’s disease.

Initially, IVIG replacement therapy for PIDD with low IgG levels was dosed at 100 to 200 mg/kg. In part to assess whether the dose was working, great reliance was placed on trough levels (the amount of serum IgG concentration immediately preceding the next infusion) as indicators of effectiveness. It was thought that an adequate trough level was roughly 500 mg/dL. However, it was later learned that not all patients have the same response when maintaining trough levels in this range. In addition, although trough levels can be used as a guide, a sufficient trough level to prevent serious bacterial infections for all types of patients has not yet been established. According to recent research published in *Clinical Immunology*, “PIDD patients receiving IVIG therapy and experiencing pneumonia are likely to be helped by increasing the IgG trough levels to at least the mid-normal range of IgG. … [And,] meta-analysis provides evidence that pneumonia risk can be progressively reduced by higher trough IgG levels up to at least 1000 mg/dL.”

While trough levels can be a useful guide for PIDD associated with low IgG levels, the same cannot be said for patients with immune-mediated diseases affecting the neuromuscular system. These disorders are treated with...
IG, but the diagnosis is not based on IgG serum levels. Therefore, using serum IgG trough levels as a benchmark is not a viable option. Complicating matters is the fact that scientists don’t fully understand how IG works in CIDP and other immune-mediated neuromuscular diseases such as multifocal motor neuropathy (MMN), myasthenia gravis (MG) and myositis. For these diseases, IG is not a replacement therapy as it is for PIDD. Instead, it is an immune-modulating therapy, meaning it adjusts the body’s innate immune response that has gone awry.

Currently, CIDP is the only neuromuscular indication that is FDA-approved to be treated with IG. The generally accepted dosing protocol for CIDP treatment with IG was determined through clinical trials. But still more studies are needed to gather data to establish more universally accepted standard protocols.

Dosing for CIDP can vary from the PI and should be based on individual response to therapy. Many insurance policies carry a clause in the reauthorization process that requires patients, once stabilized by IG, to try a lower dose of IG to see if maintenance can be attained at a lower cost. Many physicians, trying to optimize treatment and at the same time limit the cost for patients, also may take a similar approach. As with PIDD, the dose needs to be tailored to the individual patient’s needs using the clinical findings as a guide. For instance, before FDA approval of

Dosing Recommendations
For All U.S.-Approved Immune Globulin Products

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Indication</th>
<th>Administration Route</th>
<th>Dosing Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carimune NF</td>
<td>CSL Behring</td>
<td>PIDD</td>
<td>IV</td>
<td>0.4 to 0.8 g/kg every 3 to 4 weeks</td>
</tr>
<tr>
<td>Flebogamma DIF 5%</td>
<td>Grifols</td>
<td>ITP</td>
<td>IV</td>
<td>0.4 g/kg over 2 to 5 consecutive days</td>
</tr>
<tr>
<td>Flebogamma DIF 10%</td>
<td>Grifols</td>
<td>PIDD</td>
<td>IV</td>
<td>300 to 600 mg/kg every 3 to 4 weeks</td>
</tr>
<tr>
<td>Gammagard S/D</td>
<td>Baxter Healthcare</td>
<td>PIDD</td>
<td>IV</td>
<td>300 to 600 mg/kg every 3 to 4 weeks</td>
</tr>
<tr>
<td>Gammagard Liquid</td>
<td>Baxter Healthcare</td>
<td>PIDD</td>
<td>IV</td>
<td>400 mg/kg every 3 to 4 weeks</td>
</tr>
<tr>
<td>Gammagard Liquid</td>
<td>Baxter Healthcare</td>
<td>CLL</td>
<td>IV</td>
<td>400 mg/kg every 3 to 4 weeks</td>
</tr>
<tr>
<td>Gammaplex</td>
<td>Bio Products Laboratory</td>
<td>PIDD</td>
<td>IV</td>
<td>400 mg/kg every 3 to 4 weeks</td>
</tr>
<tr>
<td>Gamunex-C</td>
<td>Talecris Biotherapeutics</td>
<td>PIDD</td>
<td>SC</td>
<td>400 mg/kg every 3 to 4 weeks</td>
</tr>
<tr>
<td>Hizentra</td>
<td>CSL Behring</td>
<td>PIDD</td>
<td>SC</td>
<td>2 g/kg every 3 weeks</td>
</tr>
<tr>
<td>Octagam 5%</td>
<td>Octapharma</td>
<td>PIDD</td>
<td>IV</td>
<td>Loading dose: 2g/kg Maintenance dose: 1g/kg every 3 weeks</td>
</tr>
<tr>
<td>Privigen</td>
<td>CSL Behring</td>
<td>ITP</td>
<td>IV</td>
<td>1g/kg IV daily for 2 consecutive days (2g/kg total)</td>
</tr>
<tr>
<td>Vivaglobin</td>
<td>CSL Behring</td>
<td>PIDD</td>
<td>SC</td>
<td>1.37 x IVIG dose (in grams)/No. of weeks between IVIG doses</td>
</tr>
</tbody>
</table>

Key: CLL = chronic B-cell lymphocytic leukemia, ITP = immune thrombocytopenic purpura, IV = intravenous, IVIG = intravenous immune globulin, PIDD = primary immune deficiency disease, SC = subcutaneous immune globulin

Note: All information taken from product package inserts
Gamunex to treat CIDP, many experienced clinicians started treatment using a loading dose of 2 g/kg over two to five days. The patient was then observed and asked to immediately report any signs of recurrence. Once symptoms started to reappear, a maintenance dose of 1 g/kg was given. The patient was again observed for signs of returned symptoms. That interval of time between the infusion and the first sign of returned symptoms became the interval for maintenance therapy. For many patients, that interval was between two and four weeks.

Research presented in the *Journal of the Peripheral Nervous System* has shown that dose frequency, once established, should not be changed. In addition, the research shows that “lower dose treatment is not associated with shorter intervals between courses, and lowest effective dose is independent of weight and disease duration.” Additional studies are needed to establish standard protocols for CIDP patients. In the meantime, dosing for off-label immune-mediated indications will continue to rely on experienced physicians and peer-reviewed data to establish standard-of-care protocols.

**Whether or not an indication is FDA-approved, physicians have the option to utilize professional judgment in order to adjust the dose and/or use a particular medication for an off-label indication.**

Infusion and the first sign of returned symptoms became the interval for maintenance therapy. For many patients, that interval was between two and four weeks.

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Too Little or Too Much Can Make a Difference

Clinical trials and scientific studies help to establish maximum and minimum IG dosing standards. The clinical effects of IG dosing can have significant consequences. Knowing how much is too much and how little is too little is crucial for maximizing health outcomes and minimizing costs. Yet, because the amount of IG to prescribe can be both disease- and patient-specific, there are no clear-cut universal boundaries.

It is not well-known how much IG is too much. When treating PIDD, it is believed that after a certain amount, there is no medical benefit to increasing the dose. Currently, there are not enough studies to determine exactly what that amount is. In general, however, the goal is to prescribe enough IG to prevent serious breakthrough bacterial infections from occurring. When treating other diseases, the amount of IG to prescribe is even less clear. Using more IG than is medically necessary may result in increased costs for all, increased risk of fluid volume overload, increased risk of side effects (especially if high doses increase the propensity to speed up the infusion), and an artificially increased need for the limited natural resources needed to make IG.

No matter what the disease state, treating with too little
IG results in ineffective treatment and a poor clinical response. Because IG protocols frequently lack universal standardization, undertreatment may be more common than is realized. Undertreating may cause the patient and physician to mistakenly believe treatment is not working; cause breakthrough infections or symptoms that result in more expensive hospitalizations, treatments, testing and increased disability; decrease productivity for employers of patients; increase workload for the treating physician; and decrease quality of life for the patient.

Many factors can lead to undertreating patients. Some of the more common problems include:

• Insurance policies that attempt to standardize treatments without taking into account the treating physician’s ability to base IG dose on the clinical outcome of the patient
• Prescribers and providers not staying current on the latest research
• Limited research funding for rare diseases treated with IG
• Product shortages resulting in rationing of supplies
• Patient tolerance to treatment
• Patient compliance

Other factors also can affect dosing of IG. Specifically, the vial sizes of each product can play a small role in tailoring the dose. Each manufacturer produces a limited number of vial size options for each product, and the dose is based on the weight of the patient. If a patient’s weight requires an odd-sized dose that does not evenly match up with the vial size, the dose is generally rounded up to the nearest size available.

Clinical trials and scientific studies help to establish maximum and minimum IG dosing standards.

Because a patient’s IG dose is directly related to their body weight, obesity is one variable that may warrant a deviation from the dosing formula. Fat tissue contains proportionally more fluid than other tissues. In addition, IG has very little distribution into the fluid in fat tissue. Therefore, the dose should be adjusted down for a person when fat is a larger part of their overall body weight. Studies suggest the dose for patients with a body mass index greater than 30 kg/m² be adjusted to correlate with the ideal body weight rather than the actual body weight.³

Maximizing Patient Outcomes

IG dosing is unique and complicated. Many variables have to be considered to ensure patients get the full benefit of this expensive, lifesaving treatment. Much more research is needed to determine adequate dosing. In the meantime, following dosing recommendations and staying educated is the best way to maximize patient outcomes. ■

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

References

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Weight-Loss Strategies for the Mobility Impaired

Even individuals who find it difficult to move due to fatigue and/or disability can achieve weight-loss success by following some simple steps.

By Jill Weisenberger, MS, RD, CDE

Losing weight is tough for anyone, but it seems like a Herculean task for individuals who struggle to move around. Jogging around the block or joining a dance class at the gym to blast through extra calories is out of the question. For some, even everyday household chores are difficult. Preparing a healthful meal, for example, without the strength to cut through vegetables or the stamina to stand over a hot stove are clear hurdles to weight loss.
Such hurdles, however, are not insurmountable. Lots of planning and some simple strategies can make the elusive weight loss a reality. Here are some steps to success.

**List Personal Reasons to Lose Weight**

Because he was “running out of wardrobe” and tired of feeling short-winded, Walter Luebke, 77, of Elkhart, Ind., decided to lose weight. And, 63-year-old Nancy Wilcosky of Latrobe, Pa., changed her diet in support of her daughter who recently had weight-loss surgery. Luebke walks with a cane, and Wilcosky shuffles between walker and wheelchair because of polio syndrome. Both knew their physical limitations could hold them back, but with clear, strong motives and determination, they have both been successful. Luebke lost 25 pounds and Wilcosky is 52 pounds lighter and still dropping.

Each person’s motives to shed pounds are different. Chances for success increase dramatically when those motives are clearly defined and put in writing. Motivation waxes and wanes, so having a list to refer back to — a list to remind the individual why he or she is working so hard — helps reignite a dwindling fire.

Common reasons to lose weight are to look better, feel better, have less physical pain or discomfort, improve immune function, decrease chronic disease risk, improve chronic diseases like diabetes and heart disease, lessen heartburn, improve mobility and better enjoy social activities and family gatherings. Whatever they are, writing them down both adds a level of importance and serves as a reminder.

**Research shows that even savvy dieters eat more when large servings and lots of variety are in front of them.**

Be Accountable

Food records work. A large study from Kaiser Permanente’s Center for Health Research found that the average weight loss of nearly 1,700 participants in their weight-loss program was about 13 pounds in six months. Individuals who kept daily food records lost twice as much weight as those who kept no records.

“I never realized how much I was eating,” says 68-year-old Arlene Serkin of Bethpage, N.Y. On the advice of a registered dietitian, Serkin records everything she eats and drinks, the time she consumes them, what her mood is and how hungry she feels according to a 10-point scale. Keeping a food record keeps her accountable and honest with herself, she explains.

Serkin, who jests that she’s put together with glue because of several health issues, including osteoarthritis and vascular disease, allowed herself to substitute physical activity with food when her ailments became severe enough that her mobility was hugely limited. Now with her food record, medically supervised physical activity, stronger determination and a registered dietitian’s help, Serkin has lost 23 pounds and is still slimming down.

Wilcosky finds accountability in her daughter and a support group they attend together. Other dieters swap food records with a buddy once weekly or simply discuss successes and problems with a friend. The type of accountability is less important than just sticking with it.

**Count Calories**

The only way to lose weight is to burn more calories than you eat. Unfortunately, individuals with limited mobility just don’t run through calories like they would if
they were physically active. Thus, every calorie counts. Figure that cutting 500 calories each day will net approximately one pound lost each week. Cutting 250 calories leads to about one-half pound lost weekly. Food labels, calorie-counting books like The CalorieKing Calorie, Fat & Carbohydrate Counter and websites such as MyPyramid.gov provide most of the information needed. MyPyramid.gov also can help you determine your appropriate calorie level. The key will be estimating portions correctly. See Avoid Portion Distortion below.

Balance the Plate
Toss out all restrictive diet plans. It’s easy to fall for the newest, fastest, coolest weight-loss trend with lists of rules and taboo foods, but weight lost this way creeps back — often with interest — and doesn’t provide optimal nutrition. Each day, Luebke set out to eat a variety of foods from each food group. He counted his grains, milk, vegetables and servings from each of the other groups. No fads, just balanced eating with smaller portions.

A healthful way to balance your diet is to make two-thirds or more of your food vegetables, fruits, whole grains and beans and only one-third or less animal protein. Plan at least three food groups per meal making sure at least one is high in fiber and one is rich in protein. Be especially liberal with non-starchy vegetables like broccoli, green beans, tomatoes, carrots and cauliflower since they are packed with nutrients, very filling and low in calories. Bulking up the plate and snacks with vegetables is a sure way to tame hunger. Learn more about feeling full on fewer calories and find tasty recipes at the American Institute for Cancer Research website at www.aicr.org and in the book, The Volumetrics Eating Plan by Barbara Rolls, PhD (HarperCollins, 2005).

Avoid Portion Distortion
There’s no doubt about it: Typical restaurant and home portions are simply too big to support a healthy weight. Research shows that even savvy dieters eat more when large servings and lots of variety are in front of them. What’s more, most people significantly underestimate the amount they consume. Serkin’s nutritionist, New York-based registered dietitian Susan Weiner, urges her clients to use a kitchen scale and measuring cups to get a handle on appropriate portion sizes. “If you can’t burn a lot of calories through movement,” Weiner says, “you must monitor your portions.”

We eat with our eyes — not just our stomachs. The brain is tricked into being more satisfied with smaller portions if the food is served on smaller plates, according to research from Cornell University.2 Trade in dinner plates and large bowls for luncheon plates and cup-sized bowls. Wilcosky has found success with this method. “I’m satisfying my eye-hunger,” she says. Try this trick with flatware and serving utensils too. Eating ice cream with a baby spoon, for example, gives you more tastes from a single scoop. Avoid second and third helpings by keeping serving bowls off the table. Fill your plate from the kitchen counter, but eat at the table. Or, put extra food away before sitting down to eat. Another strategy, suggests Wilcosky, is to prepare only what you and your family will eat at one meal.

We sip about 20 percent of our calories each day, but it’s easy to ignore those liquid calories.

Avoid second and third helpings by keeping serving bowls off the table. Fill your plate from the kitchen counter, but eat at the table. Or, put extra food away before sitting down to eat. Another strategy, suggests Wilcosky, is to prepare only what you and your family will eat at one meal.

Rethink That Drink
We sip about 20 percent of our calories each day,3 but it’s easy to ignore those liquid calories. Sodas, juices, sweet tea...
and fancy coffee drinks don’t fill us up the way food does. Replacing some or all of those caloric beverages with water and other zero-calorie drinks will trim calories and your waistline. Be careful to keep drinking throughout the day, however. Even slight dehydration can sap your energy, making you less inclined to prepare a healthful meal.

**Make Smart Substitutions**

“Frying is out of the vocabulary,” says Wilcosky, who now favors the oven over the fry pan. Baking is more healthful and saves a lot of calories. Reduced-fat cheese in place of the regular variety also saves calories, and less-saturated fat is a bonus. For dessert, Wilcosky satisfies her sweet tooth with frozen grapes or pureed and frozen melon. It tastes like sherbet, she says. For sensible swaps in recipes, pick up a low-fat cookbook at your library.

**Treat Yourself**

Swearing off favorite foods is a recipe for diet failure because the forbidden item becomes even more tempting. It’s best instead to plan treats in small quantities. Buy a single bakery cookie instead of a box of cookies, for example. The key: small portions and only now and then.

**Plan Ahead**

Lifestyle changes rarely happen without a good plan and a backup plan. It’s important for dieters to recognize what is holding them back and to make a plan to overcome it. If the goal is to eat more vegetables, for example, the individual must plan how he or she will add vegetables. What’s required? For some, it will mean learning to cook vegetables, preparing a salad that can last three or four days, purchasing vegetables from the grocery, exploring frozen options or visiting a restaurant that offers several vegetable choices. Serkin recognized that her diet lacked vegetables, but used the excuse that they were too difficult for her to cut. Now she plans ahead and has her supermarket pre-cut vegetables for her. They prepare and repackage whatever she wants whether it’s one zucchini or several. And, they do it for no additional charge. Success came with a plan and taking action.

Maryland-based registered dietitian and certified diabetes educator Jamie Futterman suggests that dieters with extreme fatigue look for patterns in their day. The individual should take advantage of those times of the day when he or she feels the most energetic, she suggests. Those times are the opportunities to prepare a meal or engage in physical activity as able and permitted.

For more planning-ahead ideas and suggestions for adapting your kitchen, look to *The Essential Arthritis Cookbook: Kitchen Basics for People with Arthritis, Fibromyalgia and Other Chronic Pain and Fatigue* (Appletree Press).

**Swearing off favorite foods is a recipe for diet failure because the forbidden item becomes even more tempting.**

**Modify Exercise**

There are plenty of exercise options for people with limited mobility; however, such individuals must use extra caution and exercise only under medical supervision. Several of Futterman’s clients found success in pool walking, and Weiner recommends seated exercises with weights or resistance bands if medically safe. Collage Video (www.collagevideo.com) offers a variety of seated and specialty exercise DVDs, including chair dancing.

**Putting It All Together**

Examples of meaningful diet and exercise lifestyle changes shared by Wilcosky, Luebke and Serkin are proof that taking simple steps can lead to weight-loss success. All it takes is putting all of these steps together to get optimal weight-loss results.

**JILL WEISENBERGER** is a registered dietitian, certified diabetes educator, nutrition and health writer, speaker, spokesperson and culinary expert based in southeast Virginia. Her website, All That’s Nutrition, can be accessed at www.allthatsnutrition.com.

**References**

Understanding and Treating Multifocal Motor Neuropathy

This rare disease is typically diagnosed late or misdiagnosed, resulting in permanent disability, but patients still respond to treatment.

By Matthew David Hansen, DPT, MPT, BSPTS

Little is known or understood by most people about a great many immune and autoimmune diseases. Medical conditions such as diabetes, cerebral palsy, hemophilia and muscular dystrophy at least carry an air of familiarity. But, then there are those other diseases with alien-sounding names that are rare, as is the case with multifocal motor neuropathy (MMN).

MMN occurs in approximately one in 100,000 people, with men being affected about three times as often as women. Yet, while this is a very rare disease, understanding what the disease is and how to diagnose and treat it can mean the difference between MMN patients being cured or successfully managed, or permanently disabled.

What Is MMN?

The National Institute of Neurological Disorders and Stroke defines MMN as “a [typically slowly] progressive muscle disorder characterized by muscle weakness in the hands, with difference from one side of the body to the other in the specific muscles involved.” Symptoms frequently include general fatigue, muscle cramping and fasciculation (twitching or involuntary contractions) and, less likely, muscle atrophy (wasting). The exact pathogenesis (or cause) of the disease is not understood; however, it is now generally accepted that the condition results from an autoimmune disorder. Specifically, it appears that the body’s immune system misidentifies markers on the body’s own nerve cells as foreign, and mounts an attack. Studies have demonstrated injury and/or destruction to the peripheral motor nerve fibers and to the myelin sheath (a fatty covering that protects nerve fibers and allows for a signal to be relayed quickly), resulting in slowed or blocked nerve conduction. Weakness usually follows the distribution of individual peripheral nerves, contributing to the clinical signs of weakness on one side of the body and not the other, or mixed weakness in the same extremity.

Although mild abnormalities are often seen in the sensory nerve fibers of MMN patients as well, sensation is almost never affected. The lack of noticeable sensory involvement with MMN is one of the distinguishing symptoms from...
other progressive neuropathies, such as chronic inflammatory demyelinating polyneuropathy (CIDP), Guillain-Barré syndrome and Lewis-Sumner syndrome (multifocal acquired demyelinating sensory and motor neuropathy [MADSAM]). It is not unusual for MMN also to be initially mistaken for the ultimately fatal condition of amyotrophic lateral sclerosis (commonly referred to as ALS or Lou Gehrig’s disease) or other disorders. Needless to say, the diagnostic process can be a lengthy and frustrating one for individuals with MMN, while the “duration of disease prior to diagnosis ranges from several months to more than 15 years.”

The Story of Tony Marsalisi

Tony Marsalisi experienced this lengthy diagnostic process firsthand. Marsalisi is a private business owner who first saw a doctor in the fall of 2001 with complaints of unexplained difficulty writing. According to him, “Everything else seemed fairly normal; no strength problems or mobility issues. The doctor pretty much blew me off. I was too young to have anything major wrong with me (33 years old at the time).” After a year of persisting symptoms, Marsalisi visited another doctor and was referred to a neurologist who suspected multiple sclerosis and who ordered an MRI to be performed. When the results came back negative, Marsalisi was sent home again without concern.

Three years later in 2005, Marsalisi began noticing strength differences between his right and left arm. This time when he saw a neurologist, he was diagnosed with “writer’s cramp,” and Botox injections were recommended to “loosen the muscles” in his wrist/forearm. Not trusting the diagnosis, Marsalisi refused the treatments. When pain and numbness isolated to his right arm, wrist and hand developed in the spring of 2006, another MRI was ordered, this time revealing herniated cervical disks at the C5 and C6 levels. After being told that spinal fusion surgery would cure his problems, Marsalisi optimistically consented. Unfortunately, the operation did not cure the problem. Marsalisi describes the whole diagnosis process as “very frustrating.” “I pretty much dealt with it by myself in the beginning due to the lack of severity

**MMN occurs in approximately one in 100,000 people, with men being affected about three times as often as women.**
of my symptoms,” he says. “They were very hard to explain and, with no pain, people don’t take it very serious; they make you feel like it’s in your head.”

During the latter part of 2007, Marsalisi began having problems in his left thumb and wrist. That’s when he decided to enlist the assistance of his wife, whom he describes as being “a lot more demanding [of answers] than I am.” Together, they made an appointment to see yet another neurologist, who ordered yet another MRI. After multiple sclerosis was ruled out a second time, the neurologist referred Marsalisi to an ALS specialist who, to the couple’s dismay, told them that Marsalisi likely had some variation of ALS, Kennedy’s disease or MMN. After multiple sclerosis was ruled out a second time, the neurologist referred Marsalisi to an ALS specialist who, to the couple’s dismay, told them that Marsalisi likely had some variation of ALS, Kennedy’s disease or MMN. During the latter part of 2007, Marsalisi began having problems in his left thumb and wrist. That’s when he decided to enlist the assistance of his wife, whom he describes as being “a lot more demanding [of answers] than I am.” Together, they made an appointment to see yet another neurologist, who ordered yet another MRI. After multiple sclerosis was ruled out a second time, the neurologist referred Marsalisi to an ALS specialist who, to the couple’s dismay, told them that Marsalisi likely had some variation of ALS, Kennedy’s disease or MMN. After multiple sclerosis was ruled out a second time, the neurologist referred Marsalisi to an ALS specialist who, to the couple’s dismay, told them that Marsalisi likely had some variation of ALS, Kennedy’s disease or MMN.

There also are other things to look for. The mean age of onset for MMN is 40 years old, with 80 percent of patients falling in the age range of 20 to 50. Deep tendon reflexes may be absent (especially in affected limbs) or normal (reflexes may be brisk early in the course). And, muscle tone may be decreased or normal (no clonus, spasticity or pathologic reflexes [e.g., Hoffman or Babinski] are noted). The important thing to remember is that, in the face of real and persistent symptoms, one should not stop looking for an accurate medical explanation.

Treating MMN

Once MMN is diagnosed, most patients will require some form of treatment. The first choice in therapy tends to be IVIG in an attempt to depress the overactivity of the immune response. The Johns Hopkins Medical Institution’s Department of Neurology (JHMI) asserts that IVIG:

“… has been found to be effective in patients reported in the literature with 80% of 170 MMN patients treated with IVIg having shown improvement. … Beneficial effects from IVIg begin within days, and sometimes hours after the infusion, peak at an average of 2 weeks and the effect lasts from several weeks to months. Most patients require periodic maintenance doses of IVIg. The dose and frequency of IVIg administration needs to be individualized depending on the length of benefits received, which appears to vary between patients, but is relatively consistent in individual patients.”

A recent study conducted at the Rudolf Magnus Institute of Neuroscience at the University Medical Center in Utrecht, Netherlands, reports that 94 percent of the patients included in the study responded positively to IVI G therapy. A separate study, conducted at the same institute, suggests that the rapid clinical improvement in strength following an IVIG infusion may be due to the immunoglobulin interfering with antibody binding to gangliosides or preventing access to the antigen (the substance that stimulates an immune response), and not to structural remyelination of the nerve axons (which typically takes much longer). IG antibodies that bind to the ganglioside GM1 could be detected in approximately 50 percent of all MMN patients.

The first choice in therapy tends to be IVIG in an attempt to depress the overactivity of the immune response.

Diagnosing MMN

With upwards of 30,000 people in the United States living with MMN, Marsalisi’s experience of delayed and misdiagnosis is not unique. It can be difficult for a doctor to sort through a host of differential diagnoses; most general practitioners have never seen a case of MMN, and it’s likely that many neurologists have not either. Nevertheless, besides those signs and symptoms already mentioned, there are several other clues that may help point to MMN. For example, a positive blood test for antibodies to ganglioside GM1 (a fatty substance found within nerve cells) is supportive of MMN, particularly when concentrations are elevated. However, it should be noted that a-GM1 is also implicated in Guillain-Barré syndrome and motor neuron disease. It also should be noted that the lack of a-GM1 does not rule out the diagnosis of MMN.

There also are other things to look for. The mean age of onset for MMN is 40 years old, with 80 percent of patients falling in the age range of 20 to 50. Deep tendon reflexes may be absent (especially in affected limbs) or normal (reflexes may be brisk early in the course). And, muscle tone may be decreased or normal (no clonus, spasticity or pathologic reflexes [e.g., Hoffman or Babinski] are noted). The important thing to remember is that, in the face of real and persistent symptoms, one should not stop looking for an accurate medical explanation.

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Although IVIG is the preferred treatment for MMN, it is not the only one. JHMI indicates that cyclophosphamide, a drug used to treat various types of cancer (taken orally or intravenously) "is perhaps the only immunosuppressive agent (besides IVlg) that has shown to have consistent efficacy (50%) in the treatment of multifocal motor neuropathy with 20 of 40 cases showing improvement." The drug is not routinely used, however, because of associated toxic side effects, including increased risk of infections, bone marrow suppression, nausea and vomiting, an increased risk of hematological malignancies and other concerning conditions. JHMI reports initial positive results for the use of azathioprine (an immunosuppressant drug) and interferon beta-1a (frequently used in the care of multiple sclerosis); however, study numbers are too small to make any conclusions about their effectiveness or side effects in the MMN population. The usefulness of corticosteroids and plasmapheresis has been limited and, in fact, may worsen the symptoms of some patients after treatment.

Prognosis of MMN

Early treatment of MMN usually leads to enough of a reduction, if not a resolution, of symptoms so that permanent disability is avoided. Still, slow progression of symptoms over the years, which may lead to significant disability, is not unusual and, unfortunately, many patients aren’t diagnosed with MMN soon after they begin symptoms. On the other hand, the disease may be responsive to treatment even after many years of manifestation. Death as a consequence of MMN is extremely rare, and most patients are able to remain independent with indoor and outdoor activities, with up to 94 percent remaining employed.

In Marsalisi’s case, he experienced some immediate improvement since beginning IVIG treatments nearly three years ago and has since “leveled off — no worse, no better.” He continues to run the day-to-day operations of his business (scheduling, ordering, bookkeeping, etc.), but he is not responsible for the most physical work. Time missed from the job during infusions and difficulty writing are the most direct effects on Marsalisi’s livelihood. He is quick to note that his employees are very understanding and supportive of his absence, and he explains that he has had to train himself to write with his left hand, “which still leaves a lot to be desired.” Other fine motor skills also can be a struggle.

Outside of work, Marsalisi notes that MMN is a hard disease to explain to people. “How it affects you and how the treatments help is very confusing, and seeing as no one has ever heard of it, they don’t seem to understand [the] difficulties you have to deal with on a daily basis. My favorite line is: ‘You look good.’”

The gratitude that Marsalisi feels for the people in his life shines through his words. He thanks his wife for her support, especially now that he is receiving his infusions at home; he thanks his three teenage sons, who joke with him about his condition, calling it his “kunk” because he occasionally drops things or misses a short putt when they’re playing golf; he thanks the cancer patients at the infusion clinic and the perspective that visiting with them gives him; and he thanks his IG nurse for her flexibility and consistency.

A Rare, But Important-to-Understand Disease

MMN is but one of many diseases that society knows little about, making it a tough disease to diagnose and an even tougher one for the patient to live with — especially when not diagnosed early enough to prevent permanent disability. Even though it affects only a small population, increased familiarity with it will surely advance the likelihood of earlier diagnoses, leading to improved care and outcomes.

MATTHEW DAVID HANSEN, DPT, MPT, BSPTS, is a practicing physical therapist in Utah, and president of a healthcare consulting and fitness product company, SOMA Health, LLC. The company’s latest product, the Freedom2Move exercise program and video series, was inspired by an IG Living Readers Teleconference. Matt completed his formal education at the University of Utah in Salt Lake City.

References

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.

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\(^1\) 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, rigors, 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
Immune Globulin Intravenous (Human) Flebogamma® 10% DIF
For intravenous use only
RX only

BRIEF SUMMARY
CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE
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.

DOSEAGE AND ADMINISTRATION
The recommended dose of Flebogamma® 10% DIF for patients with PI is 300 to 600 mg/kg body weight (3.0 to 6.0 mL/kg), administered every 3 to 4 weeks.

The infusion of Flebogamma® 10% DIF should be initiated at a rate of 0.01 mL/kg body weight/minute (1.0 mg/kg/minute). If there are no adverse drug reactions, the infusion rate for subsequent infusions can be slowly increased to the 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

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- 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 osmolality 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 hyperviscosity. 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, because of the potentially increased risk of thrombosis. If signs and/or symptoms of hemolysis are present after an infusion of Flebogamma® 10% DIF, perform appropriate 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. TRALI may be managed using oxygen therapy with adequate ventilatory support.

Infusion Reactions
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 (see Dosage and Administration [2.3]).

Transmissible Infectious Agents
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. All infections suspected by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to Britisow Biologics at 1-888-474-3657. Before prescribing or administering Flebogamma® 10% DIF, the physician should discuss the risks and benefits of its use with the patient (see Patient Counseling Information [17]).

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, markedly high triacylglycerols (triglycerides), or monoclonal gammapathies, because of the potentially increased risk of thrombosis.
- If signs and/or symptoms of hemolysis are present after an infusion of Flebogamma® 10% DIF, perform appropriate 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.

Interference with Laboratory Tests
After infusion of IgG, the transitory rise of the various passively transmitted antibodies in the patient’s blood may yield positive serological results, thus the potential for misleading interpretation. Passive transmission of antibodies to erythrocyte antigens (e.g., A, B, and D) may cause a positive direct or indirect antiglobulin (Coombs’ test) result.

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, rigors, 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 (antihistactic, antihistiminic, or antienemic 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/chees pain/headache; and chills/tachycardia). Three subjects experienced four serious non-related AEs (drug abuse/depression; hernia; and sinirius). Forty-five (96%) 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 48 in 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>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>

Hemolysis
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 (5-6). Delayed hemolytic anaemia may develop subsequent to Flebogamma® 10% DIF therapy due to enhanced RBC sequestration (7), and acute hemolysis, consistent with intravascular hemolysis, has been reported. Monitor patients for clinical signs and symptoms of hemolysis. If signs and/or symptoms of hemolysis are present after Flebogamma® 10% DIF infusion, perform appropriate confirmatory laboratory testing (see Patient Counseling Information [17]).
Table 3 lists the AEs that occurred in greater than 5% of subjects during a Flebogamma® 10% DIF infusion or within 72 hours after the end of infusion, irrespective of causality.

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Subjects (%) (N=46)</th>
<th>Infusions (%) (N=601)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>28 (61%)</td>
<td>71 (12%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>17 (37%)</td>
<td>27 (5%)</td>
</tr>
<tr>
<td>Rigors</td>
<td>17 (37%)</td>
<td>37 (6%)</td>
</tr>
<tr>
<td>Back pain</td>
<td>13 (28%)</td>
<td>29 (5%)</td>
</tr>
<tr>
<td>Cough or Productive cough</td>
<td>12 (26%)</td>
<td>5 (1%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>12 (26%)</td>
<td>8 (1%)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>10 (22%)</td>
<td>13 (2%)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>10 (22%)</td>
<td>19 (3%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>9 (20%)</td>
<td>17 (3%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>8 (17%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Infusion site reaction</td>
<td>8 (17%)</td>
<td>8 (1%)</td>
</tr>
<tr>
<td>Pharyngolaryngeal pain</td>
<td>7 (15%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>7 (15%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Postnasal drip</td>
<td>7 (15%)</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>6 (13%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>6 (13%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Pain</td>
<td>6 (13%)</td>
<td>10 (2%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>6 (13%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>5 (11%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5 (11%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>5 (11%)</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>5 (11%)</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>Ear pain</td>
<td>5 (11%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>5 (11%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>5 (11%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>4 (9%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Wheezing</td>
<td>4 (9%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Body temperature increased</td>
<td>4 (9%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Neck pain</td>
<td>4 (9%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Sinus pain</td>
<td>4 (9%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Chest discomfort</td>
<td>4 (9%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Crackles lung</td>
<td>4 (9%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>3 (7%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>3 (7%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Toothache</td>
<td>3 (7%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease</td>
<td>3 (7%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>3 (7%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Respiratory tract congestion</td>
<td>3 (7%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Fall</td>
<td>3 (7%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 (7%)</td>
<td>4 (1%)</td>
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</table>

In this study, the upper bound of the 1-sided 95% confidence interval for the proportion of Flebogamma® 10% DIF infusions associated with one or more AEs was 37.8% (total infusions: 208; actual proportions: 34.6%). The average percent of infusions with AEs during or within 72 hours after the end of an infusion for each individual subject was 36.7% and the upper bound of the 1-sided 95% confidence interval was 43.9%.

AE reporting was based upon a clinical protocol precluding pre-medication against AEs. Pre-medication could be utilized only after the first 2 infusions only in those patients that exhibited adverse events.

Fifty-three of the 46 subjects enrolled in this study had a negative Coombs test at baseline. Of these 43 subjects, 10 (23.3%) developed a positive Coombs test at some time during the study. However, no subjects showed evidence of hemolytic anemia.

**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, 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, somatic nepheopathy.

**Respiratory**

Anea. Acute Respiratory Distress Syndrome (ARDS), Transfusion-Related Acute Lung Injury (TRALI), cyanosis, hypoxemia, pulmonary edema, dyspnea, bronchospasm.

**Cardiovascular**

Cardiac arrest, thromboembolism, vascular collapse, hypotension.

**Neurological**

Coma, loss of consciousness, seizures, tremor, asymptomatic meningitis syndrome.

**Integumentary**

Stevens-Johnson Syndrome, epidermolysis, pemphigus, 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**

Passive 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>61963-0005-1</td>
<td>50 mL</td>
<td>5g</td>
</tr>
<tr>
<td>61963-0005-2</td>
<td>100 mL</td>
<td>10g</td>
</tr>
<tr>
<td>61963-0005-3</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)
Two-year-old Alexa Jennings was diagnosed with opsoclonus-myoclonus syndrome (OMS), a rare (one in 10 million) autoimmune neurological disorder, in the fall of 2009.

Alexa Jennings was diagnosed with opsoclonus-myoclonus syndrome (OMS), a rare (one in 10 million) autoimmune neurological disorder, in the fall of 2009. OMS is a rare (one in 10 million) autoimmune neurological disorder. Its name describes its symptoms: opsoclonus is jiggling eye movements, and myoclonus means involuntary muscle twitching. Alexa is receiving monthly intravenous immune globulin (IVIG) treatments coupled with ACTH (adrenocorticotropic hormone) injections. So far, she has responded wonderfully. Alexa’s story was featured on the television show “Mystery Diagnosis” on the Discovery Health Channel in a segment called “The Toddler Who Stopped Walking.” We sat down with Alexa’s parents, Brooks and Becky, to learn more about her story.

Trudie: When did you first suspect your daughter was ill?
Becky: Her illness struck overnight. She was 13 months old and on Oct. 10, 2009, she went to bed able to walk and speak about six words, everything a toddler should be able to do. The next morning, she woke up with extreme balance issues, her eyes were darting back and forth and she was vomiting. We took her to a walk-in clinic and later to the emergency room. We ended up in the pediatric intensive-care unit for five days trying to get a diagnosis. The working diagnosis was a viral infection causing cerebellar ataxia, a common misdiagnosis for OMS.

Brooks: After we finally went home, she seemed to improve but then rapidly got worse. She had trembling movements in her hands and feet, her eyes would roll in [the] back of her head, and she couldn’t fall asleep. Her balance problems gave her a fear of her high chair and changing table. Pretty soon, we ruled out a viral infection and were referred by a friend to a pediatric neurologist in Houston, Texas, an eight-hour drive from our home. Alexa screamed the entire way; it was the longest day of our lives.

Trudie: When was Alexa put on IVIG?
Brooks: Treatment started with a steroid injection to curb her immediate symptoms; then IVIG was started immediately. She was given infusions for five days straight.

Becky: The neurologist broke the news to us and explained that OMS is an autoimmune disease that is typically caused by a tumor, although the tumors are not always found. So far, Alexa has no sign of a tumor. Basically, the immune system starts attacking the tumor and then gets confused and attacks the brain.

Trudie: When was Alexa put on IVIG?
Brooks: Treatment started with a steroid injection to curb her immediate symptoms; then IVIG was started immediately. She was given infusions for five days straight.

Trudie: What was that experience like with a toddler?
Brooks: Initially, it was awful. Her veins were so weak from all the IVs she’d already had and the infusions would just blow. Then, they tried to pump the IVIG faster to get it over with, but that only agitated Alexa more. Keep in mind, I’m a police officer, so I know how to restrain people, but after five hours of holding her down, I felt like I’d been fighting an army! The doctors encouraged us to hang in there and said the
disease caused the bad immunoglobulins to attack her brain and that the IVIG would grab them and flush them out. That made sense to us, so we didn’t become discouraged.

**Becky:** We credit the IVIG with helping to stabilize her. We have gradually been able to taper off the steroids.

**Trudie:** How are things now?

**Becky:** After we brought Alexa home, we began monthly IVIG infusions. We did the first two in our local hospital, and then we had a home healthcare nurse come out to show us how to do them at home. It's a piece of cake now; you turn on the TV, and four hours later it's all done.

**Brooks:** She’ll be on IVIG for several years. From what we’ve seen, I think it helps protect her immune system, in addition to helping her disease symptoms. We've both been sick and she has not gotten sick at all.

**Trudie:** What is Alexa’s long-term prognosis?

**Becky:** We can’t test her IQ until age 3, so we don’t know what brain damage may have occurred. She has a speech delay, but that was to be expected. Overall, she’s doing better than we could have hoped. As for long-term prognosis, we’ll just have to wait and see.

**Trudie:** What insurance issues have arisen?

**Brooks:** For the most part, we have not been given much grief. The ACTH is $30,000 a vial, and we use a vial a month. We’ve had a few billing and coding errors, but most have been resolved with a phone call. Of course, in a year and a half, we’ve already used up a quarter of our $2 million lifetime cap, and we have to pay certain expenses out of pocket. We’ve been researching backup plans. There are national organizations, like the National Organization for Rare Diseases (NORD), that allow you to apply for aid. We’re looking at all of our options.

**Trudie:** What advice would you give other parents of children with rare diseases?

**Brooks:** You have to become your child’s advocate. If you’re not getting answers you need, don’t be afraid to push and ask for clarification or a second opinion.

**Becky:** We had to go with our gut instinct to get her diagnosed. We left our pediatrician in the dust and drove eight hours away to see a specialist; like any parent, we’d do anything for our child. Then, educate yourself as quickly as you can, know about proper procedures, and make it a point to understand medications and side effects. At the same time, there’s a point when you have to trust the doctors and nurses and let them do their jobs.

**Trudie:** Do you have a good relationship with Alexa’s doctors?

**Brooks:** Definitely. You need your doctors to be part of your team. When this all happened, Becky and I were just a young couple with a new baby. We didn’t know how to talk to insurance companies or deal with reimbursement issues. Our doctors have fought with insurance companies on our behalf and come to our assistance. We couldn’t have done it without them.

**Trudie:** What have you learned from this experience?

**Becky:** We’ve learned it’s important to find a support network of other parents and patients battling the same disease you are. It’s the people who have been in your shoes who keep you strong and help you the most during a difficult situation.

**Brooks:** We’ve learned how strong we are. A lot of times, a crisis like this can tear a family apart. We’ve only been married six years, so this was a test and we passed. We know we can fight this together. This is “Team Jennings”; we signed on for the long haul.

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*TRUDIE MITSCHANG is a staff writer for IG Living magazine.*
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.

A Life of “Randomosity”

Immune globulin (IG) is most often prescribed as a long-term or lifelong therapy. But in many instances, the drug is a one-time, lifesaving cure. This was the case for Nicholas Burrus, who at age 4 became ill with a bad rash. His parents took him to the emergency room, where doctors said the rash was caused by a bug bite, even though there were no signs of any bite. Not satisfied with the diagnosis, Nicholas’ parents took him to another hospital, where a physician diagnosed him immediately with Kawasaki disease, a rare condition that occurs in children.

The symptoms of Kawasaki disease, which involves inflammation of the blood vessels, include fever, rash, swelling of the hands and feet, irritation and redness of the whites of the eyes, swollen lymph glands in the neck, and irritation and inflammation of the mouth, lips and throat. If not diagnosed early enough, long-term heart complications result in some cases and can be seen as early as two weeks after onset of the disease. After Nicholas was diagnosed, he was treated with intravenous immune globulin (IVIG) over several days, which cut short the course of the disease. But, today, he has congenital heart failure, and he survives with a mechanical heart valve.

Kawasaki Disease: The Culprit?

Because Nicholas was born with a heart condition, it is not known for certain whether Kawasaki disease worsened it. But, since he was at first misdiagnosed, which delayed treatment, and he has ongoing heart conditions, it is believed there is a strong chance that it did. “It is unknown if my disease was diagnosed on time or late because of how long the symptoms progressed before they got noticed,” explains Nicholas. “With some diseases, we don’t see the signs early enough.” And, afterward, rather than focusing on the connection, Nicholas’ childhood cardiologist was more concerned with keeping the damage to his heart “in check.”

Now 21 years old, Nicholas has been through three open-heart surgeries. “The heart surgeries were brutal and had long periods of recovery, especially my last one,” he says. His last one was at age 19, when his aortic valve was fully replaced with a mechanical valve. With that came new medication, Coumadin (warfarin), to regulate his blood to reduce chances of clotting, which also meant dietary changes for Nicholas. “Because of this medication, I have to avoid certain foods or eat things consistently to keep my blood levels balanced,” he explains.

After Nicholas was diagnosed, he was treated with intravenous immune globulin (IVIG) over several days, which cured him of the disease.

Transitions

By Ronale Tucker Rhodes, MS

Nicholas, who survived Kawasaki disease due to an IVIG infusion, is now living life to his fullest possible potential.
The Mind Trumps the Matter

A childhood of sickness and surgeries is bound to take its toll both physically and psychologically. But, Nicholas has weathered the storm well. “I have been jealous of others in the past, due to the fact that I got sick all the time and had to deal with painful surgeries and miss out on a lot of things,” he says. But, “honestly, I do not think much about it. I see it as something in the past and that happened. I grew up past it … I wanted to go off and focus on other things.”

Perhaps things such as “why?” Or things like facts. Thus, Nicholas’ life of “randomosity,” a term he has coined for his love of random knowledge. For instance, he asks questions like, “How does the brain calculate movement and motion? Each time you move your arm, fingers or leg, it is done in perfection.” And, “Will planting trees prevent global warming or speed it up? Trees can cool down the earth and make the ozone better, but if it’s dry like it is now, the trees might just die and be prone to fires, hence causing heat and more stuff to be stuck in our atmosphere.”

His quest to understand things extends to helping others as well. Recently, Nicholas put together a PowerPoint presentation titled “Kawasaki Disease: My Story and the Importance of IVIG” for his aunt, Mary, who works for FFF Enterprises, a distributor of IVIG. Mary wanted to have a presentation to show people “how important IVIG is when it comes to a brutal disease like Kawasaki,” says Nicholas. “I did not know much about the disease, honestly, until I started looking it up in medical dictionaries…. It is a disease that needs more study to understand what the exact cause is.”

The Miracle of IVIG

Nicholas’ story is just one example of how IVIG is used to save lives. Despite the overwhelming number of complications he has experienced because of his heart condition, most likely due to Kawasaki disease, Nicholas is alive and he has plans to live life to his utmost potential. “Right now, I am enjoying life to the fullest,” he says, “playing games, talking with people and working with some stuff for back-ends of websites. I plan on going back to school in the future, and I dream of having a job one day, perhaps when times are better. My main concern right now is my health, and it will always come first to me.”

His father recently took him on a cruise ship, and next, he dreams of going to Alaska with his dad. “For some reason, ever since I was a kid, I was obsessed with northern lights,” says Nicholas. “It boggles my mind how something like that can exist.”

RONALE TUCKER RHODES, MS, is the editor of IG Living magazine.
Pamela: I have been receiving intravenous immune globulin (IVIG) treatments since 1996. Recently, I made a request to retain a nurse who had administered my treatment for about two-and-a-half years and then left the agency.

I made this request due to the replacement nurse’s lack of skill. The last experience I had with the replacement nurse, she had to stick me a record number of six times before I was able to proceed with my infusion. It was painful, and I was definitely traumatized.

After making the request to get my more competent nurse back, I was told in order to retain her, I would also have to go with the new company she was with. It turned out that the new company was “out of network” for me, but I also was told that I would be treated as if I were “in-network.”

However, since making this change, I noticed that the cost of my infusion has nearly tripled. The brand name, dosage and everything else have remained the same. Has the cost of IVIG dramatically increased since February 2010?

Kris: Prices for IVIG have not dramatically increased since February 2010. In fact, prices have been quite stable. What you most likely are experiencing is the result of the way your product is being billed. I would caution you to get the agreement with your new provider in writing that you will not be charged for the out-of-pocket expenses above and beyond what you would have been charged using an in-network provider. Having a verbal commitment does not guarantee you will not be billed for the outstanding balance, nor does it limit your liability or risk. To further explain the price increase you experienced, I have asked service. This amount is usually considerably higher than a negotiated/contracted rate.

In most cases, this higher rate also translates to higher out-of-pocket expenses to the insured. Therefore, the incentive to the insured is to stay in network.

Karen: Typically, when a provider is contracted with an insurance company, reimbursement rates are negotiated down to a reduced (mutually agreed-upon) rate, and all claims billed by that provider are based on that reduced rate. When a provider is out of network, there is no negotiated/reduced rate established, so the provider bills at its list price. The insurance company then negotiates claims based on what they consider to be a “usual and customary” rate for that

Terry: There seems to be no specific diagnostic code (ICD-9) for multifocal motor neuropathy (MMN). What code should be used for reimbursement?

Kris: You are correct. MMN does not have a code of its own. My research showed multiple codes being used for MMN, including 357.82, 357.89 and 357.9. I asked Dr. Scott Carlson, a neurologist with the Rockwood Clinic in Spokane, Wash., to address the issue.

Dr. Carlson: There is no specific diagnostic code for this condition, and we see that with many types of neuropathies. The trick is to match the code the best you can. Both 357.89 and 357.9 are acceptable, but my favorite is 357.89. The code 357.82 is used for critical illness polyneuropathy, which is not correct for MMN.

Kris McFalls has two adult sons with chronic diseases treated with IG. She is formerly a physical therapist assistant, and currently is IG Living’s full-time patient advocate.
I BELIEVE THERE are different kinds of anger. There is anger that boils inside us. There is anger that debilitates, consumes and even fills us with fear. And, then, there is anger that fuels the fire within us and motivates us! Mark Twain once said, “In certain trying circumstances, urgent circumstances, desperate circumstances, profanity furnishes a relief denied even to prayer.” His words suggest there is justification and a place for the right anger, and that anger can sometimes provide the relief that prayer cannot. We can use our anger as a tool to open doors; it can provide us with a release that sets us on the path to finding a way to help our predicament.

Sometimes my anger turns to frustration. At these times, I just want to growl and wallow in the things that make me feel so secluded. For instance, I get mad when people don’t understand why I can’t go out in the sun! I get mad when my friends go out and I can’t keep up! I get mad when I have to take prednisone again and again! I get mad that there is never just one thing to worry about! I get really mad when people stare at me because I have a chin the size of a small city … and, yes, I am still hungry! In fact, I am mad that I am hungry!

Our illnesses give us a lot to be angry about. But, it’s OK to be mad! In fact, get mad! Get really mad! We have that right — but only for a moment. There is a Chinese proverb that says, “If you are patient in one moment of anger, you will escape a hundred days of sorrow.” This means that anger can be constructive; it can make us strong and keep us going. It can stop us from giving up!

Sometimes when I’m mad about my illnesses, instead of throwing a tantrum, I turn it into strength. My anger makes me strong enough to hold up this big chin of mine and carry on! I think to myself, “What people say can’t beat me down; only I can beat me down, and I don’t want to.” When my anger turns to strength, I let myself feel it — until the anger is gone and all I am left with is a will to be better and a bigger feeling of self-acceptance. That is the kind of anger worth having.

Getting angry is the easy part. But to be angry about the right thing, to the right degree, at the right time, for the right purpose and in the right way — that is not easy. So, when we become angry, we need to look inside ourselves and ask, “Who and what are we angry about?” Only when we are angry for the right reasons can we begin to direct that anger in a purposeful way.

When we appropriately direct our anger, we can make others aware of just how frustrated we feel at times, which can help them to understand that what we are going through is sometimes hard to take. Yes, it makes me angry that I have to rely on doctors, friends, family and pharmacists to help me live the quality life I deserve. I hope they are angry too — for our sake! Because our anger has a purpose!

ANGRY FOR A PURPOSE

By Ever Fecske

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!
Scrabble, Anyone?

By Cheryl L. Haggard

“SHE HAS WHAAT?” I gasped. The knee-buckling, mind-boggling, tongue-twisting diagnosis of Gianotti-Crosti syndrome (GCS) left three pediatricians, two dermatologists and one freaked-out mother (that’s me) literally scratching for answers as to why my immune-deficient daughter, Molly, was, well … itchy.

If you’re so lucky as to have taken a dip in the gene pool one too many times like our family, I’m sure you’ve coughed up, sneezed out and breathed in the medically unheard. We’ve gotten up close and personal with streptococci, neisseria and cryptosporidium. Some of us know how to enunciate telangiectasia with style and grace or flawlessly type reticuloendothelial without a spell checker. We know more about our bodies than we ever thought possible, and it’s music to our ears when a physician asks, “Do you think 21 days of clyndo should do the trick?”

If you’ve been a faithful IG Living reader, you know I’m the “glass half full” poster child. I am both patient and caregiver, so I must be wary not to allow a good bout with something “medically nasty” turn me into Debbie Downer (whaa-whaa).

But when GCS decided to park its freak show on Molly’s dermis, with its creepy pox-like lesions and fire-breathing irritation, I cracked. Thirteen years of cheering my kids on while they toughed out the creeping crud, and I’d seen it all and had my fill.

“Check, please!” “I’m outta here!” “See ya!” “Cheerio, Gove’na!” “Adios, amigos!” “Ciao!” “Ta-ta for
now!" and "Auf Wiedersehen."

As I slumped, defeated, next to Molly on the examination table, waiting for Dr. Luback to finish scribbling on the prescription pad, I noticed something very peculiar and familiar: Molly's GCS lesions connected, making the letter "C." Another itchy, snake-like mound resembled the letter "S."

I nudged Molly and whispered, "Is Mommy losing it, or is that an upper case 'J' by your ankle?"

"Oh my gosh, Mom! Is that a 'G' near my elbow?" Molly giggled. "I'm like a human Scrabble board!"

We were like giddy schoolgirls snickering about the new boy in town. We became engrossed with every new letter we found by connecting the dots. We certainly didn't notice Dr. Luback observing us, head cocked to one side as if she were a startled Yorkie.

I felt new hope surge through my veins. Despite the news that GCS was long-suffering — up to four months of recurrent lesions — I had found my vice: spelling!

Because Molly had missed pockets of schooling due to illnesses brought on by her immune deficiency (and her infusions and doctor appointments and blah, blah, blah), she was behind in core skills. Can I get an "Amen, Sister!"? And let me stop here and clear up any confusion there might be about the decision my husband, Mark, and I made not to home school: I have great respect for parents who choose home schooling. As a former first-grade teacher, I know how hard it is to smush information into a 7-year-old's cerebellum. I don't home school because I can't teach math past second grade. Many of my friends chide me to this day because our kids attend a public math and science school. Their favorite tease: "Who's gonna help them with their homework?"

Nonetheless, Molly and I face the dreaded weekly spelling list with great trepidation. All my tricks of the teaching trade had been useless; even chocolate failed to motivate. I was desperate to help Molly learn more than one or two words from a list of 10, and for her to bring home a spelling test better than a "+1."

Upon our return from the pharmacy, with bags stuffed full of itching and scratching remedies, I thought I'd sneak in a little spelling practice. "Hey Molly," I sweetly cooed. "I think I see all the letters to one of your spelling words on your left arm!"

Molly glared at me as if I'd really gone off the deep end. "You don't believe me?" I asked, trying to charm my puffy daughter into a little spelling practice. Molly shook her head left to right at a slow, deliberate pace, rebelling against my suggestion. "Oh, yes I do!" I chirped. Careful not to incite an itching riot with the angry red mob on Molly's arm, I gently outlined with my finger "G-I-V-E."

"OMG, Mom!" Molly squealed, "Did you just spell 'give'?"

"I sure did!"

"That's a 10-point word for me!" Molly announced in her best Gene Rayburn imitation. With a cheeky grin, Molly asked, "Scrabble, anyone?"

Back and forth, word after word, Molly and I had a ball at Mr. Gianotti's and Mr. Crosti's expense. My human Scrabble board beat me every time, but I gladly obliged. My mental irritation with GCS calmed the more we played.

Molly was able to return to school after about a week, outfitted with calamine and confidence. She was a spelling machine, armed (and legged) with sheer language power. And there I was, put back together after my GCS meltdown. "Who'd have ever 'thunk' it?" I mused, as I studied Molly walking away from the car, blowing kisses until she reached the front doors of the schoolhouse. I can hardly believe how frightened I got over some silly bumps and the two Italians who attached their names to them. In reality, that's all Gianotti-Crosti are — just words. I'm the one who made them a syndrome.

Before Molly returned home, I received a phone call from her teacher. "Molly aced her spelling test for the first time! I'm so proud of her!" Mrs. Craylor exclaimed.

She went on to say that she rewarded Molly with her choice of free-time activities, "but Molly didn't want to do her normal free-time stuff like coloring or Legos."

"That's odd," I responded. "Yes!" Mrs. Craylor agreed. "What's uncanny is she took me to the cleaners in Scrabble."

"Oh yeah?" I chuckled. "Boy howdy, yes! That girl smoked me!"

Out of curiosity, I asked: "What was the final blow?"

Mrs. Craylor painstakingly spelled: "A-g-a-m-m-a-g-l-o-b-u-l-i-n-e-m-i-a."}

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.
Coping Strategies for PIDD Preteens

Both preteens and their parents need to find ways to navigate through these difficult years.

By Mark T. Haggard

MIDDLE SCHOOL. Just saying the words brings a shudder. Girls are taller. Boys are tripping over their own feet. Changes to the adolescent body and mind mean these kids will not only have to acclimate to living in strange new shapes with new, funny odors and hair growing out from odd places, they also must adapt to changing social patterns.

It’s difficult for all kids at this age, so consider how tough it is for preteens with a primary immune deficiency disease (PIDD). In a world where popular is cool and cool is popular, it’s hard for PIDD kids to fit in when they appear to have something strange — something that not only has a name that is hard to pronounce, but that keeps them from engaging in the normally accepted activities at school. Middle school kids are known more for taunting their peers than for making them feel better, so it’s logical to see how kids who are different can so easily feel like outcasts.

As they’re already faced with living with a chronic illness, the added hurt that PIDD kids feel as outcasts becomes much more of a challenge. Some parents suggest locking their adolescents in their rooms at age 11 and letting them out at 15. But, let’s face it: That’s not a viable option. So, how can preteens find their way?

Coming to Terms with Their Disease

By the time children reach their preteen years, they are beginning to see things long-term. This means that they are realizing that their disease will remain with them for their lifetime, which is quite a revelation for a 10-, 11- or 12-year-old. How each preteen deals with this reality differs.

Rusty, an 11-year-old sixth-grader with common variable immune deficiency (CVID), says that he was surprised when he started school that nobody else got sick all the time as he does. As he has grown closer to his teen years, he has come to terms with the fact that he’s got CVID for the long term. “I gotta deal with it,” he says. “I’ve got it for my life.”

Rhett, who has been through the preteen years, has grown up with ADA severe combined immune deficiency (ADA-SCID), which requires monthly intravenous immune globulin (IVIG) infusions, as well as injections of PEG-adenosine deaminase in his leg every other day. The realization that he had a serious, lifelong condition finally settled in when he started middle school. “I would think about it all the time,” Rhett says. Ultimately, he learned to live with the fact that his disease was part of his life. “It is what it is,” he says, “and I’m willing to live with it.”

According to Erika Lawrence, a professor of psychology at the University of Iowa, the preteen years are the time when children will finally understand that their PIDD is a lifelong condition. “A variety of emotions may come up: sadness, anger, disappointment, fear, guilt or shame,” she says, and it’s important to let kids know that these emotions are normal and it is OK to feel them. Lawrence warns against children internalizing their emotions. “Getting ‘stuck in your head’ is not helpful. Withdrawing from the world is not helpful,” she explains. Instead, these emotions need an outlet. Lawrence suggests keeping a journal (on paper

As they’re already faced with living with a chronic illness, the added hurt that PIDD kids feel as outcasts becomes much more of a challenge.
or on the computer), meeting with a support group (online or in person) or talking to family members, friends or a professional counselor. Drawing or writing music and/or stories also can be good for kids who are creative.

**Learning to Fit In**

The preteen years are difficult on all kids socially, not just for those with PIDD, Lawrence says. In the elementary school years, children begin to value conformity and start to notice differences in people. But, in the middle school and junior high years, conforming becomes particularly important. This means that differences are not valued by kids in middle school. “Unfortunately,” Lawrence says of that age, “anything that makes someone different is seen as a ‘bad’ thing.” Therefore, kids with PIDD need to understand that everyone is different in some way and having PIDD is only one aspect of who they are.

But, while PIDD kids may come to understand this, all the other kids may not. For instance, Rusty plays football to make friends. He used to warn other students not to hit him in his port, but that simply made it more of a target for balls and other objects. Now, he no longer shares the location of his port with other students, nor does he willingly share the fact that he has an immune deficiency. According to Rusty, when he tried to explain his days off for IVIG infusions, his classmates tilted their heads and looked at him “kind of like dogs when they hear a strange noise.”

Lawrence advises that it’s not necessary for PIDD kids to share their condition with everyone they meet.

Lawrence advises that it’s not necessary for PIDD kids to share their condition with everyone they meet.
SUBCUTANEOUS IMMUNE globulin (SCIG) for patients with a primary immune deficiency disease offers an alternative infusion method that gives patients more freedom and autonomy than intravenous immune globulin (IVIG). Because this type of therapy is still relatively new, many patients and providers may not fully comprehend how SCIG therapy works. There is a learning curve to this therapy, and careful planning with an experienced provider is essential to a successful outcome.

Arguably, two of the most common complaints with SCIG therapy are site reactions and leaky sites. This is because SCIG treatment requires IG to be injected under the skin into the subcutaneous (fat) tissue rather than into a vein. Think of the vein as an invisible conduit, such as a flexible garden hose, and the fat as a balloon attached to the end of the hose. When the water is turned on, one expects to see a bulge accumulating in the balloon, but not in the hose. One also expects that the color and feel of the balloon may change as the volume of water in the balloon increases. If, after the balloon is full and the water is turned off, a small hole is poked into the balloon, it would slowly deflate until the balloon returns to its normal size and color. Although SCIG is not quite that simple, the analogy does help visualize why some reactions are expected.

Minimizing Site Reactions
Infusion site reactions can be mitigated by adjusting the equipment and/or needle placement. Swelling at the infusion site should correlate with the amount of fluid being infused. And, most swelling should resolve slowly over a 24-hour period. If more swelling occurs than is expected or if the swelling does not go away in a normal amount of time, adjustments can be made. Changing needle placement, changing the length of the catheter and adjusting the volume per site are a few things that can be tried.

Some redness and itching also is expected when infusing a protein such as IG under the skin. Palliative measures, such as cold or warm compresses, massaging the site and the use of hydrocortisone cream, will often ease the discomfort. It’s important to assess if the tape and dressing used to secure the site also may play an irritant role. Patient techniques associated with priming the tubing and placing and removing the needle also should be evaluated to see if they contribute to site reactions. Over time and with practice, site reactions should minimize.

Reducing Leaky Sites
In addition to site reactions, problems can arise as a result of simple human body mechanics. The body is made of pliable, moving parts having different densities. Therefore, it is understandable that when the body moves, objects such as infusion needles may need adjusting to avoid problems such as leaking at the sites of infusion.

Leaky infusion sites can be caused by a variety of factors, including wrong choice of infusion needles, poor needle placement, improper needle length, using a tissue that is denser and, therefore, less pliable, and poor technique. Solutions may include using a different site, using a different technique to secure the needle, changing the needle placement, using a longer needle and changing the style of catheter altogether.

Understanding What to Expect
Patients considering SCIG need to have realistic expectations and an experienced support team to help them adjust to this new therapy. Understanding what to expect ahead of time will help to ensure a successful outcome.

By Kris McFalls is the full-time patient advocate for IG Living magazine.

Directory of Dressings

3M
Tegaderm is an adhesive system made of polyurethane film for better contour over high-profile devices. It is a waterproof, sterile dressing that is transparent, breathable and impermeable to liquids, viruses and bacteria.
(888) 364-3577; solutions.3m.com/wps/portal/3M/en_US/SH/SkinHealth/brands/tegaderm

Smith & Nephew
Opsite is a transparent, adhesive film that is moisture-permeable, comfortable and extensible. It is resistant to water and body fluids and aids in prevention of bacterial contamination.
(800) 876-1261; global.smith-nephew.com/us/9740.htm
EMED

EMED has launched its new family of Safety SCIG (subcutaneous immunoglobulin) multi-needle infusion therapy products. The needle set configurations are designed to maximize patient comfort during insertion and use, and have been engineered to optimize the subcutaneous infusion of immune globulin by precisely controlling the amount of the medication released, and the time of release to the patient. Features include ultra-flexible polyethylene tubing to reduce chemical interchange with the infused drug; a translucent wing to facilitate insertion and provide stability for long-term use; a 27-gauge needle available in 9mm and 12mm sizes to minimize patient trauma; and hypoallergenic dressings included with each needle site for ease of placement.

(888) 550-6500; emedicaldevices.com/scig-infusion-sets-s.html

IntraPump

Neria Detach is a single-line infusion set that disconnects at a separate site, providing extra security and comfort. It has a 90-degree angled needle for easy insertion and a pre-attached adhesive, and it is made from skin-friendly latex-free tubing, which reduces the risk of contact allergies commonly associated with tubing from polyvinyl chloride. Infusions are still performed on multiple sites in the same period of time, just one site at a time, reducing problems with site absorption and drug waste in long tubing, and eliminating the need to search for multi-tubing occlusion issues. And, tubing does not need to be changed before each rate change. The set comes with a standard luer lock connection, and it can be used with any standard luer lock syringe.

(866) 211-7867; www.intrapump.com

MarCal Medical

MarCal’s Sub Q and Safety Sub Q right-angle infusion sets feature easier needle insertion and flexible wings for optimum viewing of insertion site; integrated wings on the needle to lay flat against the skin; and central position of the needle for stability and comfort. A variety of needle lengths and gauges are available (24 gauge, 27 gauge, 6mm, 9mm, 12mm and 14mm), and specialty gauges and needle lengths are available. Sets come with colored side clamps for easy identification for pull back on each site, as well as transparent dressing in a sterile package.

(800) 628-9214; www.marcalmedical.com/subQsafetySubQ.htm

Norfolk Medical

Norfolk provides a complete line of SCIG infusion sets and extension sets. The infusion sets feature two, three, four or five lumens that each have 36-inch microbore tubing with 24-, 25- or 27-gauge needles. There is a transparent clear disk with adhesive on each disk for placement stability. Needle lengths can be modified to 4mm, 6mm, 9mm and 12mm. Custom sets can be created to fit specific needs. Extension sets come without needles and feature 20-inch microbore tubing attached to two, three, four or five lumens, and allow for patients to use the needle set of their choice. A subcutaneous infusion set must be added to each extension set and connected to the luer lock connection. Six sets come in each box.

(847) 674-7075; www.norfolkmedical.com

Directory of SCIG Needles
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 Committee for Quality Assurance (detailed report cards on health plans, clinical performance, member satisfaction and access to care): www.ncqa.org
- National Institutes of Health: www.niams.nih.gov/HealthInfo/Pemphigus/Pemphigus.htm
- National Organization for Rare Disorders (disease-specific support groups and virtual communities for patients and caregivers): www.rarediseases.org
- Office of Rare Diseases Research: rarediseases.info.nih.gov
- Patient Advocate Foundation (patient access to care, maintenance of employment and financial stability): www.patientadvocate.org
- WebMD (medical reference): www.webmd.com

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

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

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

Multifocal Motor Neuropathy (MMN)

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

Multiple Sclerosis (MS)

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

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

Myasthenia Gravis (MG)

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

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

Myositis

Websites
- The Myositis Association: www.myositis.org
- Myositis Support Group – UK: www.myositis.org.uk

Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus (PANDAS)

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

Pemphigus and Pemphigoid

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

Peripheral Neuropathy (PN)

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

Online Peer Support
- Calgary Neuropathy Support Group: www.calgarypners.org

Primary Immune Deficiency Disease (PIDD)

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

- 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

- The National Institute of Child Health and Human Development (NICHD), www.nichd.nih.gov, is part of the National Institutes of Health. Go to the “Health Information and Media” tab on the website and do a search under
- American Academy of Allergy, Asthma & Immunology: www.aaaai.org
- International Patient Organization for Primary Immunodeficiencies (IPOPI): www.ipopi.org
- Michigan Immunodeficiency Foundation: www.midf.org
• 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://iddfriends.org/forum
• IDF Friends: http://iddfriends.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/clincs/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.norfolkmallcom.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]).

**5.1 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 IGSC treatment.

**Renal Dysfunction/Failure**

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

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

**Thrombotic Events**

Thrombotic events may occur with use of human immune globulin products. Patients at increased risk may include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, hypercoagulable disorders, prolonged periods of immobilization, and 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 study subjects receiving Hizentra, were local reactions (i.e., swelling, redness, heat, pain, and itching at the injection site), headache, vomiting, pain, and fatigue.

**6.1 Clinical Trials Experience**

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

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

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

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

Table 2 summarizes the most frequent adverse events (AEs) (experienced by at least 4 subjects), irrespective of causality. Included are all AEs and those considered temporally associated with the Hizentra infusion, i.e., occurring during or within 72 hours after the end of an infusion. Local reactions were the most frequent AEs observed, with injection-site reactions (i.e., swelling, redness, heat, pain, and itching at the site of injection) comprising 98% of local reactions.

**Table 2: Incidence of Subjects With Adverse Events (AEs)* (Experienced by 4 or More Subjects) and Rate per Infusion, Irrespective of Causality (ITT Population)**

<table>
<thead>
<tr>
<th>AE (≥4 Subjects)</th>
<th>All AEs*</th>
<th>AEs* Occurring During or Within 72 Hours of Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%) of Subjects</td>
<td>Number (%) of AEs (n=2264 Infusions)</td>
<td>Number (%) of Subjects</td>
</tr>
<tr>
<td>Local reactions*</td>
<td>49 (100)</td>
<td>1340 (0.592)</td>
</tr>
</tbody>
</table>

*All AEs are counted, irrespective of causality. Local reactions are defined as all injection-site reactions (i.e., swelling, redness, heat, pain, and itching at the site of injection).
The following adverse reactions have been identified and reported during the postmarketing use of IGIV products:

- **Infusion reactions**: Hypersensitivity (e.g., anaphylaxis), headache, diarrhoea, 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. It is not known whether Hizentra can cause fetal harm when administered to a pregnant woman or can affect reproductive 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. Hizentra was not evaluated in neonates or infants.

#### 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

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).

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 treatment 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 judged to have a potential increased risk of developing acute renal failure. If renal function deteriorates, consider discontinuing Vivaglobin. 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 nephrotic medicinal products, or those who are over 65 years of age), administer Vivaglobin at the minimum rate practicable.

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 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 Vivaglobin at the minimum rate practicable.

Hemolysis
Vivaglobin may 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 Vivaglobin for clinical signs and symptoms of hemolysis. If these are present after Vivaglobin infusion, perform appropriate confirmatory laboratory testing. If transfusion is indicated for patients who develop hemolysis with clinically compromising anemia after receiving Vivaglobin, 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 recipients of Vivaglobin for pulmonary adverse reactions. If TRALI is suspected, perform appropriate tests for the presence of anti-neutrophil antibodies in both the product and patient’s serum.

5.4 Transmissible Infectious Agents
Because Vivaglobin 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 been associated with the use of Vivaglobin. Report all infections thought possibly to have been transmitted by Vivaglobin to the CSL Behring Pharmacovigilance Department at 1-866-915-6958 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. The physician should discuss the risks and benefits of this product with the patient before prescribing or administering it to the patient (see Patient Counseling Information [17.2]).

5.5 Laboratory Tests
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. Passive transmission of antibodies to erythrocyte antigens (e.g., A, B, and D) may cause a positive direct or indirect antiglobulin (Coombs’) test.

6 ADVERSE REACTIONS
The most common adverse reactions (those AEs considered by the investigator to be at least possibly related to Vivaglobin administration) observed in ≥5% of study subjects receiving Vivaglobin were local injection-site reactions (swelling, redness, and itching), headache, nausea, rash, asthma, and gastrointestinal disorder.

6.1 Clinical Studies Experience
Because clinical studies 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 practice.

US-Canada Study
The safety of Vivaglobin was evaluated in a clinical study in the US and Canada for 12 months in 65 subjects with PI who had been previously treated with IGIV every 3 or 4 weeks (see Clinical Studies [14.1]). After 3 months, subjects were switched from IGIV to weekly subcutaneous administration of Vivaglobin for 12 months. Subjects were treated weekly with Vivaglobin at a mean dose of 158 mg/kg body weight (range: 34 to 352 mg/kg). The 65 subjects received a total of 3,656 infusions of Vivaglobin.

Table 2 shows the number of subjects who withdrew from the US-Canada study due to adverse events (AEs) and the AEs leading to discontinuation.

Table 2: Subjects with Adverse Events (AEs) Leading to Discontinuation, US-Canada Study

<table>
<thead>
<tr>
<th>AEs</th>
<th>Subjects with AEs At Least Possibly Related</th>
<th>Subjects with AEs Irrespective of Causality</th>
<th>Total Number (%) of Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subjects with at least 1 AE leading to discontinuation</td>
<td>4</td>
<td>1</td>
<td>5 (8%)</td>
</tr>
<tr>
<td>Injection-site reaction</td>
<td>3</td>
<td>–</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>Intestinal obstruction</td>
<td>–</td>
<td>1</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Hyperventilation</td>
<td>1*</td>
<td>–</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>1*</td>
<td>–</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

* One subject experienced hyperventilation and tachycardia.

Table 3 summarizes the most frequent AEs (experienced by more than 5% of subjects), irrespective of causality. It includes all AEs and those considered temporally associated with the Vivaglobin infusion, i.e., occurring during the infusion or within 72 hours after the end of the infusion.
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 (Rate*) of AEs per Infusion (n=3656)</th>
<th>Number (%) of Subjects (n=65)</th>
<th>Number (Rate*) 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>3 (0.001)</td>
</tr>
<tr>
<td>Asthma</td>
<td>5 (8%)</td>
<td>8 (0.002)</td>
<td>3 (5%)</td>
<td>4 (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>3 (5%)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Malaise</td>
<td>4 (6%)</td>
<td>5 (0.001)</td>
<td>3 (5%)</td>
<td>3 (0.001)</td>
</tr>
</tbody>
</table>

* Excluding infections. † Rate, number of AEs per infusion. ‡ 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 (Number of infusions: 3656)</th>
<th>Number (Rate*) of AEs</th>
<th>Number (Rate*) of AEs Occurring During or Within 72 Hours of Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs at the injection site</td>
<td>1789 (0.49)</td>
<td>1767 (0.48)</td>
</tr>
<tr>
<td>Mild</td>
<td>1112 (0.30)</td>
<td>1100 (0.30)</td>
</tr>
<tr>
<td>Moderate†</td>
<td>601 (0.16)</td>
<td>593 (0.16)</td>
</tr>
<tr>
<td>Severe‡</td>
<td>65 (0.02)</td>
<td>64 (0.02)</td>
</tr>
<tr>
<td>Unknown severity</td>
<td>11 (&lt;0.01)</td>
<td>10 (&lt;0.01)</td>
</tr>
</tbody>
</table>

* Rate, number of AEs per infusion. †Defined as those reactions that did not interfere with routine activities. ‡Defined as those reactions that interfered with routine activities.

Discontinuations due to AEs at the injection site | 3 subjects

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.

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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