Important Safety Information for GAMUNEX-C

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

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

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

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

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

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

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

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

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

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

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

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

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


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

Please see adjacent page for brief summary of GAMUNEX-C full Prescribing Information.

Evidence based. Patient proven.

Talecris To get GAMUNEX-C call 1-888-MY-GAMUNEX (694-2686)

©2011 Talecris Biotherapeutics, Inc. All rights reserved. www.gamunex-c.com January 2011 GX17-0111

The PROOF is everywhere you look

GAMUNEX-C is the IG therapy supported by robust clinical trials

Proven efficacy in more FDA-approved indications (CIDP, PI, and ITP)* than any other liquid IG1
GAMUNEX®-C
Immune Globulin Injection (Human) 10% Caprylate/Chromatography Purified

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

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

WARNING: ACUTE RENAL DYSFUNCTION and FAILURE
See full prescribing information for complete boxed warning.
• Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur with immune globulin intravenous (IGIV) products in predisposed patients.
• Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. GAMUNEX-C does not contain sucrose.
• For patients at risk of renal dysfunction or failure, administer GAMUNEX-C at the minimum concentration available and the minimum infusion rate practicable.

INDICATIONS AND USAGE
GAMUNEX-C is an immune globulin injection (human) 10% liquid indicated for treatment of:
• Primary Humoral Immunodeficiency (PI)
• Idiopathic Thrombocytopenic Purpura (ITP)
• Chronic Inflammatory Demyelinating Polyrneuropathy (CIDP)

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

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

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

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

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

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

Thrombotic events have occurred in patients receiving IGIV therapy. Monitor patients with known risk factors for thrombotic events; consider baseline assessment of blood viscosity for those at risk of hyperviscosity.
• Aseptic Meningitis Syndrome (AMS) has been reported with GAMUNEX-C and other IGIV treatments, especially with high doses or rapid infusion.
• Hemolytic anemia can develop subsequent to IGIV therapy due to enhanced RBC sequestration. Monitor patients for hemolysis and hemolytic anemia.
• Monitor patients for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI]).
• Volume overload
• GAMUNEX-C is made from human plasma and may contain infectious agents, e.g., viruses and, theoretically, the Creutzfeldt-Jakob disease agent.
• Passive transfer of antibodies may confound serologic testing.
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.

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

The opinions expressed in IG Living are those of the authors alone and do not represent the opinions, policies or positions of FFF Enterprises, the Board of Directors, the IG Living Advisory Board or editorial staff. This material is provided for general information only. FFF Enterprises does not give medical advice or engage in the practice of medicine. FFF Enterprises under no circumstances recommends any particular treatment for any individual and in all cases recommends that individuals consult with a physician before pursuing any course of treatment.

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.

Advertising in IG Living

IG Living Magazine is read by 30,000 subscribers who are patients who depend upon immune globulin products and their healthcare providers. For information about advertising in IG Living, download a media kit at www.igliving.com/Advertise.aspx. Or contact Cheryl Brooks at (800) 843-7477 x1177 or cbrooks@fffenterprises.com.

Up Front

5 Contributing Experts
Writers in this issue

6 Editorial
IG and Neurological Disease
By Ronale Tucker Rhodes, MS

7 Faces of IG Living
From our Facebook page

Did You Know?

8 Immunology 101
The Ongoing Production of IgM
By Terry O. Harville, MD, PhD

10 Industry News
Research, science, product and insurance updates

Lifestyle

32 Transitions: Determination Defies Disease
By Ronale Tucker Rhodes, MS

34 Living the Dream?
By Ever Fecske

35 Ask Kris
By Kris McFalls

36 A Spoonful of A1 Sauce
By Cheryl L. Haggard

38 LEMS Syndrome 101
By Cheryl L. Haggard

Features

14 Diagnosing and Treating Guillain-Barré Syndrome
By Ronale Tucker Rhodes, MS

19 The Effects of Exercise on Fatigue and Stamina
By Matthew David Hansen, DPT, MPT, BSPTS

26 How to Be a Teenager and Cope with a Chronic Illness
By Erika Lawrence, PhD

Sources

41 Book Corner
New and Useful Reading

42 Product Directory
Choosing an Infusion Pump
By Kris McFalls

44 Resource Center
Community foundations, associations, forums and other resources

Contents

April-May 2011
CONTRIBUTING EXPERTS

CHERYL L. HAGGARD
*PIDD Mom and Caretaker*

**LEMS Syndrome 101**
“Physicians and patients are particularly concerned about a LEMS diagnosis because small cell lung cancer (SCLC) is most frequently associated with LEMS.”

MATTHEW DAVID HANSEN, DPT, MPT, BSPTS
*Physical Therapist and President, Allied Healthcare Staffing and Consulting Agency*

**The Effects of Exercise on Fatigue and Stamina**
“Any exercise program must be tailored for the individual and must consider issues that affect that person and the management of their diagnosis.”

TERRY O. HARVILLE, MD, PHD
*Consultant and Medical Director, Special Immunology Laboratory, University of Arkansas for Medical Sciences*

**The Ongoing Production of IgM**
“IgM is typically the third most abundant immunoglobulin after IgG and IgA.”

ERIKA LAWRENCE, PHD
*Licensed Clinical Psychologist and Associate Professor of Clinical Psychology*

**How to Be a Teenager and Cope with a Chronic Illness**
“Having a chronic illness makes teenagers feel different or deficient in some way.”

KRIS MCFALLS
*Patient Advocate, IG Living magazine*

**Choosing an Infusion Pump**
“Patients often don’t realize they have a choice of pumps, and doctors usually will order whatever pump is recommended by the provider.”

---

**Connect with Other *IG Living* Readers through Monthly Teleforns!**

*IGL’s Readers Group Teleforns 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 teleforns.
- *IG Living* will send you invitations to let you know when the two-per-month, hosted, toll-free teleforns 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 Teleforns now by emailing kmcfalls@IGLiving.com or calling (888) 433-3888, ext. 1349.

---

*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
IG and Neurological Disease

How remarkable science is! Thanks to its findings, immune globulin (IG) has more therapeutic applications than we ever could have imagined. It was used for the first time in 1952 as a treatment for primary immune disease, and now, nearly 60 years later, IG is prescribed not only to treat antibody deficiency syndromes, but also autoimmune and inflammatory diseases and even specific infectious diseases in high-risk populations.

While there are many new discoveries being made for the therapeutic uses of IG, its use to treat neurological autoimmune conditions has seen particular growth. This issue, we take an in-depth look at a few of these conditions, including two of the more common, Guillain-Barré syndrome (GBS) and chronic inflammatory demyelinating polyneuropathy (CIDP), and one very uncommon one, Lambert-Eaton myasthenic syndrome (LEMS).

GBS can be a particularly devastating disease. Its symptoms come on rapidly, and while diagnosis is difficult, the importance of an early diagnosis cannot be overstated, as is evidenced by the many individuals who have suffered recovery periods lasting years, and in some cases, permanent neurological damage due to disease progression. While there is no cure for GBS, once diagnosed, most people fully recover, but relapses do occur, leaving patients to question whether they should be immunized to protect against other diseases or risk a recurrence.

CIDP is another neurological disease for which there is no cure. We talked with two individuals diagnosed with CIDP at different stages in their lives. One is a woman who at age 18 and a senior in high school was struck by this debilitating disease that left her barely able to walk. Another is a 56-year-old man who understands the importance of a therapeutic venue for those suffering from CIDP to vent and share their experiences. After being diagnosed at age 49, he started a support group in New York to help others with the “tricks of the trade” to make their lives “as meaningful, enjoyable and productive as possible.”

LEMS is a hard-to-diagnose neurological disease for which early diagnosis is gravely important, considering approximately 60 percent of these patients also have an underlying risk of cancer. To better understand LEMS, we share the stories of three individuals’ experiences from their first symptoms to, ultimately, a proper diagnosis.

Many neurological autoimmune diseases can be particularly incapacitating, resulting in reduced energy and stamina. And, while exercise is often the last thing these patients can ever imagine doing, we present in a separate article the research that shows that performing whatever amount and level possible can have both short- and long-term positive effects on their quality of life.

As IG treatment for neurological diseases continues to grow, it’s easy to see the paramount importance of understanding these diseases for correct and early diagnosis.

To your health,

Ronale Tucker Rhodes, MS, Editor
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.

IG Living

Let’s see how creative you can be. Finish this sentence:
You might have an immune dysfunction/chronic disease if…

Judi Petty
…you see more of your doctor than your spouse.

Jason Landrigan
…your legs are ice cold and the rest of your body is normal, but you are sweating buckets and it is only 70 degrees in your home.

Rosanne Lathbury
…your first-grader is trying to explain to his classmates what a BardPort is.

Allison Williams Craig
…you don’t know if you can commit to a part-time job because you might/will get sick.

Becky Wang
…you have more cupboard space dedicated to medicines and supplies than you do for food!

Cheryl Fournier
…you’re “friends” with your neurologist on Facebook!

Liz Ferguson-Hill
…your 11-year-old and his doctor can discuss everything and you just sit there and listen.

IG Living

Lots of people travel over the holidays. How do you feel about the body scanners now employed at airports? Does the extra radiation exposure bother you?

Miranda Pate Davis
Yes, with the kinds of rays being used (Compton scattering), it does bother me. The rays scatter in the skin tissue instead of being distributed throughout the entire body as with a regular X-ray. There are no official studies (despite letters of concern to the FDA), but radiology specialists at UCSF believe that the scanners may cause an alarming increase in the risk of skin, breast and testicular cancers. People over 65, children and those with immune deficiencies are at the highest risk. So, yes, having a child with [an] immune deficiency, we will not be flying until this is resolved.

Dr. Terry Harville
I am concerned about the mutations to bacteria, fungi and viruses, potentially producing “superbugs,” which may be multi-drug resistant, for which we will have no effective treatment. I am also concerned about the effects on dendritic and other immune cells in the skin, resulting in increased allergic disease and autoimmunity.

Be published in IG Living!
Enter our IG Living essay contest. For details, go to the IG Living Facebook page at www.IGLiving.com/IGLivingMagazine
LAST ISSUE, WE discussed the formation of antibodies. Antibodies are formed by combining variable and constant gene segments, with subsequent help from CD4 T lymphocytes, which stimulate the B lymphocytes to undergo “class-switch” into unique classes and subclasses of immunoglobulin, including IgM, IgD, IgG1, IgG2, IgG3, IgG4, IgA1, IgA2 and IgE. Each of the IgGs may have somewhat specific roles for immune protection. For instance, IgM and IgD have roles in the development of B lymphocytes. And, while IgD has no known specific role in immunodeficiency, it does have a role in periodic fever syndrome. In contrast, deficiencies of IgG and its subclasses IgA and IgM may be associated with specific immunodeficiencies. Now, more about the specific development and functions of these different immunoglobulin classes and subclasses. We’ll begin with the production of IgM.

IgM: Unique from Other IgGs

IgM is typically the third most abundant immunoglobulin after IgG and IgA. In contrast to the other classes and subclasses of IgGs, the ongoing production of IgM does not require CD4 T lymphocyte help. Rather, it is continuously produced by specific B lymphocytes without ever undergoing class-switch. Known as the B1 or the CD5+ subset of B lymphocytes, this subpopulation is very interesting in that it drastically changes in percentages and numbers over time. In umbilical cord blood immediately following birth, approximately 95 percent of the B lymphocytes express the CD5 marker, identifying them as B1 lymphocytes. The remaining approximately 5 percent of B lymphocytes are called CD5 negative (CD5-) or the B2 subset of B lymphocytes. Over time, the percentage of CD5+ B lymphocytes decreases and the percentage of CD5- B lymphocytes increases. CD5+ B lymphocytes reach their lowest point (approximately 5 percent) typically at 15 to 20 years of age. Correspondingly, the CD5- B lymphocytes will make up approximately 95 percent of the total B lymphocytes. These distributions persist until about 50 to 60 years of age, when, under normal circumstances, the CD5+ B lymphocyte percentage tends to increase again up to around 10 percent.

CD5 is a protein typically expressed on all T lymphocytes. Indeed, CD5 specific interaction from a CD4 T lymphocyte to a specific B2 lymphocyte receptor (CD72) provides a very important step in co-receptor signaling, allowing the CD4 T lymphocyte to activate the B2 lymphocyte, in order for it to proliferate and differentiate. In other words, it helps with somatic mutation to produce a stronger antibody, as well as with class-switch to produce a specific antibody class that will carry out its unique role. Since CD5+ B lymphocytes express CD5, they can circumvent the need for CD4 T lymphocytes. That is, they can “pair up” (CD5 to CD72, both expressed on the cell surface of CD5+ B lymphocytes) and stimulate each other to produce more IgM. But, since they lack the rest of the CD4 T lymphocyte stimulation components, there is no differentiation with somatic mutation or class-switch. And further, proliferation does not proceed the way CD5- (B2) B lymphocytes proliferate with CD4 T lymphocyte help.

CD5+ B lymphocytes must have a very important role in fetal development of the immune system, as well as with postnatal immunity in the newborn, during infancy and through childhood. As with all antibody formation during B lymphocyte development, a repertoire of IgM antibodies can be made from the CD5+ B lymphocyte subpopulation, helping to deal with pathogens before the body has ever been exposed to them. Once formed, CD5+ B lymphocytes can reproduce themselves outside of the bone marrow, again without the need for CD4 T lymphocyte help, but they do not appear to produce memory cells.

Next issue, the specific immune properties of IgM will be described in more detail.

TERRY HARVILLE, MD, PhD, is medical director of the Special Immunology Laboratory at the University of Arkansas for Medical Sciences, and a consultant for immunodeficiencies, autoimmunities and transplantation.

Editor’s Note: This Immunology 101 column, introduced in the April-May 2010 issue of IG Living, is intended to be a basic course in immunology. Each column builds upon the information introduced in each previous column. To read the columns in the order they have been published, go to the past issue archive at www.igliving.com.
April–May 2010
• Why do we have an immune system?
An immune system recognizes “self” and discriminates “non-self” (pathogens) in order to recognize and attack pathogens.

• What happens when the immune system goes awry?
Deficiencies in recognizing pathogens result in immune deficiency diseases. Overactivity, which occurs when mistaking “self” as a pathogen, results in autoimmune diseases.

June–July 2010
• What components of the immune system, not typically considered part of immune protection, actually protect us from infection?
Skin and mucosal cells act as “barriers” to keep pathogens out of the body. Mucosal cells lining the body’s conduits (ear canals, Eustachian tubes, nose, tear ducts, mouth, lungs, esophagus, stomach, intestines, anus, bladder and urethra) protect from invasion of organisms.

August–September 2010
• What are the more traditional components of the immune system?
Cellular (to be discussed in detail later) and humoral (proteins in the blood plasm) components. Antibodies are one of the more critical humoral components of the immune system that can be evaluated to measure how well a person’s immune system is working.

• How many classes and subclasses of IgGs can humans produce?
Humans have the capacity to product nine different classes and subclasses: IgM, IgD, IgG1, IgG2, IgG3, IgG4, IgA1, IgA2 and IgE, each of which has a specific role.

October–November 2010
• How are antibodies produced?
Most antibodies are produced by B lymphocytes in an “adaptive” context, which means the immune system’s CD4 T lymphocytes stimulate the B lymphocytes to proliferate and differentiate, and thereby undergo “class-switch,” which separates them into the unique classes and subclasses of antibodies listed above. Once produced, antibodies fall into one of three categories: 1) useful, 2) useless or 3) harmful. The body has special mechanisms to try to remove the useless and harmful antibodies. Deficiencies in antibodies, specifically IgG and its subclasses IgA and IgM, may cause immunodeficiencies. Harmful antibodies cause autoimmune diseases.

December–January 2011
• How are better antibodies produced?
After exposure to a pathogen, B lymphocytes can be stimulated to undergo changes to try to make an even better and stronger antibody directed against the pathogen. This process is known as “somatic mutation.”

• What is IgG?
IgG is the major class of antibodies found in the blood and body. It is the only antibody to pass through the placenta from mother to baby during the last trimester, which will gradually be replaced by the baby's own IgG antibodies between three and six months after birth.

February–March 2011
• How does the production of IgM differ from other classes and subclasses of antibodies?
IgM antibody production does not require CD4 T lymphocyte help. Instead, it is continuously produced by specific B lymphocytes without ever undergoing class-switch, known as the B1 or the CD5+ subset of B lymphocytes. IgM has a lower affinity and is more indiscriminate about what it can bind to than other classes of antibodies, allowing it to bind to a wider variety of pathogens. These properties make IgM a very suitable “first line” protection, giving the body and immune system time to “crank up” more “specific” components, which may take two to three days to a week.
Legislation

Florida Adds SCID to Newborn Screening Panel

In the United States, newborn screening began more than 40 years ago, when states and territories mandated newborn screening of all infants born within their jurisdiction for certain disorders that may not otherwise be detected before developmental disability or death occurs. Newborns with these disorders typically appear normal at birth, so when detected at birth, these diseases can be medically treated to allow most affected newborns to develop normally.

Seven other states also have voted to recommend the addition of SCID to their newborn screening panels, but screening has not yet begun. These include Colorado, Delaware, Iowa, Michigan, Minnesota, North Carolina and Rhode Island. In addition, proposals to add SCID have been made in Connecticut, Nebraska, Ohio and Pennsylvania.

On January 28, Florida voted to add severe combined immunodeficiency (SCID) to the state’s newborn screening panel, a uniform set of newborn screening tests. Florida joins five states and one territory in their decisions to add SCID to their panels: California, Louisiana, Massachusetts, New York, Wisconsin and Puerto Rico. In addition, Texas has a limited pilot SCID screening panel in place, where it tested approximately 20,000 infants in 2010.

Plasma

Grifols Updates Its PediGri Website

Grifols has redesigned its PediGri website (www.pedigri.grifols.com), a service that offers all the information on the origin and quality of Grifols plasma derivatives. On the site, healthcare professionals can access specific information on each plasma donation used in manufacturing a particular product, as well as the complete certificate of analysis for the lot and product SPC/package insert. The newly designed site offers easier, more intuitive navigation, new content and a video that explains the significance of PediGri.

Legislation

Bill Passed to Improve Clinical Trials Access

In October, President Obama signed into law S. 1674, the Improved Access to Clinical Trials Act. The new law amends the Social Security Act to provide for an exclusion under the Supplemental Security Income (SSI) program and Medicaid for certain compensation of individuals who participate in clinical trials for rare diseases or conditions.

Specifically, for SSI income exclusion purposes, the new law excludes “the first $2,000 received during a calendar year by such individual (or spouse) as compensation for participation in a clinical trial involving research and testing of treatments for a rare disease or condition,” provided the clinical trial has been reviewed and approved by an appropriate institutional review board. For Medicaid exclusion purposes, the new law provides that “the first $2,000 received by an individual (who has attained 19 years of age) as compensation for participation in a clinical trial meeting the requirements of section 1612(b)(26) shall be disregarded for purposes of determining the income eligibility of such individual for medical assistance under the state plan or any waiver of such plan.”

“This is a rare victory for the rare disease community,” said National Organization for Rare Diseases President and CEO Peter L. Saltonstall. “This legislation will support the development of new therapies by removing a barrier that might keep patients from participating in important research studies.”
**Drug Recall**

**Albuterol Inhalation Solution Voluntarily Recalled from Market**

The Ritedose Corp. is voluntarily recalling its 0.083% Albuterol Sulfate Inhalation Solution, 3 mL in 25-, 30- and 60-unit dose vials. The product, which is a prescription inhalation solution administered via nebulization for the treatment and maintenance of acute asthma exacerbations and exercise-induced asthma in children and adults, is being recalled because the 2.5 mg/3 mL single-use vials are embossed with the wrong concentration of 0.5 mg/3 mL and, therefore, represent a potential significant health hazard.

The following lot numbers manufactured by The Ritedose Corp. under NDC: 0591-3797-83, 0591-3797-30 and 0591-3797-60 are included in the recall: 0N81, 0N82, 0N83, 0N84, ONE7, ONE8, ONE9, 0NF0, OP12, OP13, OP46, OP47, 0PF0 and 0S15. Consumers should return the affected product to the place it was obtained. Wholesalers and resalers should return the product to: Total Product Destruction, Attn: Recall, 8025 Howard St., Spartanburg, SC 29303. For more information, call (803) 935-3995 or email recall@ritedose.com.

---

**Insurance**

**Report Analyzes Medicare Advantage Plans**

A new report published by the Kaiser Family Foundation examines trends in benefits and cost-sharing for Medicare Advantage plans, including health maintenance organizations (HMOs), preferred provider organizations (PPOs) and private fee-for-service (PFFS) plans. These plans are paid for by the government to provide Medicare-covered benefits to those who choose to enroll in them, although the plans have significant flexibility to modify their benefits packages.

Titled Medicare Advantage 2010 Data Spotlight: Benefits and Cost-Sharing, the report’s analysis shows that:

- Cost-sharing requirements vary widely across Medicare Advantage plans in 2010. For example, enrollees could pay anywhere between $0 and $3,325 for a five-day inpatient hospital stay, depending upon where they live and the plan they select.
  - Average cost-sharing for some Medicare-covered services has increased rapidly between 2008 and 2010 among Medicare Advantage plans — up 18 percent for an average stay in a skilled nursing facility, and up 36 percent for an average inpatient hospital stay.
  - In 2010, about four in five Medicare Advantage plans set an annual limit on enrollees’ out-of-pocket spending, providing protection from catastrophic costs that traditional Medicare does not provide. However, 31 percent of all plans have limits at about the $3,400 level recommended by the Medicare program, and 21 percent have no limit.
  - Nearly half of 2010 plans provide some coverage in the “doughnut hole” for Medicare’s drug benefit — 28 percent cover generic drugs only, and 21 percent cover generics and some brand-name drugs.

More information about the report is available at [www.kff.org/medicare/8047.cfm](http://www.kff.org/medicare/8047.cfm).

---

**Resource**

**New Magazine Teaches Children About PIDD**

Just Like Me is a 36-page free magazine, written for children ages 3 to 12, featuring educational articles about the immune system, primary immunodeficiency (PIDD) and intravenous immune globulin (IVIG) therapy. Dayna Fladhammer, the magazine’s editor, partnered with Baxter Health Corp.’s BioScience business to develop the magazine, which brings its therapeutic play kit and doll, Igi V. (pronounced “ig-e-vee”), to life. The quarterly magazine strives to give children a sense of normalcy with an otherwise difficult disease and encourages children with PIDD and their siblings to share photos, drawings, poems, jokes, suggestions and questions about the disease. Families can sign up for a free subscription to Just Like Me at [www.mygardian.com/gardian/just-like-me](http://www.mygardian.com/gardian/just-like-me).
Did You Know

Plasma

FDA Approves New Software for Plasma Collection

Fenwal Inc., a global medical technology company focused on improving blood collection, separation, safety and availability, has received U.S. Food and Drug Administration 510(k) clearance to market a new software release for its Autopheresis-C system used worldwide at blood and plasma centers to collect plasma from donors. The software includes new features designed to improve plasma collection, including automated and streamlined collection processes that reduce the need for operator intervention and help to improve work flow and reduce procedure times, and new confirmatory prompts to make accurate programming for target plasma volumes even easier.

People and Places in the News

Dr. John Bienenstock, a McMaster University, Hamilton, Ont., Canada, physician scientist who has led the development of an understanding of how the immune system impacts the whole body, has been nominated to the Canadian Medical Hall of Fame. Bienenstock pioneered the concept of the common mucosal system — the means by which the body’s different mucosal surfaces, such as the gut, respiratory tract and respiratory system, share information to fight infection.

Ken Cafferty, a businessman from Indiana, has donated $45 million to the University of Maryland School of Medicine to fund research into autoimmune diseases. Cafferty’s wife struggled for years with severe symptoms of celiac disease and was diagnosed and successfully treated.

Accentia Biopharmaceuticals Inc. has been approved to receive a $245,000 federal grant under the Qualifying Therapeutic Discovery Project to support the advancement of Revimmune, the company’s comprehensive system of care being developed for the treatment of various autoimmune diseases. The project is a tax credit provided under the new section 48D of the Internal Revenue Code enacted as part of the Patient Protection and Affordable Care Act of 2010.

The Lupus Foundation of America (LFA) has awarded six new research grants to address gaps in the science and understanding of key areas of lupus research, including pediatric lupus, reproductive health issues in people with lupus, lupus nephritis (kidney involvement) and neuropsychiatric lupus, which affects the brain and the nervous system. The LFA’s National Research Program directs LFA funding to areas of research in which other public and private organizations have not focused their efforts.

Accentia Biopharmaceuticals Inc. has entered into a strategic agreement with Baxter Healthcare Corp. to provide Accentia with the exclusive, worldwide right to purchase Baxter’s cyclophosphamide, which is marketed under the brand name Cytoxan for the treatment of designated autoimmune diseases, including multiple sclerosis.

Tanabe Research Laboratories is teaming up with Anaphore to conduct a research and development program that aims to develop protein therapeutics for autoimmune diseases, including rheumatoid arthritis, inflammatory bowel disease and psoriasis, based on Anaphore’s Atrimer technology.

Amgen is partnering with Xencor to jointly develop XmAb587, an Fc-engineered monoclonal antibody dually targeting the CD19 and CD32b pathways that is currently in phase II testing. XmAb587 is a potentially promising new treatment for autoimmune diseases.

The Mount Sinai Medical Center, Hoboken, N.J., is the second grant recipient of Octapharma’s 25th Anniversary Grants Program, which supports clinical or preclinical research focused on human protein therapies in hematology, immune therapy, intensive care and emergency medicine.

Plasma FDA Approves New Software for Plasma Collection

People and Places in the News

Dr. John Bienenstock, a McMaster University, Hamilton, Ont., Canada, physician scientist who has led the development of an understanding of how the immune system impacts the whole body, has been nominated to the Canadian Medical Hall of Fame. Bienenstock pioneered the concept of the common mucosal system — the means by which the body’s different mucosal surfaces, such as the gut, respiratory tract and respiratory system, share information to fight infection.

Ken Cafferty, a businessman from Indiana, has donated $45 million to the University of Maryland School of Medicine to fund research into autoimmune diseases. Cafferty’s wife struggled for years with severe symptoms of celiac disease and was diagnosed and successfully treated.

Accentia Biopharmaceuticals Inc. has been approved to receive a $245,000 federal grant under the Qualifying Therapeutic Discovery Project to support the advancement of Revimmune, the company’s comprehensive system of care being developed for the treatment of various autoimmune diseases. The project is a tax credit provided under the new section 48D of the Internal Revenue Code enacted as part of the Patient Protection and Affordable Care Act of 2010.

The Lupus Foundation of America (LFA) has awarded six new research grants to address gaps in the science and understanding of key areas of lupus research, including pediatric lupus, reproductive health issues in people with lupus, lupus nephritis (kidney involvement) and neuropsychiatric lupus, which affects the brain and the nervous system. The LFA’s National Research Program directs LFA funding to areas of research in which other public and private organizations have not focused their efforts.

Accentia Biopharmaceuticals Inc. has entered into a strategic agreement with Baxter Healthcare Corp. to provide Accentia with the exclusive, worldwide right to purchase Baxter’s cyclophosphamide, which is marketed under the brand name Cytoxan for the treatment of designated autoimmune diseases, including multiple sclerosis.

Tanabe Research Laboratories is teaming up with Anaphore to conduct a research and development program that aims to develop protein therapeutics for autoimmune diseases, including rheumatoid arthritis, inflammatory bowel disease and psoriasis, based on Anaphore’s Atrimer technology.

Amgen is partnering with Xencor to jointly develop XmAb587, an Fc-engineered monoclonal antibody dually targeting the CD19 and CD32b pathways that is currently in phase II testing. XmAb587 is a potentially promising new treatment for autoimmune diseases.

The Mount Sinai Medical Center, Hoboken, N.J., is the second grant recipient of Octapharma’s 25th Anniversary Grants Program, which supports clinical or preclinical research focused on human protein therapies in hematology, immune therapy, intensive care and emergency medicine.
Researchers at The Scripps Research Institute have uncovered a previously unknown regulatory mechanism in the body’s response to eliminate pathogens such as bacteria and viruses. Their findings challenge a long-held dogma in the field of immunology and have potential implication for far-ranging topics from how vaccines should be administered to the origin of autoimmunity.

The study, which focused on plasma cells (a component of the immune system known for producing large quantities of antibodies — targeted disease-fighting proteins), revealed that those cells also act in a negative feedback loop, the end result of which affects the function of other higher-ranking immune cells called follicular helper T cells. Previously, it was thought that plasma cells were simple soldiers in the fight against the body’s foreign invaders and lacking in the ability to direct the course of future battles.

“These plasma cells are not only capable of secreting highly specialized antibodies, but they are also involved in the regulation of the process that generates the mature immune response,” said Nadege Pelletier, a research associate in the McHeyzer-Williams lab and first author of the article published about the study’s results in the December issue of the journal *Nature Immunology*.

### AAAAI and AAN Release First Guidelines for Food Allergy

Working with more than 30 other professional, government and advocacy organizations, the American Academy of Allergy, Asthma and Immunology (AAAAI) and the Allergy and Anaphylaxis Network (AAN) released the first-ever set of guidelines for diagnosing and managing food allergy. While the guidelines are not binding for practicing physicians, officials at the National Institute of Allergy and Infectious Diseases hope they will help streamline diagnoses for doctors in all specialties, including pediatricians and family practitioners, as well as allergists.

The new guidelines clarify which tests are considered scientifically validated for detecting true food allergies, and outline a strategy for helping doctors distinguish patients who have sensitivities to a food, those who are not able to tolerate food, and those who have true allergic reactions, which can include anaphylactic shock and even death. They also advise, ideally, confirming the presence of four factors: a report from the patient of an adverse reaction such as a rash, intestinal difficulties, difficulties breathing or other reactions after consuming a particular food; a blood test that measures antibodies indicating an allergic immune reaction; a skin prick test with the allergen that shows an adverse reaction; and finally, the gold standard, a positive oral challenge test in which the patient ingests a small amount of the food allergen. Last, the guidelines urge doctors to follow up with any diagnoses of food allergies with additional tests at least once a year, particularly for children who are allergic to milk and eggs, since those reactions tend to disappear with age.

### Did You Know?

The Transportation Security Administration has embraced a new medical notification card that fliers can present to airport security screeners. The new cards do not exempt a passenger from screening, but they do provide a way to discreetly inform and alert a security officer about a health issue, disability or medical device that may affect screening. Travelers can find more information about the cards on a link on the TSA’s website (www.tsa.gov/index.shtm) under “Travelers with Disabilities & Medical Conditions.”
No matter what age one is when Guillain Barré syndrome (GBS) strikes, it is debilitating and tragic. Like Amanda, an active 14-year-old who suddenly became weak and lost feeling in her feet and legs. After four days in the intensive care unit and a diagnosis of GBS, she was still sick months later, in so much pain she was not only unable to do sports, and she could barely make it to school. And, like Byron Comp, a 52-year-old computer scientist who writes in his book, *Guillain Barré Syndrome — My Worst Nightmare*: “For someone like myself who spent the first 52 years of his life as an independent spirit, doing what he wanted when he wanted most of the time, my worst nightmare would be losing that independence.”

Not many people have heard of GBS. So, when struck with the sudden onset of painful symptoms that quickly worsen, individuals and very often their doctors are baffled about what is wrong. Left untreated for long, these individuals can develop permanent nerve damage and even risk death. Fortunately, there is a growing awareness of GBS, and once diagnosed, it can be treated and, in most cases, individuals do fully recover.

By Ronale Tucker Rhodes, MS
What Is GBS?
GBS is a rare autoimmune disorder in which the body’s immune system mistakenly attacks part of its peripheral nervous system (PNS), believing it to be foreign material and invading organisms. The part of the PNS it attacks is either the myelin sheath, which surrounds the axons of many peripheral nerves, or even the axons themselves, which are long, thin extensions of the nerve cells that carry nerve signals. Once injured or degraded, the nerves cannot transmit signals efficiently, and the muscles begin to lose their ability to respond to the brain’s commands. In addition, the brain receives fewer sensory signals from the rest of the body, resulting in an inability to feel textures, heat, pain and other sensations. Or, the brain may receive inappropriate signals, resulting in tingling, “crawling” skin or painful sensations. The arms and legs are most vulnerable, as the signals from the brain to those extremities must travel the longest distances.¹

A grave disorder, GBS was first described in 1859 by Jean Landry, a French physician. In 1916, Georges Guillain, Jean Alexandre Barré and Andre Strohl diagnosed two soldiers with the illness.² GBS can develop over the course of hours or days, or it can take up to three to four weeks. The first symptoms include varying degrees of weakness or tingling sensations in the legs, and in many instances, the weakness and abnormal sensations spread to the arms and upper body. As these symptoms increase in intensity, certain muscles cannot be used at all, and when severe, the patient can be almost totally paralyzed and unable to breathe on their own.²,³

GBS afflicts approximately one person in 100,000. It is called a syndrome rather than a disease because it is not clear that a specific disease-causing agent is involved. In fact, it is unknown what causes GBS and why it strikes some people and not others. But, it can affect anybody at any age, and both sexes are equally prone to the syndrome. What is known is that GBS usually occurs a few days or weeks after the patient has had symptoms of a respiratory or gastrointestinal viral infection. And, occasionally, surgery or vaccinations will trigger the syndrome.¹,³

The GBS-Vaccine Link
While experts at the Centers for Disease Control and Prevention (CDC) disagree that there is any evidence linking vaccinations with even a single case of GBS, other experts believe otherwise. However, because the associated link occurs in such small numbers, those experts don’t support forgoing vaccination.⁴

The first link between GBS and vaccinations occurred in 1976 when many cases of GBS were reported after the swine flu vaccination was given.² That year, 43 million people were vaccinated against the swine flu, 500 of whom developed GBS and 25 of whom died.² Small increases in the incidence of GBS occurring after vaccinations were also noted in the 1992-1993 and 1993-1994 flu seasons.⁵

In 2009, there were 62 cases that had a high suspicion of being GBS from among 99 million people vaccinated against the H1N1 swine flu virus, all but two of which emerged within six weeks of getting the vaccine, which translated into a rate of about six per 10 million people.

However, research shows that the rate of GBS in the general population is estimated to be 34 to 400 per 10 million people. According to Dr. Nizar Souayah, a neuromuscular specialist and assistant professor of neurology at New Jersey Medical School, although this research “suggests Guillain-Barré syndrome may be triggered in some cases by H1N1 influenza vaccination, the very low incidence of H1N1 influenza vaccine-associated Guillain-Barré syndrome makes vaccination the first-line strategy for infection prevention and supports the current guidelines for vaccination.” Dr. Souayah added, “There is more risk for not vaccinating than for vaccinating.”⁴

Case reports of GBS after administration of several other vaccines also have been published. This includes vaccines against anthrax, haemophilus influenza type b, measles, rabies, rubella, tetanus-diphtheria and polio.⁶ Most recently, there are reports of GBS after the new HPV vaccines.⁷ However, once again, the incidence of cases appears to be no higher than the background rate of GBS incidence expected in an unvaccinated population.⁶

Diagnosing GBS
Because the signs and symptoms of GBS are so varied, doctors often find it difficult to diagnose it in its earliest stages. Several disorders have similar symptoms to GBS, such as chronic inflammatory demyelinating polyneuropathy, French polio, Landry’s ascending paralysis and muscular sclerosis.¹²

To make a diagnosis, physicians need to establish a collective pattern of the signs and symptoms. For example, GBS
symptoms appear on both sides of the body, versus one or another, and symptoms appear more quickly (days or weeks) than other disorders, which often progress over months.1

Specific tests can help physicians to make a diagnosis. Since knee jerks are usually lost in GBS patients, a reflex test can be revealing. In addition, because signals traveling along the nerves are slower in GBS patients, a nerve conduction velocity test or electromyogram (EMG) can aid in diagnosis. And, GBS patients usually retain more protein than usual in their cerebrospinal fluid that bathes the spinal cord and brain, so a spinal tap, a procedure in which the doctor inserts a needle into the patient’s lower back to draw cerebrospinal fluid from the spinal column, can be performed.1,2

Treating GBS

There is no known cure for GBS, but it can be treated to lessen the severity of the illness and to accelerate recovery. The two equally effective treatments currently used for GBS include plasmapheresis (plasma exchange) and high-dose immunoglobulin (IG). With plasmapheresis, whole blood is removed from the body and processed to separate red and white blood cells from the plasma (the liquid portion of the blood). Those blood cells are then returned to the patient without the plasma, which is quickly replaced by the body. Scientists don’t yet understand why plasmapheresis works, but it does reduce the severity and duration of GBS. They speculate that the plasma portion of the blood contains elements of the immune system that may be toxic to the myelin sheath. Patients given IG therapy receive injections of these proteins in high doses, which lessens the immune attack on the nervous system. Again, scientists still don’t know how or why this works.1

Keeping the patient’s body functioning during nervous system recovery is the most critical part of treatment. In some cases, the patient may need a respirator, heart monitor or other machines to assist with breathing and other body functions. Before recovery begins, caregivers can manually move the patient’s limbs. Then, as the patient begins to recover, physical therapy is needed. Psychological counseling also may be necessary to help the patient adjust to sudden paralysis and dependence on others for help with routine daily activities.1

Depending upon how early GBS is diagnosed, recovery can be as little as a few weeks or as long as a few years. Eighty percent of people diagnosed with GBS will recover completely with only slight residual weakness. Five to 10 percent may experience more serious permanent problems, and one in 10 may experience a relapse at some later time.4

Approximately 5 percent of people afflicted with GBS will die, despite treatment.1 In a study conducted by the department of neurology at the Mayo Medical Center, Rochester, Minn., 14 of 320 patients (4 percent) admitted with GBS died as a direct result of the illness. Deaths most commonly resulted from ventilator-associated pneumonia. In comparison with 101 other patients with severe GBS admitted to the intensive care unit, the patients who died were older and more likely to have underlying pulmonary disease. In a specialized center, the primary event leading to death from GBS was ventilator-associated pulmonary infection, predominantly in elderly patients with significant comorbidity.8

Immunization for GBS Patients

Despite any proven connection between vaccines and GBS, it is known that vaccines may trigger the syndrome. Therefore, GBS patients wonder whether they should avoid vaccinations to prevent a relapse. According to Gareth J. Parry, professor of neurology at the University of Minnesota, the decision to avoid vaccinations “is a personal one that each patient must make, based on their best analysis of the risks and benefits.”9

While recurrent attacks of GBS are rare, they do occur and they have been described following vaccines. But, recurrence of GBS also may occur following infections, such as influenza. “It is important to remember that the risk of developing new GBS [or] having a recurrence of GBS … are … considerably greater following an infectious illness such as influenza than it is after vaccination,” explains Parry. “Thus, by preventing the infection, vaccinations may actually reduce the risk of one of these undesirable outcomes.” Parry emphasizes that getting a disease such as polio, typhoid, tetanus, rabies and others is so devastating that it’s easy to recommend the vaccine, even if it does cause GBS. But, he says, “It is with the less severe diseases such as influenza that the difficulties arise.”9

Because the signs and symptoms of GBS are so varied, doctors often find it difficult to diagnose it in its earliest stages.
Peter D. Donofrio, MD, who is on the medical advisory board for the GBS/CIDP Foundation International, agrees: “The patient must weigh the chances for relapses of GBS … after immunization to relapses from natural infections with the influenza virus and other pathogens, as well as the morbidity and mortality of influenza infection not affecting the peripheral nerves…. Some data exist that the relative risk of developing GBS is considerably higher after the natural flu than after vaccination.”

Depending upon how early GBS is diagnosed, recovery can be in as little as a few weeks or as long as a few years.

Unfortunately, almost all studies that have looked at the incidence of GBS following vaccination in normal populations pertain to populations that have never had GBS. But there is one study in which the researchers distributed a questionnaire to members of the British Guillain-Barré Syndrome Support Group about their illness, immunizations given after their illness, and new symptoms developing within six weeks of these immunizations. Three hundred and eleven patients with prior GBS had received an immunization since recovering from GBS. Eleven patients reported new symptoms of fatigue, weakness, numbness and paresthesia, but in most instances, the symptoms were mild and did not require hospitalization. One patient could not work or drive for six weeks. The relapses were most associated with influenza, tetanus and typhoid immunization, but some relapses were observed after immunizations with polio, hepatitis A and B, BCG, yellow fever, meningococcal and diphtheria vaccines. From that study, the researchers determined that the chance for relapse in GBS requiring treatment is about 1 percent after receiving an immunization and only 0.3 percent of patients will experience significant disability.

Parry suggests that GBS patients who are concerned about receiving an influenza vaccine answer the following questions: 1) Was the initial attack of GBS triggered by an influenza vaccine? 2) Was the initial attack of GBS triggered by influenza? 3) Is the individual at increased risk of significant complications of influenza? This includes individuals with chronic respiratory disease, such as asthma, chronic bronchitis or emphysema, people over the age of 70 years and people with other serious chronic diseases. If the answer to either of the first two questions is yes, while the answer to the third is no, then the risk of the vaccine may outweigh any benefit. If the answer to the third question is yes, while the first two are no, then the benefit of the vaccine clearly outweighs the slight risk that it will cause a recurrence of GBS. If the answer to all three questions is yes, “then I usually still recommend vaccination, but certainly emphasize to the patient the potential risk,” says Parry.

The Future of GBS?

Even though the incidence of GBS is rare, neurological scientists, immunologists, virologists and pharmacologists are all collaborating to learn how to prevent this disorder and to make better therapies available. Until then, those afflicted with GBS can only continue with the current treatment protocols and seek the insight of others who also suffer from the syndrome, such as Byron, who wrote his book to give support and hope to other victims.

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

References
Specialty solutions in Chronic Care.

Making a difference—one patient at a time.

Offering safe, convenient & reliable solutions for home infusion and critical-care products.

Immune Globulin Subcutaneous
Immune Globulin Intravenous
Antihemophilic Factors
How many people living with an autoimmune disease or primary immunodeficiency have been told by family, friends or other acquaintances that they would feel stronger and more energetic if they could just exercise a little? Well, despite the possibility that exercise is the last thing that a patient feels like doing (or hearing), those well-wishers might actually be on to something.

The positive effects of long-term exercise on stamina (energy and strength that is enduring) are well-documented in a number of healthy and patient populations. What’s more, several recent studies support the anecdotal observation that exercise has an immediate effect on energy levels as well. These findings are consistent, despite a number of potential physical and emotional causes that can be responsible for fatigue experienced by a patient, including infection, anemia and nutritional deficiencies, metabolic disorders, depression and/or anxiety, overstimulation of the adrenal glands caused by constant stress, medications and lack of sleep. Interestingly, studies seem to demonstrate a reduction in fatigue for those experiencing true (neuromuscular) weakness, where less force than normal is produced by a muscle, and for those experiencing perceived (non-muscular) weakness, where muscle strength is actually normal but a person feels that more effort is required to exact a given amount of force. Consequently, results suggest multiple mechanisms for increased energy, including physical/physiological and psychological.

Regardless of the cause of fatigue, its symptoms, in addition to lack of energy, may include difficulty concentrating, irritability, poor rationalization, insomnia, apathy (lack of interest) and weakness, and they can be debilitating to the sufferer. Therefore, the right amount, intensity and type of exercise may be the action that “primes the pump” for a more energetic, productive and enjoyable life.

Long-Term Effects of Exercise

A University of Georgia (UGA) study affirms that sedentary people can decrease fatigue by up to 65 percent and improve energy levels by 20 percent by participating in regular low-intensity exercise. The study shows that fatigue and energy aren’t necessarily exact opposites of each other. To illustrate this, think of the example of someone who feels fatigued during a long drive home from work at the end of the day, but also begins to feel energized as they get closer to home and the family, dinner or favorite television program that they know is waiting for them.

Investigators of the UGA study enlisted 36 volunteers who did not exercise regularly and had reported enduring
fatigue, yet did not meet the criteria for a medical condition (a sample that Patrick O’Connor, one of the study’s co-authors, says represents approximately 25 percent of the general population). The subjects were placed into one of three groups: the first group exercised 20 minutes, three times a week for six weeks on an exercise bike at a moderate-intensity (comparable to a fast-paced walk with hills); the second group rode an exercise bike for 20 minutes over the same time period, but at a low-intensity (comparable to an easy walk); the third group (control group) did not perform any exercise. Both the low- and moderate-intensity exercise groups experienced a 20 percent increase in energy levels over the control group; however, somewhat surprisingly, the low-intensity group had a greater reduction in fatigue levels than the moderate-intensity group (65 percent compared to 49 percent, respectively). O’Connor declared: “It could be that moderate-intensity exercise is too much for people who are already fatigued, and that might contribute to them not getting as great an improvement as they would had they done the low-intensity exercise.”

Although the right amount, intensity and type of exercise can increase energy and reduce fatigue, the fact is that overexertion is one of the greatest exacerbators of fatigue. In fact, intense and exhaustive exercise has been shown to suppress immune agents and increase the incidence of upper-respiratory tract infections (URTIs). Finding the balance point is the key. A recently released abstract of a scientific review, ahead of print, by researchers at Federal University of Sao Paulo, Brazil, proclaims: “Moderate exercise has been associated with significant disease protection and is a complementary treatment of many chronic diseases. . . The effects of chronic (i.e., long-term) exercise occur because physical training can induce several physiological, biochemical and psychological adaptations.” These modifications can include T cell proliferation, cytokine production and antibody response to vaccination; however, the primary mechanism of exercise that causes these changes still needs to be understood.

**Short-Term Effects of Exercise**

Our society is constantly searching for the next brand of “energy drink,” soda, coffee or other artificial “pick-me-up” that will help us get through the day. Those who rely on these products daily may or may not acknowledge their addictive qualities and tendency to induce tolerance (more and more is needed to elicit the same effect). However, a number of studies have supported a potentially even more concerning symptom of persistent caffeine use for the immune-deficient population: inhibition of the immune system. For example, caffeine at levels that are relevant to normal human consumption has been reported to impair lymphocyte and antibody production and proliferation. Contrastingly, science has shown that moderate exercise can promote clear increases in the levels of energy-promoting and mood-enhancing neurotransmitters in the brains of animals that are placed in regular exercise conditions — without the negative effects on the immune system.

For instance, researchers at UGA reviewed and analyzed 70 randomized, controlled trials in a study on exercise and fatigue that involved 6,807 subjects. “More than 90 percent of the studies showed the same things: Sedentary people who completed a regular exercise program reported improved fatigue compared to groups that did not exercise.” The effect of exercise on reducing fatigue was stronger than that of even stimulant medications used for the treatment of attention deficit hyperactivity disorder and narcolepsy, and benefited nearly every subgroup studied, including cancer patients and those with chronic conditions.

Another review, performed by Australian researchers, looked at 36 studies published between 1987 and 2006 that evaluated the effects of exercise and other non-drug techniques on fatigue in more than 1,700 patients with an autoimmune disease (multiple sclerosis, rheumatoid arthritis or systemic lupus erythematosus). The exercise programs that made up the studies began patients at a low-intensity level and, if they did not cause symptoms to worsen, were progressed to 15- to 30-minute sessions at least three times a week for up to 12 weeks. The authors of the paper reported that “aerobic exercise was effective, appropriate and feasible for reducing fatigue among adults with chronic autoimmune conditions.” The exercises that helped decrease fatigue in the studies included low-impact aerobicics, brisk walking, cycling and jogging.
aerobics, brisk walking, cycling and jogging. Swimming and other exercises may also help, but there weren’t enough studies in the sample that used these activities to demonstrate a statistically significant difference.

Professional literature is rich in evidence that supports the use of a graded light-to-moderate exercise program to reduce fatigue associated with a number of conditions, from chronic fatigue syndrome to post-bone marrow or stem cell transplantation. Nevertheless, the detrimental effects of a sedentary lifestyle (not exercising) are even better understood and documented. These effects include muscle wastage; loss of bone density; and increased risk of obesity, cardiovascular disease, diabetes and other complications. Inactivity also can lead to feelings of uselessness and dependence, and an otherwise poor self-image.

**Recommendations**

Perhaps family and friends are right about a little more exercise being able to improve a patient’s energy levels. However, only the patient, along with the appropriate healthcare professionals, can determine what that exercise should be. It is the family’s and friends’ responsibility to be nonjudgmental and supportive. Any exercise program must be tailored for the individual and must consider issues that affect that person and the management of their diagnosis (e.g., joint pain, reduced mobility, dizziness, exacerbations). Nevertheless, the following recommendations can be applied to most situations:

- Experiment to discover the type of exercise that is right for you. It’s important to find activities that you enjoy. It goes without saying that if you like what you are doing, you increase your chances of doing it.
- Remember that your tolerance for exercise may differ from day to day. Do what you can, and if you absolutely don’t feel that you are able to be very active on a given day, don’t be. Feelings of extreme fatigue are common around the time of an infusion and/or exacerbation of symptoms; rest up and plan on continuing your program the next day, even if you have to adapt it to how you are feeling.
- Get enough rest at night (usually recommended to be at least seven hours of uninterrupted sleep).
- Maintain a nutritionally balanced diet, and eat at regular intervals.
- Take time to regularly talk about your day, your hopes and your fears with a friend. Pent-up stress can lead to fatigue, anxiety and/or depression. Listening also can be very therapeutic and can help to put your own challenges in perspective.
- Keep an exercise journal of your activities that records how you felt immediately after and how you felt the next day. If a given amount, intensity or type of an exercise worsened your symptoms, try taking it back a notch the next time.
- Pace yourself, and stop exercising well before you feel exhaustion setting in.
- If you feel that an increase in activity or difficulty is in order, make small increases to only one component of your program at a time (e.g., frequency, duration, intensity). For example, if you walked 200 consecutive feet one day without any increase in your symptoms, try walking 225 feet the next day.
- Avoid excessive intake of alcohol and caffeine, and don’t smoke.

**Any exercise program must be tailored for the individual and must consider issues that affect that person and the management of their diagnosis.**

Although much remains to be discovered regarding the precise “hows and whys” of exercise’s effect on fatigue and stamina, science has revealed what every individual human being rediscovers for themselves nearly every day: The body and the mind are intimately connected. The objective symptoms of the body and the subjective feelings of the mind can readily influence one another. Getting up and doing something active will likely have a holistic effect on someone’s life, and if done properly, the outcome can be extremely positive.

**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.**
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)  
  - \(\geq 13.3\) log reduction of EMCV (HAV model)  
  - \(\geq 6.2\) log reduction through 4% PEG precipitation and \(\geq 5.5\) log reduction through 20 nm nanofiltration of an experimental agent considered a model for the vCJD and CJD agents \(^3\)

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

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

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

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 immunodeficiency (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

WARNING: ACUTE RENAL DYSFUNCTION AND ACUTE RENAL FAILURE
- Use of immune globulin intravenous (IGIV) products, particularly those containing sucrose, has been reported to be associated with renal dysfunction, acute renal failure, osmotic nephropathy, and death (1). Patients at risk of acute renal failure include those with any degree of pre-existing renal insufficiency, diabetes mellitus, advanced age (above 65 years of age), volume depletion, sepsis, paraproteinemia, or those receiving known nephrotoxic drugs (see Warnings and Precautions [5.2]). Flebogamma® 10% DIF does not contain sucrose.
- For patients at risk of renal dysfunction or failure, administer Flebogamma® 10% DIF at the minimum infusion rate practicable (see Dosage and Administration [2.3], Warnings and Precautions [5.2]).

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

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

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

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

Hyperproteinemia
Hyperproteinemia, increased serum viscosity, and hypernatremia may occur in patients receiving Flebogamma® 10% DIF therapy. It is clinically critical to distinguish true hypernatremia from a pseudo-hypernatremia 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 pseudo-hypernatremia 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 atherothrombosis, 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.

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 anemia 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]).

Transfusion-Related Acute Lung Injury (TRALI)
Non-cardiogenic pulmonary edema may occur in patients following Flebogamma® 10% DIF treatment (11). TRALI is characterized by severe respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever. Symptoms typically appear within 1 to 6 hours following treatment.

Monitor patients for pulmonary adverse reactions (see Patient Counseling Information [17]). 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 reconstituted 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 Grifols 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.

Adverse Reactions
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, maculopapular, rashes, tachycardia, bacterial pneumonia, and vasovagal syncope (1 patient).

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

In a multicenter, open-label, non-randomized, historically controlled clinical study, 46 individuals with primary humoral immunodeficiency received infusion doses of Flebogamma 10% DIF at 300 to 600 mg/kg body weight every 3 weeks (mean dose 469 mg/kg) or 4 weeks (mean dose 457 mg/kg) for up to 12 months (see Clinical Studies [14.1]). Routine pre-medication was not allowed. Of the 601 infusions administered, 130 infusions (22%) in 21 (47%) subjects were given pre-medications (antihypertensive, antihistamine, or antiemetic agent) because of experience with consecutive infusion-related adverse reactions.

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

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

Table 1: Treatment-related Adverse Events Occurring in ≥5% of Subjects with PI during a Flebogamma® 10% DIF Infusion or within 72 Hours After the End of an Infusion

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Subjects (%)</th>
<th>Infusions (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=46)</td>
<td>(N=681)</td>
</tr>
<tr>
<td>Headache</td>
<td>24 (52%)</td>
<td>67 (11%)</td>
</tr>
<tr>
<td>Rigors</td>
<td>17 (37%)</td>
<td>37 (6%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>15 (33%)</td>
<td>27 (5%)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>10 (22%)</td>
<td>18 (3%)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>9 (20%)</td>
<td>11 (2%)</td>
</tr>
</tbody>
</table>
Precautions [5.2]). The minimum infusion rate practicable does not contain sucrose.

If there are no adverse drug reactions, the infusion rate for subsequent infusions can be slowly increased to the intervals thereafter.

gammopathies, because of the potentially increased risk of thrombosis.

HUB and serum creatinine, before the initial infusion of Flebogamma® at increased risk of developing acute renal failure. Assess renal function, including measurement of HLA antibodies in both the product and patient’s serum.

Irrespective of Causality

Infusion or within 72 Hours after the End of an infusion, The total number of adverse events occurring during or within 72 hours after the end of an infusion, irrespective of causality, was 359, excluding non-serious reactions.

Table 3 lists the AEs that occurred in greater than 5% of subjects during a Flebogamma® 10% DIF infusion or within 72 hours after an infusion, irrespective of causality.

Table 3. 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, Irrespective of Causality

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Subjects (%) (N=646)</th>
<th>Infusions (%) (N=601)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Back pain</td>
<td>8 (17%)</td>
<td>27 (5%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>8 (17%)</td>
<td>17 (3%)</td>
</tr>
<tr>
<td>Body temperature increased</td>
<td>4 (9%)</td>
<td>6 (1%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>4 (9%)</td>
<td>6 (1%)</td>
</tr>
<tr>
<td>Pain</td>
<td>4 (9%)</td>
<td>8 (1%)</td>
</tr>
<tr>
<td>Chest discomfort</td>
<td>3 (7%)</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>3 (7%)</td>
<td>5 (1%)</td>
</tr>
<tr>
<td>Infusion site reaction</td>
<td>3 (7%)</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>3 (7%)</td>
<td>3 (0.5%)</td>
</tr>
</tbody>
</table>

Adverse Event Subjects (%) (N=46) Infusions (%) (N=601)

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

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.

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

Infusion reactions

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

Renal

Acute renal failure/uremia, osmotic nephropathy

Respiratory

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

Cardiovascular

Cardiac arrest, thromboembolism, vascular collapse, hypertension

Neurological

Coma, loss of consciousness, seizures, tremor, aseptic meningitis syndrome

Integumentary

Stevens-Johnson Syndrome, epidermolysis, erythema multiforme, dermatitis (e.g., bullous dermatitis)

Hematologic

Pancytopenia, leukopenia, hemolytic, positive direct antiglobulin (Coombs) test

Musculoskeletal

Back pain

Gastrointestinal

Hepatic dysfunction, abdominal pain

General/Body as a Whole

Pyrexia, rigors

DRUG INTERACTIONS

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. Immunglobulins cross the placenta from maternal circulation increasing after 30 weeks of gestation.

Nursing Mothers

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

Pediatric Use

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

Geriatric Use

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

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

HOW SUPPLIED/STORAGE AND HANDLING

Flebogamma® 10% DIF is supplied in single-use, individually laser etched vials containing the labeled amount of functionally active IgG. The following presentations of Flebogamma® 10% DIF are available:

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

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

DO NOT FREEZE.

When stored at room temperature (up to 25 °C [77 °F]), Flebogamma® 10% DIF is stable for up to 24 months, as indicated by the expiration date printed on the outer carton and container label. Keep Flebogamma® 10% DIF in its original carton to protect it from light.

Manufactured by INSTITUTO GRIFOLS, S.A.
Barcelona - Spain

U.S. License No. 1181
Distributed by GRIFOLS BIOLOGICALS Inc.
Los Angeles - CA 90032
Phone: 888-GRIFOLS (888-474-3657)
How to Be a Teenager and Cope with a Chronic Illness

These coping strategies for dealing with parents, friends, caregivers and even themselves can better help teens to navigate these difficult years.

By Erika Lawrence, PhD

Being a teenager is hard enough. There is tremendous pressure to fit in, to be “normal,” to conform with peers. There are few people who don’t look back on high school and shudder. It is a time when teens feel like outsiders, like they don’t belong, like they’re different in some (bad) way.
Teens also feel like they have absolutely no say over their own lives. They’re constantly answering to their parents, teachers or friends. It is one of the most challenging times of their entire lives.

Imagine how much harder it is when they add to all that a chronic illness. One of the questions teenagers often ask is: “How do I deal with people who ‘just don’t get it’?” Parents, friends and even doctors can be infuriating at times. That’s why it’s important for teens, as well as their caregivers, to understand the unique challenges they face when coping with a chronic illness, and to be armed with some strategies for dealing with these situations.

**Dealing with Parents**

People with a chronic illness know how challenging and frustrating it can be to get family members to understand the unique, complicated and unpredictable nature of their disease. They also know how difficult it is to get others to be supportive in a way that is helpful, rather than hurtful or aggravating.

But, while adults have some power in their relationships because they are on equal footing with their spouses and friends, teenagers have very little power in their relationships with their parents. Instead, they have to struggle to balance some newfound independence with their dependence on parents for food, shelter and clothing, as well as for love and support. What’s more, teens with chronic illnesses also are dependent on their parents and caregivers for help with their medical care. They have to be driven to doctors’ appointments, have their medications paid for and be helped with infusions. When they infuse in the home, parents either have to assist teens or at least supervise them to ensure the infusions are being done. When teens infuse in the hospital or clinic, parents often have to drive. As a result, teens with chronic illnesses often wind up feeling even more dependent on their parents.

Another challenge faced by these teens is dealing with parents’ reactions to having a child with a chronic illness. In some cases, parents can be as critical or dismissive as other people in their lives. However, the more common situation is for parents to become overly protective and/or extremely anxious. This makes sense, of course. Parents want to protect their children, and they worry about them and want to keep them safe. However, adolescence is the time when this feels the most suffocating and unhelpful.

So how do teenagers gain some control over their lives when they depend on their parents to stay healthy? How do they deal with overprotective parents? First, keep in mind that parents may have a hard time accepting or coping with their children’s illness. Teenagers should set aside some time to try to talk to their parents about this. Parents need a chance to tell their children how scared they are for their safety and health, how guilty they feel that they have this illness (yes, parents often blame themselves for their children’s health problems), or how much they want to lock them in their room so nothing bad can happen to them. Teenagers, in turn, need to empathize with their parents, who are feeling and/or behaving this way out of love for their children and out of a desire to be a good parent — not because they want to make their children’s lives miserable.

Second, teenagers need to ask their parents to really listen to what they say things are like for them. They need to tell their parents that they understand why they are so protective or anxious (or that they are trying to understand), but that the protectiveness and anxiety adds another layer of stress and difficulty to an already challenging situation (being a teenager with a chronic illness).

Third, once teenagers have had a chance to say how they feel, they should try to come up with a small change that both they and their parents can live with. For example, if teenagers feel a lot of pressure to stay home Friday and Saturday evenings instead of going out with friends, perhaps it could be agreed upon to go out Friday night for a few hours (perhaps two to three hours instead of five or six). Then, when they come home, they can let their parents know how much they appreciate their parents letting go a bit. If that works, they can talk again about what another step forward might be. Over time, they’ll be able to have more of the types of freedoms that other teens have, and their parents will become increasingly comfortable (or able to tolerate) giving them more freedom.
Last, if that does not work, teenagers should request that they all meet with a counselor for a few sessions. It can help a lot to have a third party to help navigate these types of discussions and move forward.

Dealing with Peer Pressure and High School

High school is all about fitting in — being normal. Having a chronic illness makes teenagers feel different or deficient in some way. There may be peer pressure to drink, which is particularly dangerous for teens who are on medications or getting infusions. Dating and becoming sexually active is more challenging with physical health problems. There also is tremendous pressure to be strong and not show vulnerability, for both teenage boys and girls. Bullying is a huge problem in schools, causing tremendous stress and depression for victims. All of this can cause stress and depression, which can worsen symptoms of chronic illness, leaving teenagers feeling more vulnerable and more like outsiders.

So how can teenagers find support and fit in at high school? First, they should identify one or two friends whom they really trust and tell them about their illness. They should do the same with one or two authority figures at school that they trust, such as a teacher, counselor or coach. Knowing they have a few people in their corner who can look out for them can make it easier to navigate everything else. This is particularly important if bullying is an issue.

Once they have identified people they can trust, teens need to figure out how to tell them. Most people want to understand, but they simply don’t know a lot about chronic illnesses. Teenagers need to educate them about their illness and how it affects them on a day-to-day basis. They also should encourage them to ask questions, and ask if they would like something to read about their illness.

It is important for teens to take their cues from the other person. They should be careful not to overwhelm others with information, but rather provide as much information as they seem interested in hearing about or able to take in at the time. They can always teach them more the next time they talk about it.

Teenagers should know that, at times, they might disappoint their friends. There are so many demands that are already put on them as teenagers. When managing a chronic illness is added to that, teens have only so much time and energy to do everything that they need and want to do. Therefore, they should be assertive and tell their friends if they cannot go out with them on Friday night because they need some time to take care of themselves. It’s OK for them to say “no.” They can also let their friends know how disappointed or frustrated they might be about that and offer an alternative that they can live with (e.g., getting together for a movie on a different night). Real friends will understand.

Dealing with Doctors and Nurses

It can be so frustrating for patients when doctors and nurses don’t know much about their chronic illness. And, finding a medical professional who is an expert — or at least knows a bit — about their specific illness is not always an option. Even if one is found, is that person within driving distance? Does he or she take the patient’s medical insurance? Is it possible to get an appointment?

Most people with a chronic illness are stuck trying to educate their doctors about their own illness, and how their illness
affects whatever symptom or problem they are experiencing that day. How do patients teach the “experts”?

Doctors can’t be expert in everything. No one can be. However, most doctors and nurses do want to understand what patients are going through, and how they can help them feel better. It is OK for patients to bring a pamphlet or sheet of information about their specific illness to their appointments. Patients also can give permission to all their doctors to speak to the specialist treating their chronic illness. It also helps to bring to each appointment a list of all their medications, the dosage and why they are taking them.

Changes in the Healthcare System

One of the key features of the current administration’s healthcare plan is to treat patients and their families; in other words, to treat the “home.” This means that people with a chronic illness will have a team of healthcare professionals to help the entire family system cope with the illness, the ways in which family members are affected, and how family members affect each other. For example, in Vermont, patients have a “healthcare coordinator” who helps families design unique care plans. This approach has been used for decades in England when women have babies, and it has been shown to be highly effective at helping individuals and families cope with changes, stressors and health problems.

Finally, Take Time for Self-Care

It is perfectly normal for teenagers to feel scared, angry, sad, disappointed, guilty and distressed at times. And, it’s OK for them to feel that way. All patients should allow themselves to have those feelings when they arise.

However, it’s important for teenagers to not let those feelings take charge. They should ask themselves these questions: “Am I so depressed that I am having trouble living my life on a day-to-day basis, or having trouble getting out of bed?” “Am I so anxious that I am not connecting with people or not going out and having fun?” “Am I so mad that I am taking it out on everyone else?” If the answer is yes to any of these questions, they need to talk to someone: a school counselor, teacher, parent, doctor or nurse. Depression, anxiety and irritability can be successfully treated; it’s not necessary to feel that way.

How can teenagers best take care of themselves?

1. Identify one or two authority figures and two to three close friends they can really talk to about how they feel.

2. Give themselves a break. Everyone feels like an outcast in high school at times. They are not alone and it is not forever.

3. Join a support group for teens — either in their community or online.

4. See a counselor for a while to have a place to get things off their chest and to have a sympathetic ear.

5. Find an outlet for their feelings and thoughts so they don’t get stuck in their heads. They can try keeping a journal, drawing or painting, listening to music or playing an instrument, or whatever works for them.

Adulthood Is Just Around the Corner

As hard as life can be for a teen, it is even more difficult for one suffering from a chronic illness. But by gaining a better understanding of how to deal with what they feel and how to reach out to their parents, friends and caregivers, they can get through this difficult time in their lives. They can grow out of their teenage years before they know it with a healthy and sound psyche.

ERIKA LAWRENCE, PHD, is a licensed clinical psychologist and an associate professor of clinical psychology at the University of Iowa where she conducts research on how couples and families cope with and adapt to chronic stressors such as illness. Lawrence also has a private practice in which she works with individuals, couples and families experiencing depression and anxiety symptoms or simply learning to cope with stress.

This article was written with the assistance of Rebecca Brock, MA, who is currently studying to earn her PhD in clinical psychology at the University of Iowa, and who specializes in the effects of support on psychological and physical health.
Gammaplex® Immune Globulin Intravenous (Human), 5% Liquid

BRIEF SUMMARY

CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION PRIOR TO USE

INDICATIONS AND USAGE

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

CONTRAINDICATIONS

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

WARNINGS

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

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

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

All infections suspected by a physician possibly to have been transmitted by this product should be reported to FFF [800-843-7477] on behalf of Bio Products Laboratory.

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

PRECAUTIONS

General

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

Hypersensitivity

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

Renal dysfunction/failure

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

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

Hyperproteinemia, increased serum viscosity, and hyperviscosity

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

Thrombotic events

Thrombotic events may occur following treatment with IGIV products. Patients at risk include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, coagulation disorders, prolonged periods of immobilization, and/or known/suspected hyperviscosity. Baseline assessment of blood viscosity should be considered in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chyomicronemia/markedly high triglycerides (triglycerides), hyperproteinemia or monoclonal gammopathies (See WARNINGS AND PRECAUTIONS: Monitoring: Laboratory Tests). For patients judged to be at risk of developing thrombotic events, administer Gammaplex at the minimum rate of infusion possible.

Aseptic meningitis syndrome (AMS)

Aseptic meningitis syndrome (AMS) may occur infrequently with Immune Globulin Intravenous (IGIV) treatment, usually beginning within several hours to 2 days after IGIV. AMS may occur more frequently with high doses (≥5 g/kg) and/or rapid infusion of IGIV. Discontinuation of IGIV treatment has resulted in remission of AMS within several days without sequelae.

Hemolysis

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

Transfusion-related Acute Lung Injury (TRALI)

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

Laboratory Tests

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

Drug Interactions

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

Pregnancy Category C

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

ADVERSE REACTIONS

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

Primary Humoral Immunodeficiencies (PI)

In a multicenter, open-label, non-randomized clinical study, 50 subjects with primary humoral immunodeficiency received 703 infusions with Gammaplex. Doses ranged from 279 to 799 mg/kg every 21 days (mean dose 465 mg/kg) to 28 days (mean dose 438 mg/kg), for up to 12 months. At some time during the study, all 50 subjects had an adverse event (AE) and in twenty-four subjects (48.0%) it was considered product-related.

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

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Subjects (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>18 (36%)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>8 (16%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>7 (14%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>6 (12%)</td>
</tr>
<tr>
<td>Pain</td>
<td>5 (10%)</td>
</tr>
<tr>
<td>Chills</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Nasal congestion</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3 (6%)</td>
</tr>
</tbody>
</table>

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

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

Manufactured by:
Bio Products Laboratory Limited
Dagger Lane
Eldree
Hertfordshire
WD6 3BX
United Kingdom.
US License No. 1811

U.S. Distributor:
FFF Enterprises, Inc.
41093 County Center Drive
Temecula, California 92591
1-800-843-7477
U.S.A.

March 2011 GPX/11/24
Enhancing life’s defenses

Gammaplex
Immune Globulin Intravenous (Human), 5% Liquid

Positive efficacy outcomes
For PI patients receiving Gammaplex there were:
> No reports of Acute Serious Bacterial Infection
> Just 0.75 days per year of subjects hospitalized
> Only 8.73 days per subject year out of work/school/day care

Low IgA levels
> The content of IgA is <10 µg/mL

Convenient infusion schedule
> Infusion rate can be increased every 15 minutes to a maximum rate of 0.88 mL/kg/min

Robust 3-step virus reduction
> An extremely low risk of viral transmission

Room temperature storage
> Gammaplex can be stored between 2°C and 25°C (36°F to 77°F) unopened for 2 years

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

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

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

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

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

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

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

Report adverse reactions to adr@bpl.co.uk

REFERENCES
For product information & inquiries, call: 772-453-9084

Please see the Brief Summary of Prescribing Information, including boxed warning, on the previous page.
CHRISTINA CARON thought that the acrylic nails she had gotten before her senior prom were causing numbness in her fingers. But, when the numbness progressed up her arms and down her legs, she began to think differently. So, in May 2000, at the end of her senior year of high school, she saw a doctor who diagnosed her with a vitamin B12 deficiency. It was a misdiagnosis, and by the time she graduated high school, she could barely walk. “No one really took it that seriously,” says Christina. “And, I ended up just going on with life. I graduated from high school and I went to my senior class trip, whitewater rafting. I could barely walk at that point, but I went anyway.”

Then, a month after graduation she went to work and fell down the stairs. In the emergency room, she was seen by an on-call neurologist who diagnosed her with Guillain-Barré syndrome (GBS). She was then admitted to the hospital and she began a week-long treatment of intravenous immune globulin (IVIG). Fortunately for Christina, IVIG treatment resulted in a dramatic improvement in her health. But a month and a half later, she relapsed and went through treatment all over again. “This just kept happening,” explains Christina, “so I got a referral to the Mayo Clinic in Boston, and they were the ones who diagnosed me with chronic inflammatory demyelinating polyneuropathy (CIDP).”

While the correct diagnosis came just six months after experiencing her first symptoms, Christina says: “I honestly thought I was dying. It seems silly now that I know what it is, but it was really scary not knowing.”

A Determined Outlook

At age 18, the CIDP diagnosis may have been a relief, but it also was an added burden to what should have been the start of a new chapter in her life. “I remember when I was diagnosed with CIDP, knowing it could potentially be with me the rest of my life was a little daunting, and it took a little for me to get over that,” she says. “But it was still good to know that IVIG was working for me.”

Christina first began IVIG treatments every week, but the frequency gradually decreased to biweekly, and now, after 11 years, she only needs treatment every 12 weeks.

Always a determined person, Christina wasn’t going to let her illness get in the way of what she had planned for herself.

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.
illness get in the way of what she had planned for herself. “I learned early on that I had to be an advocate for myself, and I think that really strengthened my outlook,” she explains. “I couldn’t sit there and feel sorry for myself, because no one else was going to.”

And, although she was frustrated when she had to miss out on things that others were doing or on the days after treatment when she didn’t feel well, she says that looking back, she is glad this happened to her. “It has made me an extremely stronger person than I would have been,” Christina says. “It has made me realize what is important.”

A Happier Chapter in Life

Five years after Christina’s diagnosis, she met her husband, Jeremy. She tells the story like it was yesterday: “We were on our first date, and he thought I was nervous,” laughs Christina, because her hands were shaking. “So, I said I probably should tell you this so you know right away.” She told him that the shaking in her hands was caused by damage to her nerves, caused by CIDP. The irony is that Jeremy not only was familiar with the symptoms of CIDP, but with IVIG treatments. In 2002, while Jeremy’s family was vacationing in Canada, his dad had gotten up in the middle of the night and had fallen down paralyzed. He was diagnosed with GBS and treated with IVIG.

Shortly after marrying, Christina and Jeremy wanted to start a family, but Christina was afraid. “When I was first diagnosed, I had a neurologist who was old school,” explains Christina. “He said I didn’t need to understand why, but that I would never be able to have children. That was clearly devastating to me. But, when I went to the Mayo Clinic, they made it very clear to me that this was not the case.”

Still, she wasn’t sure. What if she had a relapse with the physical stress of pregnancy? Or, what if she couldn’t continue with her IVIG treatments? Christina did some research about CIDP, but she found that “the majority of people who have it tend to be between 45 and 60, so there weren’t really cases of young women who had CIDP who I could use [as an example] to see if everything was going to be OK. It was unknown.”

Kris McFalls, IG Living’s patient advocate, put Christina in touch with another neurologist who reassured her that from his perspective there wasn’t any concern. A year later, Christina was pregnant, and her daughter, Abigail (Abby), was born in March 2010.

Contrary to Christina’s concerns, she learned that instead of having to discontinue her IVIG treatments, she had to increase them. “It was three months into the pregnancy, and I started to get weak, which is normally the first symptom of needing treatment, [even though] I had just had treatment a month prior,” says Christina. So, her immunologist decided that she would have treatment every six weeks (twice as often). In addition, rather than taking Solu-Medrol prior to treatments, she opted to switch to Benadryl.

Today, Christina is back to her normal treatment protocol, receiving IVIG every 12 weeks. When asked if she feels the pregnancy had any long-lasting effect on her energy level, she says, “I would say that I am more tired, but I don’t know if that’s because of the CIDP or because I have a baby.”

Looking on the Positive Side

While there are no support groups near to where she lives, Christina is a member of the GBS/CIDP Foundation and receives its newsletter. But, mostly, she relies on her own positive attitude to deal with her illness. CIDP “will only define you as much as you let it define you,” she says. “It’s awful, quite frankly, to have it affect your life, but there are so many diseases that have no cure, no hope. The great news is there is a treatment that can make you feel better. That’s the amazing thing.”

After reflecting on the 11 years of dealing with CIDP, she says it amazes her who she is today.

RONALE TUCKER RHODES, MS, is the editor of IG Living magazine.
IN MY DREAM, I am jumping out of bed and running to the shower — full of energy to start my day. There is so much to do! It’s almost wedding day! Not mine, but another lovely bride’s, and I am doing just what I love! Yes, today, I am going to the Los Angeles Flower Mart to buy 12 dozen roses, daisies, purple orchids and bundles of other beautiful flowers for centerpieces and bouquets for the wedding tomorrow.

Then, reality hits. My alarm goes off at 5:30 a.m., and I can’t move. After three minutes, I manage to roll over on my back, but my body is stiff. My ribs are crackling and sore as I try to sit up. My heart is beating fast, and my knees don’t want to straighten out.

I have things to do! I force myself through the pain and stand up. I figure that once I stand up things will be easier. Blah! I slowly get dressed and my sister, who is also my lovely assistant, helps me to get my shoes on. We have our list and are heading to the car when “grrrr” goes my stomach. I run to the bathroom. We head again to the car when the lovely noise and cramps start again. “Bbbbbuuuuuuuuuuuuuuuuuu.” I run back to the bathroom. This happens four times before we are able to pull out of the driveway. I don’t think my stomach likes waking up before 8 a.m.

When we get back from the Flower Mart, we begin getting the arrangements ready for the big day. We start by cutting every stem, taking off all of the leaves, getting the vases ready with water and foam, and then separating and organizing each stem by type and color. We have 27 arrangements to make and less than a day to complete them.

Stems are flying and flowers are being secured. We are working fast, and everything is turning out beautifully! I couldn’t be happier that I managed to make 27 centerpieces, three bouquets, three corsages and eight boutonnieres in a little more than six hours.

As we sit down for a nice, well-deserved dinner, even relishing in our success couldn’t make my pain go away. That’s when I realized I had been standing up for more than eight hours; I don’t think I sat down once. My legs are stiff, and I feel as if I have just finished running a marathon. I just need to go to bed.

Comparing my dream with reality: I was way off! I had this magical idea about how I wanted things to happen, but I left a few things out of the equation when I dreamed about my day. The main thing: my compromised health. I have to accept the fact that I can’t keep going and going without getting tired or at least taking a break. I didn’t have to get the job done in six hours. I could have spread out the work and taken some breaks in between. Shoulda, coulda, woulda … right? But, when my adrenaline was pumping and I felt like I could work for days, reality overcame the truth and I became the dream! I was seeing results, and I couldn’t get enough.

What have I learned from this? Regardless of what my body is saying, sometimes I need to be a fortuneteller and predict that if I don’t take a break, I will suffer for it later. I need to remember the truth and try to stay away from the dream. At least until I fall asleep.

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!
Myrna: Why does my “sed rate” rise dramatically after infusion?

Kris: I asked Dr. Melvin Berger to reply to your question.

Dr. Berger: The “sed rate,” or sedimentation rate, is also known as the “erythrocyte sedimentation rate” (ESR). When anticoagulated whole blood is put into a long, thin tube, which stands up vertically, the rate at which the erythrocytes (red blood cells) settle or “sediment” due to gravity is recorded. Normally, the red blood cells have a little bit of electric charge on their surface (like static electricity), which causes them to repel each other so they do not sediment very quickly. The normal rate is only a few millimeters an hour. However, if there are increased amounts of certain proteins in the blood, the protein molecules may stick to the surface of the red blood cells by static electricity and neutralize the negative charge of the cells. In that case, the normal repulsion decreases, and the cells sediment faster, so the ESR, or sed rate, is increased.

The amount of the proteins in the blood that can neutralize the charge on the cells increases rapidly when the body is fighting an infection, or when there is inflammation someplace in the body. When these proteins, called “acute phase reactants,” increase, the ESR increases. The red blood cells also may sediment faster if they are coated with antibodies against their surface molecules — like the sugars that make up the blood group antigens (A, B, Rh(D) positive, etc.). The sed rate test, therefore, gives diagnostic and monitoring information much like taking a patient’s temperature, but it is much more sensitive.

Normally, IgG infusions do not increase the sed rate. But, if the sed rate does go up after an infusion, it may mean that there is chronic infection present that is not being recognized by the body due to antibody deficiency. It is not unusual for patients with antibody deficiency to have chronic (subclinical) sinus and/or bronchial infections of which they are unaware. If that is the case, when an IgG infusion is given, the antibodies alert the body to the presence of the infection, white blood cells rush to the site to fight the bacteria, and there is an “acute phase response,” which may raise the sed rate. Sometimes, the response is strong enough to cause flu-like symptoms and/or fever. And, this situation can occur repeatedly if the response is not sufficient to totally get rid of the infection; it may even suggest that antibiotics are needed.

Most of the current IgG products contain some antibodies against blood group antigens, like those of the A, B or Rh(D) types. The plasma of normal people (from which IgG is made) usually contains antibodies against blood group antigens different from their own. Modern methods of manufacturing IgG preserve these antibodies, so it is possible that some patients who receive IgG, particularly high doses intravenously, will have some antibodies binding to their red blood cells after an infusion. While this may temporarily increase the sed rate, it rarely causes clinical problems. A Coombs test can determine if the red blood cells have bound antibodies from the infusion.

Megan: Recently, I had pain in my ribs, and an ultrasound of my spleen showed it was enlarged. I was told that there is not a significant way to reduce the spleen size except with radiation. Are you aware of common variable immune disease (CVID) patients developing an enlarged spleen, and do you know how it can be treated?

Kris: The function of the spleen is to filter the blood to remove abnormal blood cells. An enlarged spleen can be caused by a buildup of lymphocytes as a result of infections. According to the Immune Deficiency Foundation’s Patient and Family Handbook (www.primaryimmune.org/publications/book_pats/e_ch02.pdf), it is not unusual for someone with CVID to have an enlarged spleen. If you have not already, you should consult with your immunologist to help determine the cause of your enlarged spleen before deciding on treatment.
**A Spoonful of A1 Sauce**

By Cheryl L. Haggard

**ONE OF MY** favorite movie moments is when Mary Poppins serenades her reluctant, damp-footed brood to convince them that a “spoonful of sugar makes the medicine go down.” Frankly, I’d love a taste of her magical rum punch when I need to take over-the-counter cough syrup. Despite cheering myself on with: “Past the lips! Through the gums! Look out stomach: Here it comes!” I can’t help but make the “eewie” face after chugging the prescribed tablespoons of bitter elixir.

Modern pharmaceuticals have done a marvelous job taking Ms. Poppins’ advice to create flavor preparations for liquid medications. These prescription enhancers come dangerously close to the taste of my favorite miniature jelly bean treats: strawberry, buttered popcorn, coconut and peanut butter ‘n’ jelly. And despite it not quite being a clone of our beloved Mary’s rum punch (roll that “r”!), I appreciate knowing a little touch of the “grape” in my PIDD kids’ Augmentin does help the elixir pass the taste bud test.

Those early years of unsweetened prescriptions seem like a dream, or more like a nightmare! My toddlers’ footed pajamas bear scars, where spit-up, forced-down, miss-aimed and foul-tasting antibiotics didn’t quite make it down the infected’s hatch. The ache of frustrations past are unwelcome memories — some so vivid they seem too close for comfort. If bribing or holding the uncooperative didn’t work, my husband, Mark, and I resorted to literally choking down the bacteria-killing swill. After hours of battling, we’d be covered in more medicine than what was in the kid. Spent and wiping sticky, green sinus goo off my nightshirt, I’d point at myself and sob dramatically, “I wish they’d make a drug for this!”

These memories are now tucked gently into my cerebellum in case I need a swift reminder of how grateful I am to have made it to the pill-swallowing stage with our now pre-pubescent patients. No more failed attempts. No more hiding prescriptions in Jell-O, applesauce, pudding, ice cream or yogurt (not that my kids fell for those tricks anyway). No more unforgiving amoxicillin spots. Spray ’n Wash is now for “normal people” stains.

We thought we had made it to the top of the mountain, and there was no looking back. Until our PIDD kid Caleb (age 11) got a horrific thrush infection.

“So, we need to treat the thrush before we can go after the sinus infection,” Dr. Stubach announced while
penning a prescription into her computer.

I nodded in numb obedience. I wanted to ask how the medical community treats thrush in older kids, but somehow my mouth and fearful memories of thrush infections from long ago didn’t want to connect.

“OK, I just emailed Caleb’s script to your pharmacy and I want him to get two treatments in by bedtime,” Dr. Stubach instructed, as she ripped the prescription off the pad and handed it to me.

Caleb was busy fiddling with a potty-protector paper airplane he had just constructed, too busy to care about his impending medicinal future.

“Um, uh, OK,” I muttered, looking fearfully at my innocent, foul-breathed boy.

Reading the prescription, my deepest fears bounced right off the square watermarked paper.

All I needed to see were the words “swish in mouth” and “gargle” to know we were in for a very long five days.

You might think, “Well, all she’s gotta do is get the medicine flavored.” You’re exactly right. Except for one thing: Caleb can’t stand any of the 21 or so flavors offered. Believe me, we’ve tried.

“OK, Son,” I cooed, sucking exactly 5 mls of liquid into the syringe. “All you have to do is rinse your mouth out with a little bit of this stuff for a few seconds and then you’re back in the saddle,” I said, standing over the kitchen sink just in case.

The look on my son’s face as I thrust the syringe in his direction told me this was not going to go well. It’s as if he had just sucked on a green lemon, as he sniffed and inspected the trapped liquid. I have to admit, it just didn’t look appetizing; even I couldn’t imagine noshing on the impossible.

Two sniffs, a stiff, defiant pucker and a “there-is-no-way” look on Caleb’s face drew the battle line.

I dropped the syringe in defeat. I can’t fight this battle, I thought.

Wallowing in demise, I hung my head, wondering how Caleb was ever going to do this. Then, what to my wondering eye did appear, but a bottle of A1 Steak Sauce drew near.

“What in the world ... ,” I said.

“It’s OK, Mom! I’ve had a stroke of genius!” Caleb gushed.

I stood in awe as Caleb drew fresh medicine into the syringe and squeezed it into his mouth, followed by about three shots of A1.

You see, like most PIDD kids, Caleb has suffered through numerous (too many to count) ear, sinus, throat and lung infections, so his taste buds are, for the most part, shot. Not to mention, he has an age-appropriate disdain of the lower part of the nutrition pyramid.

Caleb has overcome his taste bud deficiency by choosing to nosh on spicy, vinegary and uber-tart foods. In order to savor meat, for example, he pours a lake of A1, piles on the Pappy’s and liberally squirts lemon all over his beloved protein. I’ve often wondered if catsup has turned up in his blood draws!

All my worries were for naught. Caleb’s creative seasonings did the trick and he was able to recover nicely from the thrush infection. In fact, I think he had a bit of fun grossing us out with his mouth rinses (as if his sinus washes weren’t bad enough!).

Six days later, Caleb and I took a trip to our local big box store to pick up his antibiotic, steaks and a gallon jug of A1 to restock the fridge.

“That’s an interesting combination,” the pharmacist commented.

“Planning a barbecue?”

“Naw, just getting the medicine to go down a wee easier,” I winked.

As we made our way out, a woman behind me in the pharmacy tapped me on the shoulder.

“Scuse me,” she said. Her too-familiar disheveled, desperate, baggy-eyed look with an obviously ill baby on her hip brought back memories of those awful first infections. “Will you repeat what you said to the pharmacist about ‘the medicine going down’?”

“Sure!” I replied.

I wasn’t even through with Caleb’s concoction when she turned and darted toward the condiments aisle. Scurrying as fast as she could, Kleenex and pea-green snot flying, she waved and shouted, “Thank you! Thank you so much!”

“Hey, Mom, isn’t that the woman you were talking with just a minute ago?” Caleb asked as we were driving away.

As my window slowly came down, she came over to the car and asked, “So what do you do to get him to eat veggies?”

Suddenly, I got my own stroke of genius. I grabbed the A1 and caressed it silently as if I were Vanna.

Later that night, Caleb got his first taste of my newest side dish: A1-smothered broccoli.

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.
LEMS Syndrome 101

Lambert-Eaton myasthenic syndrome (LEMS), a rare neuromuscular disorder, is difficult to diagnose and is frequently associated with cancer. Three people show how a positive attitude is what it takes to live with the disease.

By Cheryl L. Haggard

IS IT POSSIBLE for three people who have never met each other to cite chapter and verse of each other’s life stories? It is possible, if they share the diagnosis of Lambert-Eaton myasthenic syndrome (LEMS).

LEMS is an autoimmune disease that manifests as a neuromuscular (brain and muscle) disorder. LEMS is caused when the autoimmune response interferes with the release of acetylcholine (ACh), a neurotransmitter that activates muscles, regulating many bodily functions and helping carry messages from nerve cell to nerve cell in the brain.

The Mysterious Symptoms of LEMS

Before Sharon Southern was diagnosed with LEMS, she kept asking herself: “What’s wrong with me?”

Sharon’s professional life as an employee of an Australian airline and her passion for swimming were interrupted by sudden onset of chronic dry mouth and muscle weakness in her extremities. “My mouth was so dry, I had to keep sipping water just so I could swallow,” Sharon says. “Then I started having bouts of diarrhea, then terrible constipation. When I noticed my left eye was beginning to droop and my body, especially my legs, became weak, I thought to myself, ‘You’re becoming a hypochondriac, and you’re only 38 years old!’”

Bill Oehlke had a similar experience with LEMS. Climbing and lifting were all part of Bill’s daily routine as a fire chief. But after 11 years of progressively struggling with muscle weakness, even to the point of needing to push himself up with his arms from seated and prone positions, Bill’s wife of over 46 years knew something just wasn’t right. “When I couldn’t finish talking, chewing and swallowing, I thought I was next.”

Susan Harper, a social worker who lives with LEMS, can relate to Bill’s experience. “I was angry at myself, thinking my muscle weakness was due to laziness,” she explains. “When I was able to feel the bones in my legs, I was afraid that the next step was to plan my funeral.”

The real next step for Susan, Bill and Sharon was to seek the best possible medical opinion for their mysterious and maddening symptoms, and get the proper diagnosis.

Proper diagnosis protocol is important to achieving an accurate diagnosis, particularly because LEMS has an underlying cancer risk, as much as 60 percent.

How LEMS Is Diagnosed

LEMS is easily misdiagnosed. After Susan was misdiagnosed with myriad diseases, including chronic inflammatory...
demyelinating polyneuropathy (CIDP) and multifocal motor neuropathy, and then rediagnosed with Sjogren’s syndrome, lupus and connective tissue disorder, her third neurosurgeon concluded she might have been dealing with myasthenia gravis (MG), which has some symptoms similar to LEMS. She was then referred to a fourth neurosurgeon, who performed a series of diagnostic tests and scans that could distinguish between MG and LEMS.

The diagnostic tests included an electromyogram (EMG), which measures the electrical activity of muscles at rest and during a contraction, as well as nerve conduction studies (NCS), which measure how well and how fast the nerves can send electrical signals. With these tests, a physician can quickly and accurately begin to crack the code of a patient’s common complaints of weakening extremities, dry mouth and bladder dysfunction.

Dr. Robert Friedman, who consults on MG and LEMS cases for the Muscular Dystrophy Association, explains that there are clear clinical differences between the diseases. Proper diagnosis protocol is important to achieving an accurate diagnosis, particularly because LEMS has an underlying cancer risk, as much as 60 percent. “In myasthenia gravis, when you repeat the nerve stimulation, the muscle response declines rapidly, whereas in LEMS, it’s the complete opposite,” explains Dr. Friedman. “As LEMS patients exercise, they typically get stronger and stay stronger with proper medication.”

Along with EMG and NCS testing, blood work to detect antibodies to acetylcholine receptors is key to confirming LEMS. According to Dr. Friedman, this is where the rubber meets the road. Some 85 percent to 90 percent of people with LEMS test positive for antibodies against voltage gated calcium channel (VGCC), a protein that allows calcium entry into nerve cells, which is required for acetylcholine release. There is evidence that cancerous cells inappropriately make VGCC, triggering the immune system to make anti-VGCC antibodies. “Once a patient tests positive for voltage gated calcium channel antibodies, we confirm LEMS and go looking for a tumor,” Dr. Friedman continues. “LEMS suddenly takes a back seat, and we go after cancer.”

And timing is everything. “After a positive VGCC antibody test, we begin with everything available to us to find the neoplasm, including PET [positron emission tomography], CT [computed tomography], MRI [magnetic resonance imaging] and chest X-rays,” Dr. Friedman explains, although sometimes it may take up to five years before a tumor is detected. And, “because of the high risk of cancer in LEMS patients, we must routinely check for carcinoma. It’s always looming in the back of our minds.”

Physicians and patients are particularly concerned about a LEMS diagnosis because small cell lung cancer (SCLC) is most frequently associated with LEMS. What is interesting is that 3 percent of patients with SCLC have LEMS, and almost all SCLC sufferers with LEMS have a smoking history. The good news is this: If cancer is not found within two years, the chances of a LEMS patient developing cancerous tumors decrease.

**Ultimately, a good marriage of medical therapy and support systems can create positive quality-of-life outcomes for patients with LEMS.**

Treating LEMS

According to Dr. Friedman, successful treatments depend on the patient. Ultimately, a good marriage of medical therapy and support systems can create positive quality-of-life outcomes for patients with LEMS.

Prior to cancer treatment, or in LEMS patients without cancer, immunosuppressant drugs, intravenous
immune globulin (IVIG) and/or plasmapheresis (a plasma exchange where antibodies are removed from the blood) are quite helpful. According to the Muscular Dystrophy Association, IVIG is essentially an infusion of antibodies that might work by dialing down the immune system's production of its own antibodies, much as warm air tells a thermostat to stop pumping out heat.

For many LEMS patients, symptom relief is achieved with Mestinon, which allows more ACh to accumulate, improving the transmission of electrical impulses, and/or 3, 4-diaminopyridine (DAP), an FDA-designated orphan drug for the treatment of LEMS. “When I arrived home after my first dose of DAP, I sat down and went to cross my legs,” Susan recalls. “In the past, I needed to use my hands to lift my legs. I was able to lift my leg with just my leg! In fact, I almost kicked myself in the head as this was such a dramatic change.”

Living with LEMS

For Bill, Susan and Sharon, a positive attitude is the common denominator for living with such an uncommon disease.

“They made me a permanent greeter at church because I’m so well-known,” Bill joked. “Not known because of my LEMS, but because I’m such a likable guy!” After almost 16 years living with LEMS, Bill defied the cancer statistics. He published two books about the fire department and was working on a third when, in February 2008, he passed away due to complications from LEMS.

Within months of Susan’s LEMS diagnosis, she was found to have a 0.5 millimeter spot in one lung that has been carefully monitored. This past December, she had her five-year CT scan, and since there is no change in the spot, she is considered to be cancer-free, which, says Susan, “is an incredible boost to my morale!” To keep her mind and her body sharp, Susan took to the art of cross-stitch and sends her finished products “to people sicker than I am,” she says. “I was tired of existing as a human being instead of a human doing.” Some of her work is being used by an online group called Love Quilts, which creates and gives cross-stitched quilts to ill children. Her work also has been sold to support a children’s hospice and an air ambulance in England. In addition to cross stitch, Susan started an online support group for people with LEMS.

Nine months after being diagnosed with LEMS, Sharon was diagnosed with breast cancer and had a mastectomy “that almost took my life,” she explains. She suffered an internal bleed and had to have several blood transfusions. “Lying in my hospital bed after my mastectomy, I had to make a choice about my illness,” Sharon recalls. “I made the decision: ’I don’t just plan to survive, I plan to thrive.’” Now, five years later, she is cancer-free. And, whenever she feels temporary emotional twinges related to her LEMS, she will mentally rehearse her father’s favorite saying: “I complained I had no shoes, until I saw a man with no feet.”

Related Organizations

Muscular Dystrophy Association: www.mdusa.org
Myasthenia Gravis Foundation of America: www.myasthenia.org
National Organization of Rare Disorders (NORD): www.rarediseases.org
American Autoimmune Related Diseases Association: www.aarda.org
Autoimmune Information Network: www.aininc.org
LEMS Yahoo Group: groups.yahoo.com/group/Lambert-Eaton/join

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.
After the Rain: Overcoming Diabetes, Lupus, Arthritis, Sarcoidosis, Prednisone, Obesity

Author: David Dobson
Publisher: Xlibris Corp., www.xlibris.com

David Dobson was told at age 38 that he wouldn’t live past 40. Now, at age 45, he is in perfect health and enjoying a healthy and active lifestyle. This book, written with Dobson’s lighthearted sense of humor, explains how after many years living with diabetes, sarcoidosis, lupus, obesity and arthritis, his health turned around in a very short period of time, and now he no longer has to rely on any medications. Chapters look at the various diseases and how the diet, exercise and lifestyle components play a role.

Autoimmune Diseases of the Endocrine System

Author: Robert Volpe
Publisher: CRC Press, www.crcpress.com

This book is a comprehensive, easy-to-read discussion of the organ-specific autoimmune endocrine diseases, emphasizing new contributions and trends for research and management. It begins with a brief chapter introducing the general principles of immunology, followed by discussions covering topics such as immunogenetics and animal models and how they can be applied toward interpreting human autoimmune endocrine diseases, autoimmune thyroid diseases, insulin-dependent diabetes mellitus hypophysitis, and Addison’s disease. The book also discusses future trends toward gaining an understanding of these disorders and possible therapeutic principles.

Combination Treatment in Autoimmune Diseases

Author: W.B. Harrison and B.A.C. Dijkmans (eds)
Publisher: Springer Publishing, www.springerpub.com

Published in 2002, this book consists of contributions from the most prominent experts in this field. In the first section, the general principles of combination treatment are discussed, from rationale and methodology to benefits of risks in daily practice. The second section concerns specific diseases. The last section is devoted to the future, and the editors hope to come back with an issue that will look back and determine whether the experts’ predictions have come true.

Time to Care: Personal Medicine in the Age of Technology

Author: Norman Makous, MD, with Bruce Makous
Publisher: TowPath Publications, www.brucemakous.com

In Time to Care, Dr. Norman Makous, who has spent 60 years providing personal care to his cardiology patients, examines how the high cost of technology-based care has caused the economic squeeze in healthcare that has already led to the rationing of medical services. He proposes that the patient-doctor relationship can be brought back to the center of the healthcare system to humanize treatment, improve quality and reduce unnecessary spending. The book is filled with dozens of real-life case anecdotes that illustrate the crucial role of the patient-doctor relationship and how medical practice has changed in recent decades.
Choosing an Infusion Pump
By Kris McFalls

LITTLE ATTENTION is paid to infusion pumps, which are used to deliver medications to patients in a controlled manner, unless there is a problem. This is because the choice of which infusion pump to use is typically made by the infusion provider. Patients often don’t realize they have a choice of pumps, and doctors usually will order whatever pump is recommended by the provider. And although cost is a factor, safety, reliability and ease of use also are considerations.

Cost Consideration
Providers have to weigh cost as an important factor when deciding which pump to carry, especially since the prices vary greatly. In fact, some pumps can cost as much as a nice used car. Additionally there are maintenance costs. Electronic pumps, in particular, require yearly maintenance to ensure they are clean and calibrated correctly. Failing to properly maintain equipment could result in a malfunction of the pump, fines for the provider and harm to the patient. And, since the cost of maintenance is typically not paid for by insurance, in most cases, it falls on the provider.

If deciding to purchase a pump on their own, most patients have a durable medical equipment (DME) benefit that will cover part of the cost. However, many insurance companies limit the reimbursement for all DME to $2,500, leaving all extra costs, including maintenance, up to patients.

Another cost consideration when choosing a pump is supplies. Several pumps require the use of proprietary supplies, such as specialized tubing or syringes, that add further costs to the infusion process.

Taking into account all of the cost factors, it’s easy to see why providers limit their supply of infusion pumps to one or two models.

Other Considerations
Besides the cost of a pump, there are other important considerations, such as ease of use and reliability. Being able to consistently control the rate of a pump can be an important factor that helps prevent rate-related side effects. Many of the electronic pumps do a very good job controlling the rate. Additionally, many of the electronic pumps include alarms to alert the caregiver about possible problems, such as occlusions and air in the line.

Infusion pumps, significantly more portable than traditional intravenous drips with a pole setup, can provide increased mobility to patients receiving home infusion. Often, backpacks or fanny packs are used to hold the pumps to help give the patient more freedom of movement and a decreased risk of snagging the infusion line when ambulating.

IG patients choosing subcutaneous IG (SCIG) instead of intravenous IG (IVIG) find utilizing a syringe driver pump is especially helpful. IG is already a viscous solution, but SCIG products are higher in concentration and even higher in viscosity. Having a good syringe driver pump that can deliver the medication with even pressure in a controlled manner is paramount for comfortable and successful treatment.

Consider All Factors
All factors must be considered when choosing an infusion pump. Ideally, doctors, patients and pharmacists should team up to consider all options to find a solution that will work best for each patient to ensure optimal treatment.

KRIS MCFALLS is the full-time patient advocate for IG Living magazine.

Directory of Infusion Pumps

Moog
The 4000 Clinical Management System is a multi-therapy ambulatory electronic infusion pump capable of continuous, PCA, PCEA, subcutaneous, TPN, intermittent and variable modes. It can be easily programmed with menu-driven protocols and context-sensitive help screens. It measures 5.1-by-4.0-by-2.5 inches and weighs 17.5 ounces.
(800) 970-2337; www.moog.com/products/medical-pump-systems/infusion-pumps/4000-cms

IntraPump
The Crono S-PID50 has a small and compact size, runs on batteries and was designed with subcutaneous immuno-globulin in mind for the home setting. It offers continuous administration and bolus administration of medications and has a very high
PSI and occlusion alarms, appropriate for highly viscous medications. A liquid crystal display (LCD) shows relevant information to patient and physician with respect to settings, delivery time and diagnostics. 
(866) 211-7867; www.intrapump.com

**MarCal Medical**

The Graseby 3400 offers a wide range of infusion rates. Unlike many other syringe drivers, it is compatible with many syringe sizes and tubing, which makes it cost-effective, as there are no dedicated disposables. The operation is simple, and it features an easy-to-read display. It runs on batteries and also requires at least yearly maintenance. 
(800) 628-9214; www.marcalmedical.com

**Micrel Medical Devices**

The Micrel MP101 syringe driver provides infusion therapy for a wide range of applications. It is an efficient infusion system for delivery of small volume medications, and can be used in both the homecare and hospital setting. Features include a simple rate setting with an LCD display, clear identification of alarms detected and a double microprocessor. It is lightweight and portable, has an ultra-low battery consumption, and comes with a shoulder holster for ambulatory use, plastic carrying case, operating instructions and a set of batteries. 
30 210 6032333 (Greece); www.micrelmed.com

**RMS Medical Products**

The Freedom 60 pump requires no electricity or batteries; the patient just needs to wind it up. It utilizes proprietary tubing to administer subcutaneous infusions at predetermined rates. It is very portable and effective and requires no preventive maintenance. While it may be a bit larger than some of the ambulatory competitors, its ease of use has made it a popular choice for subcutaneous therapies. 
(800) 624-9600; www.rmsmedicalproducts.com/Freedom60info.htm

---

**THE QUALITY YOU DESERVE**

CRONO S-PID 50 ambulatory infusion pump

For optimal results with subcutaneous therapy

- Delivers maximum PSI
- Easily adjustable rate
- Greatest accuracy
- Best suited for Hizentra™

920 Minters Chapel Rd, Suite 200, Grapevine, TX 76051 
1-866-211-7867 | www.intrapump.com
Sources

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

General Resources

Other Organization Websites
These organizations provide information about various disease states, which can be found by conducting a search of the disease state name.

- Advocacy for Patients with Chronic Illness: www.advocacyforpatients.org
- Alliance for Plasma Therapies (fair access to plasma therapies): www.plasmaalliance.org
- American Autoimmune Related Diseases Association (AARDA): www.aarda.org
- American Chronic Pain Association (ACPA): www.theacpa.org
- Band-Aides and Blackboards: www.lehman.cuny.edu/faculty/jfleitas/bandaides
- Cleveland Clinic: www.clevelandclinic.org/health
- eMedicine from WebMD: emedicine.medscape.com
- FamilyDoctor.org: www.familydoctor.org
- Johns Hopkins Medicine: www.hopkinsmedicine.org
- KeepKidsHealthy.com (pediatrician’s guide to children health and safety): www.keepkidshealthy.com
- Mayo Clinic: www.mayoclinic.com
- National Committee for Quality Assurance (detailed report cards on health plans, clinical performance, member satisfaction and access to care): www.ncqa.org
- 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.csblehring.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 Polynueropathy (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
Mitochondrial Disease
Websites
- United Mitochondrial Disease Foundation: www.umdf.org

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

Multiple Sclerosis (MS)
Websites
- All About Multiple Sclerosis: www.mult-sclerosis.org/index.html
- Multiple Sclerosis Association of America: www.msaa.com
- Multiple Sclerosis Foundation: www.msfacts.org
- National Multiple Sclerosis Society: www.nationalmssociety.org
Online Peer Support
- Friends with MS: www.FriendsWithMS.com
- MSWorld’s Chat and Message Board: www.msworld.org

Myasthenia Gravis (MG)
Websites and Chat Rooms
- Myasthenia Gravis Foundation of America (MGFA): www.myasthenia.org
Online Peer Support
- Autoimmune Information Network Inc.: www.aininc.org

Myositis
Websites
- The mission of The Myositis Association, www.myositis.org, is to find a cure for inflammatory and other related myopathies, while serving those affected by these diseases. (703) 299-4850
- The Cure JM Foundation www.curejm.com (760) 487-1079

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

Primary Immune Deficiency Disease (PIDD)
Websites
- The Immune Deficiency Foundation (IDF), www.primaryimmune.org, is the national patient organization dedicated to improving the diagnosis, treatment and quality of life of persons with primary immunodeficiency diseases through advocacy, education and research. (800) 296-4433
- 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 "Autoimmune Diseases.
- American Academy of Allergy, Asthma & Immunology: www.aaaai.org
- International Patient Organization for Primary Immunodeficiencies (IPOPI): www.iopoi.org
- Michigan Immunodeficiency Foundation: www.midf.org
Sources

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

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

Scleroderma

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

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

Stiff-Person Syndrome (SPS)

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

Other Resources

Education and Disability Resources
- Individuals with Disabilities Education Improvement Act of 2004: http://idea.ed.gov/explore/home
- National Disabilities Rights Network: www.ndrn.org
- 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.”
- U.S. Department of Health and Human Services, Office of Civil Rights: www.hhs.gov/cosb
- U.S. Department of Health and Human Services, Office of Civil Rights: www.hhs.gov/cosb
- U.S. Department of Health and Human Services, Office of Civil Rights: www.hhs.gov/cosb

Medical Research Studies
- ClinicalTrials.com: www.clinicaltrials.com
- ClinicalTrials.gov: www.clinicaltrials.gov
- World Allergy Organization: www.worldallergy.org

Food Allergies
- Allergic Disorders: Promoting Best Practice: www.aaaaa.org
- American Partnership for Eosinophilic Disorders: www.apfed.org
- Food Allergy and Anaphylaxis Network: www.foodallergy.org
- Food and Drug Administration: www.fda.gov
- 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.cslehring-us.com/s1/cs/enus/1151517250474/Web_Product_C/1151517249408/ProductDetail.htm
- 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.safeyardsmedicinalproducts.com
- Grasby Marcal Medical: www.marcalmedical.com
- Intra Pump Infusion Systems: www.intrapump.com
- Micrel Medical Devices: www.micrelmed.com
- Norfolk Medical: www.norfolkmedical.com
- Repro Med Systems, Inc: www.rmsmedicalproducts.com
- Smith Medical: www.smiths-medical.com/brands/cadd

Have something to add to these pages? Please send your suggestions for additions to the IG Living Resource Directory to editor@IGLiving.com.
Hizentra is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of human immune globulin or to components of Hizentra, such as polysorbate 80. Hizentra is contraindicated in patients with hyperprolinemia because it contains the stabilizer L-proline (see Description [11]). Hizentra is contraindicated in IgA-deficient patients with antibodies against IgA and a history of hypersensitivity (see Description [11]).

5. WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity

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

Individuals with IgA deficiency can develop anti-IgA antibodies and anaphylactic reactions (including anaphylaxis and shock) after administration of blood components containing IgA. Patients with known antibodies to IgA may have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions with administration of Hizentra. Hizentra contains ≤50 mcg/mL IgA (see Description [11]).

5.2 Reactions Reported to Occur With IGIV Treatment

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

Renal Dysfunction/Failure

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

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

Thrombotic Events

Thrombotic events may occur with use of human immune globulin products. Patients at increased risk may include those with a history of atherosclerosis, multiple cardiovascular risk factors, advanced age, impaired cardiac output, hypercoagulable disorders, prolonged periods of immobilization, and/or known or suspected hyperviscosity. Because of the potentially increased risk of thrombosis, consider baseline assessment of blood viscosity in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia, markedly high triglycerides (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>
<thead>
<tr>
<th>AE (≥4 Subjects)</th>
<th>All AEs*</th>
<th>AEs* Occurring During or Within 72 Hours of Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (%) of Subjects (n=49)</td>
<td>Number (Rate) of AEs (n=2264 Infusions)</td>
<td>Number (%) of Subjects (n=49)</td>
</tr>
<tr>
<td>Local reactions</td>
<td>49 (100)</td>
<td>1340 (0.592)</td>
</tr>
</tbody>
</table>
Table 4: (Continued)

<table>
<thead>
<tr>
<th>AE (≥2 Subjects)</th>
<th>All AEs*</th>
<th>AEs* Occurring During or Within 72 Hours of Infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number (%) of Subjects (n=49)</td>
<td>Number (Rate†) of AEs (n=2264 Infusions)</td>
</tr>
<tr>
<td></td>
<td>(Rate‡) of Subjects (n=2264 Infusions)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Rate§) of AEs (n=2264 Infusions)</td>
<td></td>
</tr>
<tr>
<td>Other AEs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>13 (26.5)</td>
<td>40 (0.018)</td>
</tr>
<tr>
<td>Cough</td>
<td>8 (16.3)</td>
<td>9 (0.004)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7 (14.3)</td>
<td>8 (0.004)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6 (12.2)</td>
<td>6 (0.003)</td>
</tr>
<tr>
<td>Back pain</td>
<td>5 (10.2)</td>
<td>11 (0.005)</td>
</tr>
<tr>
<td>Nausea</td>
<td>5 (10.2)</td>
<td>5 (0.002)</td>
</tr>
<tr>
<td>Abdominal pain, upper</td>
<td>5 (10.2)</td>
<td>5 (0.002)</td>
</tr>
<tr>
<td>Rash</td>
<td>5 (10.2)</td>
<td>7 (0.003)</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>4 (8.2)</td>
<td>7 (0.003)</td>
</tr>
<tr>
<td>Migraine</td>
<td>4 (8.2)</td>
<td>5 (0.002)</td>
</tr>
<tr>
<td>Pain</td>
<td>4 (8.2)</td>
<td>5 (0.002)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>4 (8.2)</td>
<td>6 (0.003)</td>
</tr>
<tr>
<td>Pharyngolyngeal pain</td>
<td>4 (8.2)</td>
<td>6 (0.003)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>4 (8.2)</td>
<td>5 (0.002)</td>
</tr>
</tbody>
</table>

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

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

- **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, 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 menigitis syndrome.
- **Integumentary:** Stevens-Johnson syndrome, epidermolysis, erythema multiforme, dermatitis (e.g., bullous dermatitis).
- **Hematologic:** Pancytopenia, leukopenia, hemolyis, positive direct antiglobulin (Coombs') test.
- **Gastrointestinal:** Hepatic dysfunction, abdominal pain.
- **General/Body as a Whole:** Pyrexia, rigors.

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

7 DRUG INTERACTIONS

7.1 Live Virus Vaccines

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

7.2 Serological Testing

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

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

8.3 Nursing Mothers

Hizentra has not been evaluated in nursing mothers.

8.4 Pediatric Use

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


Manufactured by:
CSL Behring AG
Bern, Switzerland
US License No. 1766

Distributed by:
CSL Behring LLC
Kankakee, IL 60901 USA

Based on March 2010 version
Before prescribing, please consult prescribing information, a brief summary of which follows. Some text and references refer to full prescribing information.

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

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

3 WARNINGS AND PRECAUTIONS
3.1 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 serious hypersensitivity reactions.

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.

4.5 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, asthenia, and gastrointestinal disorder.

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]).

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 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>31 (48%)</td>
<td>159 (0.04)</td>
<td>30 (46%)</td>
<td>104 (0.033)</td>
</tr>
<tr>
<td>Headache</td>
<td>24 (37%)</td>
<td>35 (0.01)</td>
<td>18 (28%)</td>
<td>24 (0.007)</td>
</tr>
<tr>
<td>Gastrointestinal disorder</td>
<td>16 (25%)</td>
<td>28 (0.08)</td>
<td>12 (18%)</td>
<td>20 (0.005)</td>
</tr>
<tr>
<td>Fever</td>
<td>12 (18%)</td>
<td>18 (0.005)</td>
<td>11 (17%)</td>
<td>15 (0.004)</td>
</tr>
<tr>
<td>Nausea</td>
<td>11 (17%)</td>
<td>22 (0.006)</td>
<td>10 (15%)</td>
<td>16 (0.004)</td>
</tr>
<tr>
<td>Rash</td>
<td>10 (15%)</td>
<td>17 (0.005)</td>
<td>8 (12%)</td>
<td>11 (0.003)</td>
</tr>
<tr>
<td>Sore throat</td>
<td>7 (11%)</td>
<td>8 (0.002)</td>
<td>5 (8%)</td>
<td>5 (0.001)</td>
</tr>
<tr>
<td>Allergic reaction</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>Skinfold 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>Anemia</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>2 (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>

Discontinuations due to AEs at the injection site: 3 subjects

* 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.
§ Defined as those reactions that made it impossible to perform routine activities.

Of the three subjects who discontinued the study due to injection-site reactions, one withdrew on Day 1 (Infusion 1) of the wash-in/wash-out period after a moderate injection-site reaction and a mild headache; one withdrew on Day 22 (Infusion 4) of the wash-in/wash-out period following severe injection-site reactions for two weeks; and one withdrew on Day 78 following a mild injection-site reaction.

Local reactions decreased substantially after repeated use.

Table 5 summarizes the most frequent adverse reactions (experienced by at least 3% of subjects) and considered by the investigator to be at least possibly related to Vivaglobin administration.

Table 5: Incidence of Subjects With Adverse Reactions (Experienced in ≥3% of Subjects) and Rate* Per Infusion in the US-Canada Study

<table>
<thead>
<tr>
<th>Related Adverse Reactions (≥3% Subjects)</th>
<th>Number (%) of Subjects (n=65)</th>
<th>Number (Rate*) of AEs per Infusion (n=3656)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse reactions at the injection site*</td>
<td>60 (92%)</td>
<td>1787 (0.49)</td>
</tr>
<tr>
<td>Other AEs reactions</td>
<td>21 (32%)</td>
<td>59 (0.016)</td>
</tr>
<tr>
<td>Headache</td>
<td>7 (11%)</td>
<td>9 (0.002)</td>
</tr>
<tr>
<td>Nausea</td>
<td>4 (6%)</td>
<td>9 (0.002)</td>
</tr>
<tr>
<td>Rash</td>
<td>3 (5%)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Gastrointestinal disorder</td>
<td>3 (5%)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Fever</td>
<td>2 (3%)</td>
<td>2 (0.001)</td>
</tr>
<tr>
<td>Skin disorder</td>
<td>2 (3%)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>2 (3%)</td>
<td>2 (0.001)</td>
</tr>
<tr>
<td>Urine abnormality</td>
<td>2 (3%)</td>
<td>3 (0.001)</td>
</tr>
</tbody>
</table>

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

6.2 Postmarketing Experience

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

Vivaglobin

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

General

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

- Renal: Acute renal dysfunction/failure, osmotic nephropathy
- Respiratory: Apnea, Acute Respiratory Distress Syndrome (ARDS), TRAIL cyanosis, hypoxenia, pulmonary edema, dyspnea, bronchospasm
- Cardiovascular: Cardiac arrest, thromboembolism, vascular collapse, hypotension
- Neurological: Coma, loss of consciousness, seizures, tremor, aseptic meningitis syndrome
- Integumentary: Stevens-Johnson syndrome, epidermolysis, erythema multiforme, bullous dermatitis
- Hematologic: Pancreatitis, leukopenia, hemolysis, positive direct antiglobulin (Coombs') test
- General/Body as a Whole: Pyrexia, rigors
- Musculoskeletal: Back pain
- Gastrointestinal: Hepatic dysfunction, abdominal pain

7 DRUG INTERACTIONS

7.1 Live Virus Vaccines

The passive transfer of antibodies with immunoglobulin administration may interfere with the response to live virus vaccines such as measles/mumps/rubella and varicella (see Patient Counseling Information [17.2]).

7.2 Serological Testing

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

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

8.3 Nursing Mothers

Vivaglobin has not been evaluated in nursing mothers.

8.4 Pediatric Use

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

8.5 Geriatric Use

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

Manufactured by: CSL Behring GmbH
Marburg, Germany
Distributed by: CSL Behring LLC
Kankakee, IL 60901 USA
US License No. 1765
Based on April 2010 Revision.
If you live with primary immunodeficiency disease (PIDD)...

Make the leap to Hizentra

The Sub-Q Ig therapy that fits your life
- Self-administer on your schedule
- Ready-to-use Sub-Q Ig
- Room temperature storage—no refrigeration required
- From the maker of Vivaglobin®, Immune Globulin Subcutaneous (Human)

To learn about the benefits of Hizentra, visit www.LearnAboutHizentra.com
Ask your doctor about Hizentra today.

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.

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.
Now it’s easy when

YOU CHOOSE

your delivery dates!

Visit MyFluVaccine.com to secure YOUR best delivery dates.

Choice
Select from a broad portfolio of products

Convenience
Choose your delivery dates

Safety
Count on a secure supply

YOU PICK THE QUANTITY • YOU PICK THE DATE • WE DELIVER

MyFluVaccine | (800) 843-7477 | www.MyFluVaccine.com

Brought to you by FFF Enterprises, Inc., the nation’s largest and most trusted distributor of flu vaccine and critical-care biopharmaceuticals.