IG Dosing
An Individualized Approach

Autoimmune Disease & Drug-Drug Interactions

Understanding & Treating Multiple Sclerosis

Self-Prep for IG Therapy: To Prepare Is to Empower
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.
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.

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

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

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

WARNINGS AND PRECAUTIONS
- IgA deficient patients with antibodies against IgA are at greater risk of developing severe hypersensitivity and anaphylactic reactions. Have epinephrine available immediately to treat any acute severe hypersensitivity reactions.
- Monitor renal function, including blood urea nitrogen, serum creatinine, and urine output in patients at risk of developing acute renal failure.
- GAMUNEX-C is not approved for subcutaneous use in ITP patients. Due to a potential risk of hematoma formation, do not administer GAMUNEX-C subcutaneously in patients with ITP.
- Hyperproteinemnia, with resultant changes in serum viscosity and electrolyte imbalances may occur in patients receiving IGIV therapy.
- Thrombotic events have occurred in patients receiving IGIV therapy. Monitor patients with known risk factors for thrombotic events; consider baseline assessment of blood viscosity for those at risk of hyperviscosity.
- Aseptic Meningitis Syndrome (AMS) has been reported with GAMUNEX-C and other IGIV treatments, especially with high doses or rapid infusion.
- Hemolytic anemia can develop subsequent to IGIV therapy due to enhanced RBC sequestration. Monitor patients for hemolysis and hemolytic anemia.
- Monitor patients for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI]).
- Volume overload
- GAMUNEX-C is made from human plasma and may contain infectious agents, e.g., viruses and, theoretically, the Creutzfeldt-Jakob disease agent.
- Passive transfer of antibodies may confound serologic testing.

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

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

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

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

Talecris Biotherapeutics, Inc.
Research Triangle Park, NC 27709 USA
U.S. License No. 1716
08939771/08939782-BS
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Autoimmune Disease and Drug-Drug Interactions

“With autoimmune diseases, patients are almost guaranteed a drug therapy regimen that is comprised of multiple medications to treat the various manifestations of the disease.”

Understanding and Treating Multiple Sclerosis

“These are exciting times for the 400,000 individuals in the U.S. and the 2.5 million worldwide who suffer from MS and its related symptoms!”

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. And, we want you to be a part of it! Our blog, which has a new entry posted each Friday, provides interesting perspectives on topics such as living with IG, people to be admired, support and encouragement, current news of interest and things you just need to know. We encourage you to comment with your opinions and stories. And, better yet, if you have a blog you’d like to post, send it our way!

IG Living’s Facebook page has hundreds of fans who respond to our questions that are posted each Monday through Friday. Together, these fans share their life stories and thoughts. What’s more, they are making a connection with one another that otherwise wouldn’t be possible.

So, be a part of it now at www.igliving.com/blogengine and www.facebook.com/IGLivingMagazine.

Connect with Other IG Living Readers through Monthly Teleforsums!

IGL’s Readers Group Teleforsums allow readers to connect with others to share their experiences living with chronic diseases. Here’s how you can participate:

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

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

Sign up for the Teleforsums now by emailing kmcfalls@IGLiving.com or calling (888) 469-9720.
Immune Disease and Autoimmunity

According to the Department of Health and Human Services’ Office of Women’s Health, autoimmune disease and disorders ranked No. 1 in the top-10 list of most popular health topics requested by callers to the National Women’s Health Information Center. The reason? It is one of the top-10 leading causes of death in female children and women in all age groups up to 64 years of age.

Today, between 80 and 100 autoimmune diseases have been identified, and it is suspected that there are an additional 40 diseases that have an autoimmune basis. While the exact cause of autoimmune disease is unknown, it is believed to be a combination of genetic and environmental factors. And, it is documented that many with autoimmune diseases are those who also have been diagnosed with an immune deficiency.

One of those autoimmune diseases is multiple sclerosis (MS), which is becoming increasingly widespread. It is estimated that 250,000 to 350,000 people in the U.S. have been diagnosed with MS, with approximately 200 new cases diagnosed each week. But, it also is suspected that many more people with MS have yet to be diagnosed because, as with many autoimmune diseases, it sometimes doesn’t present until its acute stages. As we discuss in our article Understanding and Treating Multiple Sclerosis, the disease is quite complex, and while immune globulin (IG) is not the standard treatment for MS, it is now occasionally being used as a secondary treatment for those who have been in long periods of remission.

As if the complications of immune disease aren’t challenging enough, they are greatly increased with an autoimmune disease. It’s not uncommon for such patients to suffer long-term damage and to be prescribed multiple courses of treatment.

As Amy Ehlers, director of pharmacy at NuFACTOR Specialty Pharmacy and author of the article Autoimmune Disease and Drug-Drug Interactions explains: With autoimmune diseases, patients are almost guaranteed a drug therapy regimen that is comprised of multiple medications to treat the various manifestations of the disease. And with this, of course, comes the danger of drug interactions. She discusses many different disease states and their treatments that may present some potential complications.

Luckily, there have been no known interactions between autoimmune disease medications and IG. However, even with IG therapy, patients often continue to be plagued by a high rate of infection. Therefore, as more and more diseases are treated with immune globulin, it becomes more important than ever for physicians to determine what the appropriate dosing regimen is for each patient. In this issue, we present three recent studies that examine the relationship between infection and IG replacement dosing regimens — all of which strongly suggest that treatment needs to be individualized for each patient. These are new findings that counteract the traditional method of IG dosing. It is hoped that, in the near future, these findings will become the basis for treatment guidelines that will improve infection outcomes for IG patients.

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
What is it that your doctor does well that you wish all patients could experience?

Donna Altomare Rehb Mentz
Listen, comment and be concerned — always there for me no matter what. Once I was hospitalized and my husband left a message for him. He called right away, and it turns out he was on vacation in Utah! He’s the chief of his department and also a professor. Even his secretary locates him for me if I need him. He says: “I’m never too busy for you!” I am very lucky to have him for a doctor.

Malin Inger
My doctor and his nurses make me feel that we are in this mess together and that they’ll do everything they can to help me. They respect and value my “body” knowledge (I usually can tell which bacteria are having a party even before the test results have come back positive). They make me feel welcome every time I need to phone them or pay them a visit.

Connie Johnson Worthen
Our son is now 20, going from a child to an adult. Our doc has always wanted to know what he is up to, goals, likes and dislikes. She is awesome and has also called others for opinions. Bedside manner matters; that should be a required class when docs go to school!

Rachel Rich
My doc chuckles at just the right moment. I’ve got a sense of humor, too, so it lifts my spirits.

Mark Leventhal
He listens and is truly a compassionate human being, along with being a nationally recognized immunologist with over 300 peer-reviewed publications. He wore a string tie and had a ponytail when I first met him, and his license plate is T-Cell. Best of all, he responds to emails generally within 15 minutes and trusts his nurse practitioner to handle much of his patients’ mundane problems.

Carrie Lee Lyons
… that no matter how bad you think you are, it could always be worse, so look on the bright side.

Lisa Webb Tuttle
… to make every day special with a memory!

IG Living
Finish this sentence: The most important thing chronic disease has taught me is …

Shannon Walker Zack
Garfield, because he does what he wants when he wants to.

Michelle Pallotti
Bugs Bunny: “What’s up, Doc?”

Tim Lee
Elmer Fudd. Always huntin’ G.

Gail Moore
Ziggy — always seeing a brighter side even though the cloud follows me.
Did You Know

IG Self-Prep: To Prepare Is to Empower

By Kris McFalls

PEOPLE WITH immune-mediated diseases that require immune globulin (IG) treatment don’t get to choose their disease; their disease chooses them. Unfortunately, these chronic diseases can cause feelings of helplessness and lack of control that, if not managed well, can lead to worsening of symptoms and progression of disease. Therefore, patients need to be encouraged to take an active role in their healthcare. It’s a fact that patients who are empowered to manage their disease and treatments are more satisfied with their care and have better quality outcomes.

When it comes to IG treatments, there are a few choices that patients can make. Primary immune deficient patients have the options of subcutaneous immune globulin (SCIG) or intravenous immune globulin (IVIG). Many patients using IVIG also have the possibilities of home infusions and clinic- or hospital-based infusions. Factors that drive patients’ decisions include insurance, nursing, cost, side effects and convenience.

Yet, even though patients’ choices can be limited, there are things they can do to help prepare for a positive infusion experience. Learning about the products, understanding the possible treatments for side effects, and preparing supplies ahead of time can help make the process go more smoothly.

Product Choice

A number of IG products are on the market today, and more are scheduled to enter the market in the next couple of years. Each IG product is branded; there are no generics. As such, each is uniquely made using different ingredients and sterilization processes. Additionally, IG comes in different concentrations. Some IG products need to be refrigerated, while others can be stored at room temperature for up to 36 months. And, while most IG products come in a ready-to-use liquid preparation, a couple of others still require mixing in the pharmacy before they can be infused.

Choice of product is often guided by what inventory is available when the patient initially begins IG treatment. Patients can help guide the doctor’s future decisions by keeping track of how they have responded to products in the past. Keeping an infusion log that records the lot number, vial size, expiration date and rates of infusion will help doctors decide if a certain product is right for them.

Faster May Not Be Better

The time it takes to receive a treatment also determines whether the patient has a good experience. Of course, patients would like to get in and get out as fast as possible. Likewise, infusion staff would like patients in and out as quickly as possible. However, faster is not always better. Sometimes faster means more side effects, which could have negative consequences for the patient. Additionally, more side effects mean more attention is needed from the infusion staff. Patients who are mentally prepared to take as much time as needed to prevent side effects will have a better-quality experience.

Side Effects Drive Choice

Probably the most influential driver behind patient choice of product and route of therapy is the patient’s response to treatment. Side effects brought on by IG infusions can be
frustrating and tough to manage. Patients can help control side effects by becoming more educated about them and the options to treat them. Keeping a health diary that tracks symptoms before and after therapy can help doctors decide whether to change the product, dose and rate, or to add pre- and/or post-infusion medications. Patients also can help themselves by staying well-hydrated the day before, the day of and the day after treatments.

**Be Prepared**

Being prepared for each infusion, whether it is IVIG or SCIG, also helps to keep infusions running smoothly. Patients in an infusion clinic or hospital understandably get frustrated with the amount of time it takes just to get an infusion started. However, they should keep in mind that because IG is a very expensive medication, hospitals will not prepare an infusion until the patient is on-site. If possible, patients receiving IVIG in a clinic or hospital can request to use a liquid product. Doing so eliminates the need to mix the product, which can shorten the amount of time it takes a pharmacy to prepare the product for infusion.

Many IG products require refrigeration either to maximize its shelf life or simply to keep the storage environment consistent. IG, however, should be infused at room temperature but should never be warmed by anything other than body heat or sitting out at room temperature. Patients receiving therapy at home can assist this process by taking the product out of the refrigerator once they know the infusion nurse is on the way, or in the case of SCIG, the morning they plan to do their infusion.

Patients also can make infusions run smoother by preparing their infusion supplies. Once supplies arrive, they can use the time during an infusion to get supplies ready for the next one. This is accomplished by first making a list of supplies needed for the next infusion, and then placing them into a zip-lock bag ready for use. In the case of SCIG, patients can prepare separate infusion bags as soon as their supplies arrive. When it is time for an infusion, the patient can simply grab the next bag and get started, rather than spend time fumbling through supplies.

**Empowerment Equals Satisfaction**

Having a chronic disease does not render a patient helpless. Indeed, giving patients more control over how treatment is given empowers them. And, patients who are empowered ultimately are more satisfied with their care.

**KRIS MCFAULS** is the patient advocate and a staff writer for IG Living magazine.

**Sources**  
Research

New Target Identified for Scleroderma Therapy

Investigators at Northwestern University Feinberg School of Medicine have identified the molecule Egr-1 (early growth response factor 1) as a new therapy target for scleroderma, an autoimmune disease for which there currently is no cure. Affecting an estimated 300,000 people in the U.S., most frequently young to middle-aged women, the disease causes progressive thickening and tightening (fibrosis) of the skin and also can lead to serious internal organ damage, and sometimes death.

John Varga, MD, professor of medicine and dermatology at Feinberg and a physician at Northwestern Memorial Hospital, led a research team that included Northwestern scientists from pathology, plastic surgery, immunology, and pulmonary and critical care medicine. In one study, the team reproduced scleroderma in mice to show that the levels of the protein Egr-1 become highly elevated in the scar tissue. In a second study, the team used mice where the gene for Egr-1 was genetically deleted to demonstrate protection from the development of skin and lung fibrosis, in contrast to the genetically normal mice. Because the understanding of scleroderma and fibrosis represents a major unmet medical need, fresh insights into the disease process might open the door for novel therapies.

“The implications of our discovery are broad-ranging because fibrosis, or scarring, underlies not only scleroderma but also other more prevalent diseases such as pulmonary fibrosis, kidney fibrosis, liver cirrhosis, radiation-induced scars and many others,” says Dr. Varga. “The role of Egr-1 in fibrosis that we have identified is likely to apply to all of these conditions.”

These findings, along with similar research findings from the University of Pittsburgh School of Medicine, were published in the American Journal of Pathology.

Healthcare

HealthWell Foundation Launches SLE Fund

The HealthWell Foundation, a nonprofit organization providing financial assistance to insured patients facing a variety of chronic and life-altering illnesses, has launched a new fund to support treatment of systemic lupus erythematosus (SLE), the most common form of lupus. The fund provides copayment assistance to people who are living with SLE who cannot afford the high-cost medication. “Critical to taking advantage of the latest therapeutic option for any disease is the ability to afford that option,” said HealthWell Foundation President Mary P. Sundeen.

“As a direct result of the generosity of our donors, the HealthWell Foundation stands ready to reduce the cost-sharing obligations that many insured patients face when trying to access gold-standard and recently approved medications.” Application information for the SLE fund, as well as information on making a financial donation to support this and other funds, can be found at www.HealthWellFoundation.org.

Did You Know?
The Neuropathy Action Foundation is encouraging patients or physicians who are having trouble obtaining intravenous immune globulin (IVIG) to report it to the FDA as soon as possible by calling (800) 835-4709 or emailing CBERP roduct Shortages@cbcr.fda.gov.
Research

Daclizumab May Help Treat MS

Results from a Phase II clinical study show that the addition of daclizumab to interferon beta (IFNB) led to a significant reduction in the number of new or enlarged multiple sclerosis (MS) lesions when compared to IFNB alone in patients with active relapsing forms of MS. The trial, called CHOICE, also showed that daclizumab led to an increase in a subset of the natural killer (NK) cells that help regulate the immune system.

Daclizumab is a humanized monoclonal antibody that binds to CD25, a high-affinity receptor that is expressed at low levels on resting T cells, which are a type of immune cell, and at high levels on T cells that can become activated in response to autoimmune conditions such as MS. In the study, daclizumab 2mg/kg was administered subcutaneously every two weeks in combination with IFNB, which reduced the number of new or enlarged gadolinium contrast-enhancing lesions (Gd-CELs) by 72 percent versus IFNB therapy alone. The presence of Gd-CELs is thought to indicate inflammation within the central nervous system that corresponds with MS disease activity. In addition, treatment with daclizumab resulted in a seven- to eightfold increase of CD56 NK cells, which was associated with a decrease in disease activity.

Phase II study results provided evidence for Biogen Idec and Facet Biotech to continue the development of daclizumab in two registrational trials in MS. The Phase IIb SELECT trial is evaluating the efficacy and safety of monthly subcutaneous daclizumab as a monotherapy versus placebo, and is currently enrolling patients. The Phase III DECIDE trial is expected to be initiated in the second quarter of 2010.

Medicines

FDA Approves Shire Autoimmune Drug

Shire’s Firazyr (icatibant) has been approved by the U.S. Food and Drug Administration (FDA) to treat acute attacks of hereditary angioedema (HAE) in patients ages 18 years and older. HAE, which affects fewer than 30,000 people in the U.S., results from improper function of C1 inhibitor, a protein that regulates how certain immune system and blood-clotting pathways function. Individuals with the condition can develop rapid swelling of the hands, feet, limbs, face, intestinal tract and other internal organs, which can lead to disfigurement, disability and death. “Firazyr provides a new option to treat acute attacks of HAE and, because it can be self-administered through an injection in the abdominal area, patients can treat themselves upon recognition of an HAE attack,” says FDA Office of Drug Evaluation II Director Curtis Rosebraugh.

Research

“Bouncer” Protein Halts Rheumatoid Arthritis

Researchers at the Feinberg School of Medicine have figured out how the immune cells of rheumatoid arthritis (RA) patients become hyperactive and attack their joints and bones. They found that the cells lose their “bouncer,” a burly protein that keeps immune cells from going into their destructive mode through the cartilage and bone. When the scientists developed and injected an imitation of the protein into an animal model of RA, it halted the disease progress. The findings were reported on in Arthritis & Rheumatism.
**Education**

IDF Launches Nursing Course on PIDD and IG Therapy

The Immune Deficiency Foundation now offers a free accredited online continuing education (CE) course for nurses. The five-credit CE course will consist of four presentations that will focus on the nurse’s role with IG therapy, PIDDs and the difference between subcutaneous immune globulin (SCIG) and intravenous immune globulin (IVIG). The presentations include:

- Overview of IG Therapy and Disease States in Which It Is Utilized, by Jordan Orange, MD, PhD, University of Pennsylvania School of Medicine, Children’s Hospital of Philadelphia;
- Primary Immunodeficiencies, Combined T-Cell and/or B-Cell Immune Defects, by Mark Ballow, MD, SUNY Buffalo School of Medicine and Biomedical Sciences, Women and Children’s Hospital of Buffalo;
- Intravenous Immunoglobulin Therapy (IVIG), by Kristin Epland, MSN, FNP-C, Midwest Immunology Clinic, Plymouth, Minn.; and
- Subcutaneous Immunoglobulin Therapy (SCIG), by M. Elizabeth Younger, CRNP, PhD, Johns Hopkins University, Baltimore, Md.

The course is sponsored by an unrestricted educational grant from CSL Behring. To register, interested nurses can go to [http://primaryimmune.org/healthcare-professionals/continuing-education-course-for-nurses](http://primaryimmune.org/healthcare-professionals/continuing-education-course-for-nurses).

**Research**

Celiac Disease on the Rise in the U.S.

Two studies show that celiac disease is on the rise in the U.S. One study suggests that nearly five times as many people have celiac disease today than during the 1950s. Another report says that the rate of celiac disease has doubled every 15 years since 1974. The disease is now believed to affect one in every 133 U.S. residents.

Celiac disease is an inherited autoimmune gastrointestinal disorder that causes the body’s immune system to attack the small intestine, which compromises the body’s ability to digest food and extract vital nutrients. Researchers believe that the disease is increasing for the same reason other autoimmune diseases are on the rise: Our Western environment is overly clean and sanitized. According to Carol McCarthy Shilson, executive director of the University of Chicago Celiac Disease Center, the “hygiene hypothesis” is that people in industrialized countries are more at risk for celiac disease because their bodies have not had to fight off as many diseases. Another version of the hypothesis reasons that the cleanliness of industrialized society has caused a fundamental change in the composition of the digestive bacteria contained within the gut.

**Hotline**

First Psychologist Hotline Debuts

Call for Therapy is a new 24/7 platform where patients and psychologists can find each other on demand in real time. Instead of someone having to locate a psychologist, make an appointment and then wait to see the doctor, they can call the hotline for instant advice and treatment over the phone. David Gonen, MD, president of Call for Therapy, says: “We found people were having trouble using the old-fashioned therapy system. Our service gives you someone to guide you through your situation — someone who is understanding, professional and there expressly to listen to you.” In addition to a hotline that can be called at (888) 537-6403, Call for Therapy is a live community at [www.CallforTherapy.com](http://www.CallforTherapy.com).
**Research**

**New Approach Found to Treat Inflammatory Autoimmune Disorders**

Scientists at Duke University Medical Center have discovered a new way to fight inflammation using molecules called polymers to mop up the debris of damaged cells before the immune system becomes abnormally active. The discovery, published August 15 in the journal *Proceedings of the National Academy of Sciences*, offers a new approach to treat inflammatory autoimmune disorders such as lupus and multiple sclerosis, which are marked by an overactive immune response.

The idea for the new approach stemmed from earlier findings that showed dying and diseased cells spill nucleic acids (the building blocks of life that include DNA and RNA) that then circulate at high levels in the bloodstream and send powerful signals to the immune system that something is amiss. Once activated, the immune system launches an attack to fight whatever caused the cell damage. Under normal circumstances, this inflammatory response eventually restores order. But, in some cases, the inflammatory response becomes persistent and out of control, leading to tissue damage and causing symptoms such as fever and pain.

Working to interrupt this cycle, the Duke scientists focused on a set of molecules called nucleic acid binding polymers that were designed to infiltrate the nucleic acid inside of cells and deactivate specific immune triggers. They found that because the inflammatory nucleic acids are outside of cells, whereas DNA and RNA normally function inside cells, that the polymers could bind to the external nucleic acids without disrupting intracellular functions of DNA and RNA.

The approach worked in experiments on mice. And, it is believed that it has numerous potential applications, not only for autoimmune disorders, but for acute tissue damage of several bacterial and viral infections, shock and injuries. Patents have been filed on the finding, and the researchers are pursuing the development of therapies.

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**Research**

**GSK Developing Gene Therapy for ADA-SCID**

GlaxoSmithKline is moving forward to develop and commercialize a new gene therapy for adenosine deaminase deficiency-severe combined immune deficiency (ADA-SCID), which is also known as “bubble boy disease.” The investigational gene therapy uses gene transfer technology in which stem cells are harvested from the patient’s body, the correct form of the gene is inserted into the cell, and the cells are then reintroduced to the patient. GSK licensed the investigational gene therapy from the San Raffaele Telethon Institute for Gene Therapy in Milan, Italy, in 2010, and it has recently signed a two-year, $7.7 million deal with Italian biotechnology company MolMed for it to develop a production process for the gene therapy.

ADA-SCID is caused by the alteration of a single gene that prevents the body from producing the ADA enzyme, which helps create disease-fighting immune cells. Patients who have the condition can’t fight bacteria or viruses. Treatment is usually a bone marrow transplant from a donor, but even when the stem cells come from a closely matched or related donor, the risk of rejection remains. Using the patient’s own cells poses less of a risk of immune rejection compared with bone marrow transplants.
Insurance

Insurance Premiums Up 9 Percent in 2011

Average annual insurance premiums for employer-sponsored family health coverage increased to $15,073 in 2011, up 9 percent from 2010, according to the Kaiser Family Foundation/Health Research & Educational Trust (HRET) 2011 Employer Health Benefits Survey. On average, workers pay $4,129 and employers pay $10,944 toward those annual premiums. The study also finds 31 percent of covered workers are in high-deductible health plans, facing deductibles for single coverage of at least $1,000, including 12 percent facing deductibles of at least $2,000. Covered workers in smaller firms (three to 199 workers) are more likely to face such high deductibles, with half of workers in smaller firms facing deductibles of at least $1,000, including 28 percent facing deductibles of $2,000 or more.

The 13th annual Kaiser/HRET survey of small and large employers provides a detailed picture of trends in private health insurance costs and coverage. This year’s survey also looked at employers’ experiences with several already implemented provisions of the 2010 health reform law affecting employer coverage. In particular, the survey estimates that employers added 2.3 million young adults to their parents’ family health insurance policies as a result of the health reform provision that allows young adults up to age 26 without employer coverage on their own to be covered as dependents on their parents’ plan.

Medicines

Octagam 5% Returns to Market in U.S. and Europe

The U.S. Food and Drug Administration (FDA) and the Committee for Medicinal Products for Human Use in Europe have approved the return of Octagam 5% (human normal immunoglobulin 50 mg/ml) to the market. Marketing authorization was suspended in August 2010 in the U.S. and in September 2010 in Europe after a massive voluntary recall by Octapharma due to an increase of thromboembolic events (TEEs). To determine the biochemical root cause(s) of the TEEs in concerned Octagam batches, Octapharma conducted a number of tests, which identified FXIa as the major procoagulant activity. In response, FXIa was successfully removed through corrective and preventive measures in the manufacturing process. Now, Octapharma has implemented post-marketing studies to ensure product safety.

“We are extremely pleased that the FDA has authorized the market return of Octagam 5%,” said Octapharma USA President Flemming Nielsen. “Our collaboration with the FDA over the last year has enhanced awareness of the industry-wide concerns regarding procoagulant activity and TEEs. Octapharma has always believed that patient safety comes first, so the Octagam 5% that we will return to the U.S. market ... will enjoy the highest level of safety scrutiny available today and the same level of tolerability that our patients have come to expect from Octapharma therapies.”
Insurance

Twelve New Diagnoses Added to Compassionate Allowances List

In July, 12 new medical diagnoses were added to the Social Security Administration’s Compassionate Allowances program. Established in 2008 with a list of 50 diseases, the program expedites review of applications for disability benefits by quickly identifying those that meet Social Security’s standards. These additions are important for people with rare diseases who, historically, have encountered problems when applying for assistance because those making decisions are not familiar with their diseases. With patient advocates submitting diseases for consideration, along with input from medical experts at the National Institutes of Health and leading medical centers, there are now 100 diseases on the list. For a complete list of compassionate allowances, go to http://www.ssa.gov/compassionate_allowances/conditions.htm.

Insurance

Initiatives to Lower Medicaid Costs and Improve Care

The U.S. Department of Health and Human Services is launching two initiatives to help states save money and better coordinate care for the nine million Americans enrolled in both Medicare and Medicaid. The first, the Alignment Initiative, is an effort to more effectively integrate benefits under the two programs. Currently, lower-income seniors and people with disabilities must navigate two separate programs: Medicare for coverage of basic acute healthcare services and drugs, and Medicaid for coverage of supplemental benefits such as long-term care supports and services, help with Medicare premiums and cost-sharing for those who need additional assistance.

The second is a new process that provides faster state access to Medicare data to support care coordination, a tool that will help states seeking to coordinate care, improve quality and control costs for their highest-cost beneficiaries. For example, a state that wants to expand its long-term care and behavioral healthcare management program to serve low-income seniors and people with disabilities needs data on their Medicare-covered hospital, physician and prescription drug use. With Medicare data, states can identify high-risk and high-cost individuals, determine their primary health risks and provide comprehensive individual client profiles to its care management contractor to tailor interventions. More information on this initiative can be found at www.cms.gov/CMCSBulletins/CMC SB/list.asp#TopOfPage.

Did You Know?

Because rheumatoid arthritis (RA) is hard to diagnose in its early stage, doctors must diagnose based on factors that are clearly related with the disease, including swollen areas in the wrist, hand or finger joints; morning stiffness in the joints for at least one hour; swelling around three or more joints at the same time; X-ray changes in the wrists and hands; arthritis affecting symmetrical joints on both sides of the body; and a high level of rheumatoid factor in the blood.

— The American College of Rheumatology
Insurance

Part D Drug Premiums to Decrease in 2012

The average monthly premium for Medicare Part D prescription drug coverage will decline in 2012, according to the U.S. Department of Health and Human Services (HHS). The average monthly drug plan in 2012 will cost about $30, approximately $1 lower than 2011 averages. In addition, nearly 900,000 Medicare beneficiaries whose prescription drug purchases place them in the so-called “doughnut hole” have benefited from the new 50 percent discount on covered name-brand drugs. “The marketplace created by the Medicare Part D structure continues to be vibrant and highly competitive,” said Mary R. Grealy, president of the Healthcare Leadership Council. “To succeed, Part D plans have to keep premiums affordable and provide value, and seniors are benefiting.”

Legislation

Supreme Court to Rule on Healthcare Law Constitutionality

In September, the Justice Department said it would forgo an appeal to the full U.S. 11th Circuit Court of Appeals in Atlanta, which ruled 2-1 in August that the healthcare reform law’s requirement that people buy health insurance is unconstitutional. The suit before a three-member panel of the court was brought by 26 states, the National Federation of Independent Business and several individuals. Opponents of the law had expected the government to ask for the so-called en banc hearing to delay a ruling by the U.S. Supreme Court until at least 2013. The decline of the appeal and the subsequent request by the Obama administration for the Supreme Court to hear the case clears the way for arguments on the constitutionality of the healthcare law in the spring and a decision by June, in time to land in the middle of the 2012 presidential campaign.

Legislation

Partnership for Patients Meeting Participant Goal

Nearly 4,500 organizations — including more than 2,000 hospitals — have pledged their support for Partnership for Patients, meeting the Obama administration’s hospital goal in less than three months. Partnership for Patients aims to reduce preventable harm in hospitals by 40 percent in the next three years, including a reduction in the number of preventable in-hospital medication errors, central-line associated bloodstream infections, falls and other injuries. It also seeks to help patients heal successfully after discharge, targeting unnecessary return visits to reduce 30-day hospital readmissions by 20 percent over the next three years. According to the U.S. Department of Health and Human Services, the partnership has the potential to save up to $35 billion in healthcare costs, including up to $10 billion for Medicare. And, over the next 10 years, the partnership could reduce costs to Medicare by about $50 billion and result in billions more in Medicaid savings.

People and Places in the News

Rebecca H. Buckley, MD, has been elected as a member of the National Academy of Sciences for her life-saving research in pediatric immunological diseases. Dr. Buckley is the J. Buren Sidbury Professor of Pediatrics and professor of immunology at Duke University Medical Center.

Thermo Fisher Scientific Inc. has acquired Phadia, a global leader of blood tests for the clinical diagnosis and monitoring of allergies and autoimmune diseases.

Trine Jorgensen, a Cleveland Clinic Department of Immunology researcher, has received a $1.1 million grant from the U.S. Department of Defense (DoD) to study why lupus is so much more prevalent in females than males. She is one of two researchers nationally to receive a DoD grant for lupus research. The other $1.2 million grant went to a researcher with Boston’s Brigham and Women’s Hospital.
Legislation

Legislation Protects the Treatment of Rare Diseases

Two new bipartisan bills, H.R. 2672 and S. 1423, both titled Preserving Access to Orphan Drugs Act, have been introduced to safeguard the development of drugs and therapies that treat patients with rare diseases by eliminating barriers to innovation. Under the current law, most plasma protein therapies, despite being approved for marketing by the U.S. Food and Drug Administration solely for the treatment of one or more rare diseases or conditions, would not qualify for the orphan drug exclusion from the annual pharmaceutical fee. In the U.S., a rare disease or condition is generally defined as one affecting fewer than 200,000 people. The new bills would modify the law to ensure that manufacturers can exclude the sale of all drugs and therapies that are FDA-indicated solely for the treatment of one or more rare diseases from their annual fee liability.

“The majority of patients who rely on plasma protein therapies are coping with a very rare disease for which no alternative treatment exists,” said Julie Birkofer, Plasma Protein Therapies Association senior vice president, North America. “This legislation preserves access to therapies and drugs for rare disease patients and helps to ensure that research and development into new therapies for orphan diseases continues to be encouraged and remains unencumbered.”

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Immune globulin (IG) replacement therapy is the standard treatment for primary immune deficiency disease (PIDD), either via intravenous (IV) or subcutaneous (SC) routes. Yet, even with IVIG and SCIG treatments, patients continue to suffer acute breakthrough and chronic infections. This is because IG treatment is not a standardized, one-size-fits-all treatment. And, because dosing strategies are unique to each patient, there is sometimes confusion about what is the optimal dosing strategy.

Individual IG Dosing Strategies

By Ronale Tucker Rhodes, MS, and Kris McFalls

Studies that examine the relationships between therapeutic doses of IG, trough IgG levels and infection rates shed new light on how IG replacement therapy should be prescribed for individuals.
A History of Dosing Regimens

In the U.S., there is no one national guideline for IgG dosing, as there is in the United Kingdom and Australia, for example. However, there are several different published IgG dosing guidelines that recommend satisfactory IgG trough levels for patients, yet all of them differ somewhat. And, there is the U.S. Food and Drug Administration’s minimal criterion for efficacy, which states that the IgG treatment should achieve less than one serious infection per patient per year. Most of the published guidelines regarding IgG trough levels recommend patients achieve a level of around 600 to 800 mg/dL with a dose of 400 mg/kg of Ig every three to four weeks. The problem, then, says Dr. Melvin Berger, a specialist in allergy and immunology and pediatric medicine in Cleveland, Ohio, and the senior medical director of clinical research and development at CSL Behring, is that some patients may need a biological trough level of only 600 to achieve less than one serious infection per year, whereas other patients may need a trough level of 900 to attain the same measure of health. Therefore, it has been questioned whether treatment protocols that use IgG trough levels as a determinant of the IgG dose patients receive during therapy are most effective for reducing infections.

According to Dr. Berger, there have been about 10 studies over the years that have looked at IgG dose and effect, comparing lower and higher doses in PIDD patients. All those studies except one, he says, have found that the higher dose was more effective in lowering the incidence of infection. Additionally, several recent studies have shown that while general dosing guidelines are a great starting place, each patient needs individualized dosing to prevent infections.

Study: Lucas et al. (2010), Oxford University

An extensive study published in the Journal of Allergy and Clinical Immunology by a group led by Dr. Helen Chapel at Oxford University in the United Kingdom examined the relationships among therapeutic IgG doses, trough serum IgG levels and infection rates over 22 years in a single clinic. Its objective was to provide data to support the hypothesis that each patient requires an individualized IgG dose to prevent breakthrough infections, rather than to achieve a serum IgG trough level.

The study followed the practice in Dr. Chapel’s clinic to adjust IgG doses in real time in accordance with infection episodes, rather than to achieve a particular trough IgG level. Patients without chronic lung disease were started with initial doses of 0.4 g/kg per month of Ig, and patients with bronchiectasis were treated with initial doses of 0.6 g/kg per month. Those doses were then adjusted in line with breakthrough infections. If there were no serious breakthrough infections, those patients with a rate of three moderate bacterial infections per year got an increase in IgG dosage of around 0.15 g/kg per month, usually given as SCIG or IVIG every two weeks.

It has been questioned whether using IgG trough levels to determine the IgG dose during therapy is most effective for reducing infections.

Ninety patients with confirmed common variable immune deficiency (CVID) and 15 with X-linked agammaglobulinemia (XLA) were included in the study. (The group of XLA patients was analyzed in this study for comparison.) To participate, CVID patients were selected if they had a serum IgG level <6.0 g/L (600 mg/dL) and either a serum IgA level of <0.8 g/L or a serum IgM level of <0.5 g/L or both; if they were over 4 years of age at diagnosis; and if there were no other conditions or therapies associated with antibody failure. Patients were excluded if there was less than 12 months of data or noncompliance with therapy or monitoring. The same exclusion criteria were used for XLA patients for comparison purposes.

To collect the data, the Oxford PID Database was created in which demographic and infection data correlating to IgG therapy were logged. The specific information logged included data on infections (infection site, pathogen type and treatment details), administration route of Ig, IgG dose in grams per kilogram per month, and clinical complications. Baseline data were entered from patient notes at the start of IgG therapy or on referral to Oxford for patients previously diagnosed.

Additional data on treatment and response were collected over a follow-up period of 22 years, and then validated and analyzed. The entry point for each patient into the
analysis was the point at which the serum IgG level was stable (defined as ≤1.5 g/L variation from the mean trough IgG over at least four months). Data were analyzed for IgG, IgA and IgM levels against time for each patient, commencement of replacement therapy and dose changes. In addition, the analysis allowed for seasonal variations in infections. And, confirmation of bacterial infection was made using radiologic/laboratory/microbiological findings and responses to antibiotics.

Results of treatment with therapeutic IG doses adjusted in accordance with infection data rather than to achieve a particular trough IgG level showed that overall bacterial infection frequency was low (2.16 infections per patient-year), and the incidence of serious infection was particularly low. And, in any period, the mean trough IgG level correlated strongly with the replacement dose of Ig, but there was a weak relationship between infection score per patient-period and mean trough IgG.

**Studies show that patients need individualized dosing to prevent infections.**

According to the study’s authors: “This study provides evidence to support the clinical view that the trough IgG and dose of replacement therapy to maintain minimal infectious burden is unique to the individual.” They conclude by stating: “The goal of replacement therapy should be to improve clinical outcome and not to reach a particular IgG trough level.”

**Meta-Analysis of SCIG: Dr. Berger (2011)**

Dr. Berger substantiates the Oxford study’s conclusions with his meta-analysis that summarizes seven studies conducted on SCIG. The analysis, which was published as a letter to the editor in the *Journal of Clinical Immunology*, notes that having a consensus targeted trough level is complicated, in part because of the differences in pharmacokinetics of SCIG versus IVIG therapy. Consensus is further complicated by the different regulatory authorities of individual countries and the different practices of different physicians.

The seven studies utilized four different SCIG preparations from three different manufacturers. In total, the reports include data from 322 SCIG patients who were treated in multiple settings and who received treatments on a weekly basis. Trough levels were reported after 12 to 16 weeks of SCIG therapy. All studies defined serious bacterial infections (SBIs) according to published FDA guidance. Non-serious infections other than SBIs such as sinus or upper-respiratory infections with fever were defined by the treating physician. Mean trough levels in the different studies were reported to be between 810 and 1250 mg/dl (8.1 to 12.5 g/l).

A total of seven SBIs were reported in four of the seven studies, all of which were pneumonias. The remaining three studies reported no SBIs. Studies with a higher mean trough level did not demonstrate a lower incidence of SBIs. Therefore, no linear correlation could be made between the annualized incidents of SBI and the mean steady trough levels of the different studies. In contrast, however, the incidence of non-serious infections showed that a decrease in the number of infections correlated significantly with a higher steady-state serum IG level, and there did not appear to be a plateau above which higher IgG levels did not correlate with lower incidence of infection.

Dr. Berger concluded: “For any individual patient, factors other than the IgG dose and resulting serum IgG level unquestionably contribute to the type and the frequency of infections which may occur. Therefore, treatment regimens, doses, and target serum IgG levels should be individualized to optimize treatment effects and costs for individual patients.”

**Meta-Analysis of IVIG: Dr. Orange (2010)**

Although pharmacokinetics of SCIG and IVIG are not similar, the belief that higher serum IgG levels correlate with lower infection rates also was shown to be true in a meta-analysis published in *Clinical Immunology* that evaluated the incidence of pneumonia with varying doses of IVIG. Conducted by Dr. Jordan S. Orange, a pediatric immunologist at Children’s Hospital of Philadelphia and consultant to Baxter Healthcare, Talecris Biotherapeutics (now Grifols) and CSL Behring, and colleagues, this was the first meta-analysis to enumerate the relationship between IgG trough levels and pneumonia in PIDD patients treated with IVIG.

As previously discussed, serum trough IgG levels of PIDD patients historically have been used as a guide to determine appropriate levels of IVIG therapy. However, a sufficient trough level to prevent SBIs has not been established. And, while many immunologists have considered 500 mg/dL a minimum target trough level, the level of benefit gained above 500 has been debated.

Pneumonia was chosen for this meta-analysis because it...
is one of the most frequent manifestations of PIDD that can result in hospitalization and require the use of intravenous antibiotics. Additionally, it is one of the primary validated SBIs used to determine efficacy of IG therapy.

A total of 17 clinical studies reported from 1982 to 2009 comprising 676 total patients and 2,127 patient-years of follow-up were included in the meta-analysis. Of the total studies conducted in the United States, Canada, Europe, the Middle East and Argentina, 11 were prospective and six were retrospective. All the studies included PIDD patients predominately diagnosed with CVID and XLA. However, no patients with subclass deficiency were enrolled in 14 of the 17 studies. Other PIDD diagnoses such as hyper-IgM, hypogammaglobulinemia and ataxia telangiectasia also were included.

Incidence rates of pneumonia were analyzed at serum trough levels of 500, 600, 700, 800 and 1,000 mg/dL (10 g/l), and at doses of 100, 200, 300, 400, 500 and 600 mg/kg. The median IVIG treatment interval between doses was 24.6 days. Results were highly statistically significant and showed that pneumonia incidence declined by 27 percent with each 100 mg/dL (1 g/l) trough increment.

Dr. Jordan and colleagues concluded that “PIDD patients receiving IVIG therapy and experiencing pneumonia are likely to be helped by increasing the IgG trough levels to at least the mid-normal range of IgG,” which they defined as up to at least 1,000 mg/dL. No apparent plateau in efficacy was observed. However, they stated additional research “is needed to determine whether a general threshold trough of optimal protection against pneumonia may exist above 1,000 mg/dL.”

From Paper to Practice?

What do these research findings mean for PIDD patients being treated with IG? Is it possible that they could result in a national guideline for IG dosing in the U.S. such as those guidelines in effect in Australia and the U.K.? Dr. Berger doesn’t see a need for a national guideline. “I don’t know what role published guidelines actually play,” he says. “There’s no obligation for a doctor to follow a published guideline. In general, the idea of a guideline is just a suggestion of where to start. It’s not an end unto itself. I think most doctors probably recognize that.” However, guidelines should not be used by payers to limit doses that patients receive or to restrict doctors’ prescribing practices.

What these findings do provide, however, is evidence-based guidelines from which treatment protocols can be developed that will result in a higher quality of life for a large portion of PIDD patients. For instance, Dr. Berger says, “What is the goal of therapy? To keep the patient barely alive or to produce a normal citizen who can go to school or work?” The goal, he says, is the latter and that can be achieved only by reducing the number of infections. So, since these studies show that higher doses of IG

Study findings provide evidence-based guidelines that can be used to develop treatment protocols that result in a higher quality of life for PIDD patients.

A lot more is known about multiple sclerosis (MS) today than a few years and even just a few months ago. In 1970, scientists knew of one gene linked to MS. In 2007, that number increased to three genetic links, and in early August 2011, scientists announced that there are 57 genetic links with the confirmation of 23 previously identified genes, 29 newly identified genetic variants and five genetic candidates worthy of further study. These are promising times for the 400,000 individuals in the U.S. and the 2.5 million worldwide who suffer from MS and its related symptoms!1

Understanding and Treating Multiple Sclerosis

By Amy Scanlin, MS

While research has greatly increased our understanding of what causes MS, much still needs to be learned. In the meantime, new treatments have been developed and many more are in the pipeline.
**What Is MS?**

MS is a chronic disease affecting the central nervous system that, in turn, prohibits the nerve cells in the brain from communicating with the spinal cord. When the protective fatty myelin sheaths surrounding the axons of the brain and spinal cord are damaged or scarred (demyelination), the result is a reduced ability to perform everyday activities, reduced cognitive function, impaired or lost vision, and even loss of bladder control and paralysis. The term multiple sclerosis refers to the numerous lesions, or scleroses, that form when the nervous system is attacked.

MS attacks more women than men, and it is typically diagnosed between the ages of 20 and 40, although it can be seen at any age. It is more common in Caucasians than African-Americans, but those men and African-Americans who do have MS tend to have more severe attacks. The incidence of MS is higher in persons who have a close relative with the disease, and if it is a first-degree relative, there is a 12- to 20-fold increase in risk.² The rate of MS also is higher in those who spent formative years farther from the equator, where there is less sunlight. Interestingly, children who are born in one area and migrate to another prior to age 15 are thought to take on the risks of MS of their newly adopted area.² So, if a child is born closer to the equator and then moves farther away, they take on the same risks for MS as the population of the area to which they moved.

**In early August 2011, scientists announced that there are 57 genetic links to MS.**

To be diagnosed with MS, doctors must confirm two separate incidences of demyelinations, or lesions, in the white matter; two or more remissions of neurological deficits; and have the diagnosis confirmed by an MRI. Doctors also look for “increased IgG synthesis with positive oligoclonal bands (OCBs) in the spinal fluid.”²

Some people with MS can live for years without symptoms, while others become disabled rather quickly. It is a disease whose progression is difficult to predict.

**Causes of MS**

The latest study in which 57 genetic links to MS were identified was a major breakthrough for scientists who for years have been looking at a variety of possible theories on the causes of MS — from the controversial Italian researcher Dr. Paolo Zamboni’s theory of blocked veins, to more widespread theories of immunologic causes.

Now, scientists can say that about 80 percent of the 57 genes identified that are associated with MS are immunologic and that inflammation of the immune system triggers MS attacks. Although scientists don’t think MS is a hereditary disease, they know that it is a function of one’s genes, perhaps interacting with environmental factors, and perhaps also in conjunction with a vitamin D deficiency, which can cause the immune system to attack the nervous system.

Many of these newly identified genes also are involved in the functioning of T cells, which attack foreign invaders, and about one-third of them are associated with other autoimmune disorders such as Crohn’s disease and type 1
diabetes, two conditions often found in those with MS. Yet, even with so much information starting to come together, scientists think that these new gene variants may still account for only a small portion of the big picture. The rest is yet to be discovered.

**Symptoms and Subtypes of MS**

Symptoms of MS can occur as discrete attacks or as a relapsing form, or the symptoms can accumulate over time, as with progressive MS. Symptoms also may completely disappear between attacks, but the underlying effects during those attacks are the cause of the neurological problems that later occur.

The different types of MS are categorized according to the course of the symptoms. There are four types: relapse-remitting, secondary progressive, primary progressive and progressive relapsing.

### The different types of MS are categorized according to the course of the symptoms.

The majority of MS patients have the relapse-remitting form, potentially with long periods between symptoms and no indication that a relapse is about to occur. After a relapse, any deficits suffered can disappear or remain, compounding over time with each subsequent relapse. A typical number of attacks with relapse-remitting MS is one to two per year.

Many patients initially diagnosed with a relapse-remitting form of MS develop secondary progressive MS. These patients begin to have a neurological decline between attacks without any periods of remission. The typical time for developing secondary progressive MS is less than 20 years, and in women, this development happens around the time of menopause.

Those with primary progressive MS never go into remission after the first onset of symptoms, and this subtype is usually diagnosed at about the age of 40. The least common subtype of MS is progressive relapsing, and these patients have a steady neurological decline once symptoms begin, as well as clear attacks.

### Treatment for MS

Developing treatments for MS is expensive, averaging about $1 billion to bring a drug to market at an annual treatment cost of between $40,000 and $50,000. Today's treatments for MS include attempts to lessen the progression and long-term impacts of the disease, as well as to reduce the number of flare-ups and attacks.

One of the top 10 medical breakthroughs in 2010, voted on by the Cleveland Clinic, was Gilenya capsules (manufactured by Novartis International AG). Gilenya was approved as the first oral treatment for MS by the U.S. Food and Drug Administration (FDA) for reducing the number of relapses, as well as for reducing the physical symptoms of MS. Another drug recently approved by the FDA is Ampyra (manufactured by Acorda Therapeutics). Ampyra has been shown effective as the first treatment to target the symptoms that severely compromise MS patients’ ability to walk, and it has shown to be effective for those with all types of MS.

Two more promising drugs are predicted to come to market in 2012. Sanofi and its subsidiary Genzyme are developing alemtuzumab (Campath) with Bayer HealthCare. The monoclonal antibody is already used to treat leukemia, or T-cell lymphoma, and it also is used in conditioning regimens for bone marrow or kidney transplantations. Results from the Phase III clinical trial show a 55 percent reduction in relapse at two years in adults with relapsing-remitting MS treated with alemtuzumab. The companies expect to file for United States and European Union approval of the drug for MS in early 2012. They have already been granted a fast-track designation by the FDA.

The second promising drug is BG-12 (BG00012, dimethyl fumarate) from Biogen Idec, which is an investigational oral therapy in Phase III clinical development as a monotherapy for the treatment of relapsing-remitting MS, and in Phase II clinical development for rheumatoid arthritis. BG-12 received fast track designation in MS from the FDA, which may expedite U.S. regulatory review.

Other methods of treatment for MS include powerful autoimmune-suppressing corticosteroids administered intravenously over the course of a few weeks to help lessen the risk of long-term damage of attacks. While many doctors and patients feel this type of therapy is effective, some studies have shown little to no long-term difference between control and study groups. More research is needed to determine whether corticosteroids actually work.
The American Academy of Neurology recommends physicians consider the blood-cleansing procedure of plasma exchange (plasmapheresis) on a short-term basis as a secondary therapy for those with rapidly progressing MS who are unresponsive to corticosteroids. This therapy has not shown to be effective for those with secondary or primary progressive MS; however, it has shown to be successful to treat other immune disorders.

Other therapies such as IVIG or Mitoxantrone often are used as secondary treatments for those patients with long periods of clinical remission. In fact, several published European studies have confirmed the benefits of IVIG therapy in those patients with clinically definite relapsing-remitting multiple sclerosis. These studies demonstrated a reduction in the acute relapse rate and the number of contrast-enhanced lesions on monthly MRI scans. Most importantly, the patients receiving multiple sclerosis treatments in the form of IVIG therapy spent significantly more time in an improved or stable neurological state as compared with the placebo groups, suggesting a better quality of life for the IVIG patients during remission.

Managing Day to Day
While many years ago it was advised that patients with MS not do any form of exercise for fear of exacerbating painful symptoms, today that is not the case. Patients working closely with a doctor and physical therapist can develop appropriate programs that show promise in not only reducing symptoms of MS but improving cardiovascular function and strength, bone density, bowel health, mood and overall quality of life.

Aerobic exercise has a positive effect on the parts of the brain most affected with MS, including fewer and smaller lesions and improved cognitive capacity, as evidenced by higher scores on cognitive testing. Researchers also have found that fitter MS patients have more gray matter, or cell bodies, in the brain, as well as less deterioration of white matter, or fibers that connect the gray matter areas, which are both significant to the brain’s ability to process information.

In addition, mindful meditation can help manage depressive feelings and fatigue. A study conducted in Switzerland of those with both relapse-remitting and secondary progressive MS found that patients can see great emotional benefits from a mind-body connection.

Before getting started with a fitness program, patients should speak to a doctor to determine what programs might be appropriate. They should be especially careful to avoid tripping and slipping hazards by having a bar or steady object close by. And, they should avoid becoming overheated, as many with MS feel symptoms are greatly exacerbated when the body temperature rises. For these reasons, water exercise is a particularly popular choice, provided there are non-skid surfaces in the locker room and along the pathway to the pool.

Also popular are yoga and tai chi, gentle strength training protocols, and both arm ergometers and bicycles. Again, any exercise program should only be undertaken with doctor supervision and modified as needed.

Future Outlook
As more genes are identified and researchers learn more about the role the immune system plays in the development of MS, patients can expect more personalized treatments while researchers look at new opportunities for drug development. There are numerous trials under way in the treatment of MS, and many are showing promise.

In the prevention of relapse, one Phase II trial found that a liquid injectable form of the monoclonal antibody daclizumab reduced the rate of recurrence. There also are positive indications that alemtuzumab, an intravenous therapy delivered over two years, five days a week for the first year and three days per week in the subsequent year, may be a new therapy.
worthy of further exploration after a Phase III study revealed a 55 percent reduction in relapse rate.14 The FDA has designated alemtuzumab a “fast track product.”

In order to prevent MS and better treat its symptoms, scientists need a better understanding of the role inflammation plays on its progression, the role of environmental interactions, as well as the specific molecules involved in attacks. One consideration of an environmental interaction is how tobacco smoking interacts with the presence of the Epstein-Barr (EB) virus. Those with a history of multiple mononucleosis attacks caused by the EB virus or who have higher levels of the virus’ antibodies in the blood and who have a history of smoking are nine times more likely to develop MS than those without the EB gene.15

Another environmental consideration is how vitamin D, gained from sunlight exposure, has shown to be an important factor in the prevention of MS. Alterations of genes in both vitamin D hormone receptors and synthesis have been associated with increased instances of MS, especially in combination with estrogen, which along with vitamin D prevents inflammation of the central nervous system. When women enter puberty, they become more dependent on estrogen for the autoimmunity protection of vitamin D. As women produce less estrogen in menopause, their ability to use vitamin D decreases and their MS risk factors increase. This is the time when doctors see progression from relapse-remitting to secondary progressive forms of MS. Scientists are looking at the possible links of estrogen replacement and vitamin D supplements to prevent that transition.5

The good news is that progress is being made in new therapy and treatment trials, which are providing more and more information each day. In the meantime, the Multiple Sclerosis Society offers links to online social networking communities where patients who have been diagnosed can share their stories. Visit www.nationalmssociety.org/online-community to learn more.

AMY SCANLIN, MS, is a freelance writer specializing in medical and fitness writing.

References
Autoimmune Disease and Drug-Drug Interactions

By Amy Ehlers, BS, PharmD, BCPS

Patients with autoimmune diseases who often take multiple medications can take a number of steps to prevent adverse drug events.

There were over 3.7 billion prescriptions dispensed in the United States in 2010, along with $17 billion in over-the-counter (OTC) drug sales and $5 billion in natural supplements. With each prescription that leaves the pharmacy or OTC/natural supplement that is purchased, there exists a potential for a drug interaction. In a study published in the Dec. 24/31, 2008, issue of the Journal of the American Medical Association, University of Chicago researchers interviewed approximately 3,000 individuals ages 57 to 85 about their use of prescription and OTC drugs and dietary supplements, and found that one in 25 was potentially at risk of having a major drug-drug interaction.

According to the Centers for Disease Control and Prevention's National Center for Health Statistics, in 2004, nearly half of all Americans were taking at least one prescription medication, and one in six individuals was taking three or more. With autoimmune diseases, patients are almost guaranteed a drug therapy regimen that comprises multiple medications to treat the various manifestations of the disease. For instance, multiple sclerosis (MS) is an immune-mediated inflammatory disease that attacks myelinated axons in the central nervous system, destroying both the myelin and the axons. The treatment for MS involves drug therapy for both the underlying immune disorder and the symptoms of the disease, which usually include fatigue, numbness, tingling and muscle spasms or weakness. This means that a typical MS patient may take four or more medications on a regular basis to help manage their disease.
Distinguishing Between Side Effects and Adverse Drug Events

It is important to distinguish between a side effect and an adverse drug event. A side effect, which also may be referred to as an adverse drug reaction, is an expected and known effect of a drug that is not the intended therapeutic outcome. These may decrease over time or be significant or serious enough to warrant changing the drug therapy. An adverse drug event, on the other hand, is an injury that occurs from using a drug at a normal dosage and may occur from the use of one drug or the interaction between two or more agents.

To better illustrate the differences between side effects and adverse drug events, let’s look at the drug gabapentin (Neurontin). This drug is frequently prescribed to help treat nerve pain. Common side effects of gabapentin include dizziness, drowsiness and visual disturbances such as blurred or double vision. These are considered side effects because they are predicted outcomes of using the drug and typically decrease over time. This is why many patients, when beginning gabapentin therapy, are slowly titrated to reach their optimal dose. By giving the body an opportunity to slowly adjust to the gabapentin, these side effects are usually far less severe than if the full dose is started initially. A known adverse drug event exists between gabapentin and naproxen (Aleve, Naprosyn). When naproxen is taken together with gabapentin, the absorption of gabapentin is increased. This means that a patient who was once on a stable dose of gabapentin with little to no side effects may suddenly complain of things such as dizziness or blurred vision. If the naproxen use is limited, these will resolve, but if the naproxen use continues long-term, the gabapentin dose may need to be decreased.

Preventing Adverse Drug Events

A number of things can be done to help prevent adverse drug events.

Become educated. Patients need to take the time to become educated about each medication that they are prescribed. By law, each time a new prescription is dispensed, the pharmacist must make the offer to counsel on the medication. Many people visit the pharmacy at the end of a long day that may have gone like this: The appointment is at 9 a.m., and the patient arrives at the physician’s office at 8:45 a.m. They sit in the waiting area until 9:15 a.m., when they are taken back to have vital signs taken and then told to go back to the reception area to wait again. At 10 a.m., they are taken back to an examination room, where they sit patiently until 10:30 a.m., when the doctor appears. At 11 a.m., they are ready to leave the physician’s office to head to the lab to have the ordered lab tests done. At the lab, because they didn’t have an appointment, they wait until almost 12:30 p.m. to have blood drawn. They then grab a quick lunch and then drive to the pharmacy to have their prescription filled around 1 p.m. The pharmacy technician tells them that it won’t be ready for a while, so they walk around the store and wait. When their name is finally called at 3 p.m., they rush to the counter to pick up the medication and when the pharmacist asks if they have any questions and attempts to counsel them on the new prescription, they say: “I’ll read the information when I get home.” They then sign the log that declines counseling and finally head home.

Patients need to take the time to become educated about each medication that they are prescribed.

Reading the drug information sheets may seem to be the easiest thing to do, yet according to a 2007 article in the Journal of the American Pharmacists Association, 50 percent of all patients throw them away at home without reading them. By skipping the information about the expected side effects and other medications and OTCs to avoid, they have placed themselves at a much higher risk to experience a drug interaction or adverse effect of the medication.

Communicate. If a new drug is started and something
doesn’t feel right, patients need to speak up! A perfect example of the need to communicate is an MS patient who is using any of the interferon beta drugs (Avonex, Betaseron or Rebif). Depression and/or suicide ideation of attempt is a well-documented risk with any of these products. While it is not uncommon for patients dealing with a chronic illness to manage or experience episodes of depression, if this is something that is new to them, they need to talk to their physician or pharmacist. The depression most likely can be controlled, allowing them to have an improved quality of life.

**Follow directions.** It’s important for patients to follow the directions given to them by their physician or pharmacist regarding their medication and any required lab tests or follow-up visits. For instance, many drugs that rheumatoid arthritis patients use have a risk of causing liver dysfunction, especially methotrexate. If their physician recommends having their liver enzymes checked on a routine basis (perhaps every three months), patients should make sure to keep those lab appointments so that they can be appropriately monitored. People often don’t see signs of liver failure until significant damage has been done. Another example is with the tumor necrosis factor blocker medications such as adalimumab (Humira), etanercept (Enbrel) or infliximab (Remicade). These medications increase the risk of tuberculosis or hepatitis B, particularly in patients with a prior history of these diseases. Patients should disclose any prior history of exposure or treatment of these illnesses and be tested for active disease prior to initiating these specific drug therapies.

**Dealing with Multiple Physicians**

Trying to prevent adverse drug events can be a greater challenge when there are multiple physicians involved in a patient’s healthcare. If each physician is not fully aware of all prescription, OTC and herbal items that a patient is currently using, it becomes more difficult to safely adjust their medication therapy.

A few things can be done to help with this. One is to maintain a thorough and updated list of all medications, both prescription and OTC, and herbal items currently being taken with the name, dose, frequency, reason for using and date started. For every physician appointment or admission to the hospital, providing this complete medication history may help prevent a patient from being a victim of one of the 1.5 million medication errors that occur in the United States each year.

Providing this list to the pharmacy is important as well. If a patient is unable to have all their medications filled by one pharmacy, which is ideal, they should make sure that each pharmacy has the complete list of those medications, as well as which pharmacy is dispensing what medication. Specialty pharmacies find this especially useful, as often they are treating only one portion of a patient’s disease. Without the patient telling them their routine medications, they may find it difficult to help fully participate in the patient’s healthcare team. In addition, if the patient is unable to keep a complete medication list as suggested, they or any of their treating physicians can always contact the pharmacy to have them provide this list on their behalf.

Another important thing that a patient can do when a new medication is added to their drug regimen: Ask why. Is the proposed drug treating an old problem in a new way, or is it treating a new symptom that just started? If it is treating a relatively new concern, it may be possible that this is a temporary side effect that may resolve with time, or the current regimen may need a dose adjustment. Adding a new drug is not always the best choice and may not be needed in some instances.

**Always a Risk**

With any medication, there is a chance that there will be a drug interaction or side effect. This is something that is often referred to as “risk versus benefit.” The important thing for patients to remember is that just because there is a possibility of risk, it does not mean that it will occur, and with proper steps and management, the risk can be significantly decreased.

**AMY EHLERS, BS, PharmD, BCPS, is the director of pharmacy at NuFACTOR Specialty Pharmacy. She has a bachelor’s and doctorate degree in pharmacy, and is board certified in pharmacotherapy.**
**By Kris McFalls**

**Allison:** I was just informed by staff at the infusion clinic where I receive my intravenous immune globulin (IVIG) that Medicare will no longer pay for infusions for anyone whose levels are over 600. Doesn’t Medicare realize that the cost for doctor visits and hospitalizations will be higher than the cost for IVIG?

**Kris:** IVIG reimbursement under Medicare Part B in infusion clinics is managed by Medicare administrative contractors (MACs). In your particular case, IVIG coverage is addressed by LCD #L25820.

Medicare policy stipulates that IVIG is medically necessary to treat primary humoral immunodeficiency for those with a diagnosis of congenital agammaglobulinemia, common variable immunodeficiency, Wiskott-Aldrich syndrome, X-linked agammaglobulinemia and severe combined immunodeficiency. LCD #L25820 further stipulates that 1) blood level results that demonstrate a significant deficiency in gamma globulin levels must be drawn before the initial treatment; 2) a serum trough IgG level should be measured every three months prior to the infusion, and the dose of IVIG should be adjusted accordingly; 3) while infusions are usually given every four weeks, the interval should be adjusted, depending on the serum trough IgG concentrations and the patient’s clinical condition; 4) serum trough levels should be maintained at 400 to 600 mg/dl, a value close to the lower limit of normal; and 5) while a patient rarely needs his or her serum trough level greater than 600 mg/dl, if greater levels are needed, documentation should support the rationale.

LCD #L25820 also allows for coverage of IVIG for patients with recurrent severe infection and documented severe deficiency or absence of IgG subclass, as well as for patients with clinically significant functional deficiency of humoral immunity as evidenced by documented failure to produce antibodies to specific antigens and a history of recurrent infections. For patients with an IgG subclass deficiency, the LCD states that a serum IgG subclass trough level should be monitored at least every three months prior to the dose of IVIG, along with clinical progress of signs and symptoms for which IVIG therapy is required. And, for patients with a functional deficiency, the deficient antibody(ies) should be monitored at least every three months prior to the dose of IVIG, along with clinical progress of signs and symptoms for which IVIG therapy is required. In these cases, it is important to note that doctors still must use the code for one of the five allowed for primary humoral immunodeficiency diagnoses in order to get reimbursed.

While there is language in the Medicare LCD similar to what your infusion clinic staff referred, the LCD allows doctors to justify needing more IG based on the patient’s clinical response. Furthermore, some patients have normal or near normal serum IG levels, but they have other problems that require IG. As is referenced in the text for patients with an IgG subclass deficiency or functional deficiency, the LCD appears to allow for coverage of IVIG in those patients.

The staff at your infusion clinic is justified in their concern about reimbursement, but they may need further information before making a unilateral decision for all PIDD patients. I would suggest your infusion clinic reimbursement specialist request further explanation from the MAC contractor. I would also suggest you reach out to the Immune Deficiency Foundation (IDF) and make them aware of your circumstances. IDF has conducted advocacy efforts on this issue in the past and should be equipped to fight this battle again.

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

By Ever Fecske

I'M A PUSHER. I push and I push myself until there is nothing left. I suppose it is my struggle to try to find a balance between illness and normalcy. I want to do everything. The word no is not in my vocabulary.

“Will you make 100 cupcakes for a party tomorrow?” Yes!

“Will you drive me to the airport at 3 a.m.?” Yes!

The answer should be no, but that word never even pops into my head. Instead, I think of how I can complete the task, always putting the needs of others before my own.

My lack of saying no has led me to a feeling of utter exhaustion. I am my own worst enemy by packing in as many things to do in a day as I can. I thrive on being so busy — mostly because it allows very little time or energy for me to think about how tired I am.

Case in point: As part of my “maintenance” regimen, I receive IV Remicade infusions every six weeks to maintain the health of my lungs and to slow down the disease process. This is a very strong drug, and I should take it easy afterward in case there are any side effects. But, as usual, I expect everything to go as smoothly as my immune globulin infusions.

Wrong! One day after my Remicade infusion, I got in my car, still relatively drugged up from the Benadryl, drove home to pick up my sister, and then drove to pick up a cargo van so that I could then pick up supplies for an event I was designing. Imagine me driving on the freeway in an old van with no back windows and no rearview mirror, hung over and sleepy.

I began to feel a little nauseous and dizzy, so I told my sister that I thought we should stop. Fortunately, my mom worked right down the street, and we found her in the back courtyard throwing a marketing barbecue. No wonder, I thought. I'm hungry! I haven't eaten anything since the morning. I remember a huge plate of food, but I don't remember eating. I started feeling woozy, I lost my peripheral vision, and I had the most intense pressure in my head. A woman came to talk to me and I had no idea what she was saying. I went to my mom and tried to tell her that something was wrong, but my words made no sense. I wanted to say “tree,” but it came out “dress.” I was becoming more and more panicky, and I started drooling out of the right side of my mouth.

Finally, I managed to ask her to take me to the emergency room. Was I having a stroke? Was this going to last forever? I couldn't see anything! I didn't know what I was going to do about the van and the things I needed to pick up. But, why was I thinking about the van when I couldn't even control my saliva?

We made it to the ER, and the doctors sent me for an MRI of my brain. After staying the night for observation, I was told that no, I didn't have a stroke. But, I may have had an infusion-induced migraine. What? All that was due to my infusion?

The experience sure puts things in perspective. As much as I hate to admit it, I do need to say no to doing too much, especially on infusion days. While the word no rarely passes my lips, it needs to have more of a presence in my vocabulary.

Lesson learned!

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!
Most married couples start their journey together vowing to endure seasons of sickness and health. Few are tested as severely from day one as Patricia Jane Edelman and her husband, Roy, of 47 years. Patricia sent her story to IG Living as an essay submission during our recent contest. Because her story really resonated with our editors, we want to share it with our readers.

**Patricia:** I met my husband in 1961 on my first day in a new high school. I was 15 years old. As he walked through the room with his then-girlfriend, our eyes met briefly, and the thought that went through my mind was: “I’m going to marry him someday.” We did not formally meet or speak for another six months, but once we met, there really was no one else for either of us.

**Trudie:** Tell us how you met your husband.

**Patricia:** I met my husband in 1961 on my first day in a new high school. I was 15 years old. As he walked through the room with his then-girlfriend, our eyes met briefly, and the thought that went through my mind was: “I’m going to marry him someday.” We did not formally meet or speak for another six months, but once we met, there really was no one else for either of us.

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**Trudie:** Tell us about your diagnoses.

**Patricia:** While I have been progressively ill for many years, my husband suffered primarily from progressive osteoarthritis, which has ultimately left him wheelchair-bound. He acquired hypogammaglobulinemia in 2003, progressing to a diagnosis of common variable immune deficiency (CVID) a few years ago, and he has been on infusions every three weeks since 2003. After many years of progressive illness, I finally received definitive diagnoses of dermatomyositis, Sjogren’s (secondary to the dermatomyositis), seronegative inflammatory polyarthritis and relapsing polychondritis, hypogammaglobulinemia and some osteoarthritis.

**Trudie:** What’s it like to live with so many illnesses under one roof?

**Patricia:** Even though we are frequently sick, usually uncomfortable and always wary of the next infection or complication, I would change nothing. After all, when I recited my wedding vows in 1964, this was all included, no surprises.

**Trudie:** What helps you stay positive?

**Patricia:** Of course, our faith is primary in keeping us positive. We do not want to fail God in coping with trials or troubles and are “content wherein we find ourselves.” We are confident that our lives and circumstances have meaning. We fully accept that while we may never know it, how we respond to our circumstances may have far-reaching effects on people we will never know. Truthfully, we are positive people by nature and though there are times when we are not as happy about our circumstances as we would like, we always have an underlying joy in life that carries us through. Practically speaking, I find it helpful every now and then to allow myself 30 minutes to feel sorry for myself. Then I move on.
**Trudie:** Tell us your definition of the vow “for better or worse.”

**Patricia:** Dare I think this is the “worse”? Not at all. We are still in love. We are still happy. We have children, grandchildren and great-grandchildren who love us. We still live unassisted in our own lovely home in glorious retirement. We have found hobbies we can pursue that are interesting and fulfilling, and the Internet and telephone allow us to keep in close touch with our many friends and relatives. I am tempted to say that instead of the “worse,” this may very well be the “better.”

**Trudie:** What did you and your husband do for work prior to retirement, and how did your illnesses impact your career decisions?

**Patricia:** For the first eight years of our marriage, during the Vietnam War, my husband was in the U.S. Navy, from which he received an honorable discharge for disability. In 1973, we answered the call of God to ministry and both of us were Salvation Army officers for 25 years prior to our retirement in 2001 due to our illnesses. For 24 years, we did not allow our physical conditions to prevent us from doing our work, but in 2000, my dermatomyositis flared and left me unable to work. This, combined with my husband's doctors' urging that he retire, led to our retirement 11 years early.

**Trudie:** What does the vow “in sickness and in health” mean to you?

**Patricia:** We meant it when we entered into that covenant at the ripe old age of 17, and our determination has never wavered. Is one of us doing poorly? The other picks up the slack. Are we having a particularly good week? Time to take a trip to town or rent a movie. We never embraced the idea of a “cut-and-run” marriage in which only the good times were to be honored and the bad times called for quick exit and a search for someone and something easier. It is in our illnesses that we have grown and have truly come to know each other in all our strengths and weaknesses — in other words, as whole persons, not as idealized constructs that could not and would not have failed to disappoint on every level.

**Trudie:** How did living with chronic illness affect your parenting?

**Patricia:** Frankly, we just never let it make a difference. If one of us happened to be out of commission temporarily, the other made sure everyone got to their activities and did everything that needed doing. We never felt hampered or crippled or held back. Rather, we had each other's back. I am not sure to this day that the children really had any idea that we were actually ill, except for the occasional hospital stay for my husband through those years, unrelated to immune issues.

**Trudie:** You also have a positive attitude about “for richer or poorer.” Tell us about that.

**Patricia:** We are blessed to be financially secure at this time, but we know full well that material security is fleeting at best. “Richer” for us encompasses not only our home and other possessions, but also our rich and turbulent family life, our steady friends and our ability to find joy in small things — a good book, the many hobbies we can engage in even with our limitations, a short drive in the country or a trip to the local Walmart just to look around.

**Trudie:** What advice do you have for other married couples dealing with chronic illness?

**Patricia:** Do not let your illness define you. You are not your illness. You are separate, valuable, competent people who can and will find ways to help each other, each compensating for the other’s weaknesses and drawing upon the other’s strengths. Be willing to give and accept help and compassion, and never be afraid to express the frustrations and anger and unexpected joys that come with chronic illness.

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“MRS. HAGGARD, may I speak with you privately?” Ms. Maddie, Caleb’s preschool teacher quietly asked in my ear. “How’s about over there,” she pointed, where “Art Street” and “Play House Drive” meet.

I swallowed hard and nodded in silent submission as circle time was in progress. A “mommy sighting” for a bunch of homesick 3-year-olds suffering with separation anxiety can easily start an uncontrollable riot.

I followed Ms. Maddie to our destination, my eyes fixed to the sway of her Holly Hobbie skirt and my ears keeping time with the smacking of her well-loved Birkenstocks against her cracked heels. Ms. Maddie would be a great candidate for the reality show “What Not to Wear.” I giggled, snapping myself out of the spontaneous fear funk Ms. Maddie had put me in. Unfortunately, my momentary happy high was about to come to an end.

“Caleb mentioned something to the group this morning that begs clarification, Mrs. Haggard,” Ms. Maddie pontificated, in her sappy-sweet, uber-sugary tone. Wringing my sweaty palms I thought, “Ugh, here we go again!” Despite my numerous attempts at explaining Caleb’s CVID (common variable immune deficiency), and the too-many-to-mention illnesses, treatments and DME (durable medical equipment) that goes along with the aforementioned, Caleb’s CVID has interrupted another 3-year-old “love-in” for Ms. Maddie.

“What can I help you with this time?” I asked.

“Caleb said something about breathing in ‘bubbling drugs’ through what he called a ‘smoker.’ Can you explain?”

For a moment, I thought Ms. Maddie was smoking something, and I was concerned I’d get a contact “high”! She actually thought Caleb was describing his nebulizer as something my college dorm mate liked to use on occasion!

The nebulizer isn’t the only strange but true medical DME gadget along this family’s path of chronic illness that has elicited some uncomfortable moments. After 14 years of legal pharmaceuticals and their paraphernalia, I thought I’d seen it all, until I was diagnosed with plantar fasciitis. The description for this in Cheryl’s...
Dictionary of Medical Terms is: I’d rather step on a hot nail than walk.

“Well, that should hold ya’ for a while. We’ll see you in six weeks for a follow-up,” Dr. Gilson explained as he finished fiddling with my air cast. Two injections later, the bottom of my right foot was numb and cozy in its new “home”: a black contraption that wrapped around my ankle and my foot, delivering pillows of air that I controlled. It was heaven, despite its appearance.

After saying my goodbyes to Dr. Gilson’s staff, I limped toward the elevator and decided to take my numb foot on a much-needed trip to the nearest big-box store. “Walking” around the store, picking up this and that was awkward — not just because of my foot, but because of the stares, occasional pointing and the little ones constantly asking, “Lady, what’s that thing on your foot?” or “What does that thing do?” Being polite, I’d say, “I have an owie and I just have a funny-looking black band-aid, that’s all. I’ll be OK.”

Some folks were kind, keeping to themselves, but others were plain mean! One mother actually gave me a snide look and held her tot close to her when I happened to be in the dairy section to pick up my favorite yogurt. It really was puzzling to me that I somehow irriated the plantar fascia of my foot, and then tried to inject a little about primary immune deficiency and how it affects so many parts of our bodies.

“No, no, no.” Mr. Nice Guy said, shaking his head. “Yer other foot. What ya’ do to get it?”

“Well, I was just telling you about my illness and, uh, what?” I stammered. “Don’ play coy with me, sister. C’mon, tell me. Was it drugs? How ‘bout gambling? My brother got himself in a heckuva mess with gambling.”

Mr. Nice Guy kept speaking to me, but his words were just background noise to what I was thinking.

“OK, so you gonna tell me or what? C’mon now, what did they throw you in jail for?” Mr. Nice Guy asked, pointing right at my big black band-aid.

It was as if a lightning bolt had my name on it. Mr. Nice Guy thought my air cast was an ankle bracelet — and not the pretty, jewelry-type bracelet! I’m talking about the kind of ankle bracelet made famous by Lindsay Lohan. The kind of ankle bracelet Mr. Nice Guy and the rest of the big-box store patrons thought I had, which can tell the authorities if I’ve been drinking, doing drugs or even if I left my house — not what the latest fashion statement is. This explains the glares, snubs and stares from other shoppers as well. They probably thought I was an escaped criminal; no wonder they looked at me with such contempt! Mr. Nice Guy thought I was a bad “good” girl! Hilarious!

As soon as I stopped laughing, I explained to Mr. Nice Guy that I was a good girl with very bad genes. Mr. Nice Guy and I parted ways with a good laugh and an even better story to share.

I do have to confess: Since meeting Mr. Nice Guy, I’ve caught myself thinking more about this homebound ankle bracelet thing. How bad could it be, really? I mean, to stay home and not have any outside commitments for a while? That sounds more like heaven, not punishment! Count me in for not having to take my turn to drive the carpool, or take this one to ballet and that one to saxophone lessons. Or, take this one for shots or that one for a blood draw. What about the cleaners, or the grocery store? The vet or the dentist? Do they count? How about PTA meetings or rushing to the post office? Paying bills? What about taking overdue books to the library or…

Cheryl L. Haggard is a stay-at-home mom and has three children, two of whom have CVI. She and her husband, Mark, also operate Under the Hood Ministries at www.underthehoodministries.org.
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.

EMPATHY IS OFTEN a misused term. It’s not uncommon to hear someone say that they empathize with someone’s situation. But, to truly empathize with another, we must be able to identify with the other’s experience by having the same or an acutely similar experience. Therefore, it is common to hear patients with a primary immunodeficiency (PIDD) — a diagnosed disease in only approximately one in 1,200 people — say that others simply don’t “get it.” Not Annette Zampelli. She “got it” starting at a very young age, despite the fact that she didn’t “know it” — even when she was caring for PIDD patients.

Not Seeing the Forest for the Trees

ANNETTE ZAMPELLI was a nurse caring for PIDD patients when she was diagnosed with CVID. Since her diagnosis and starting treatment with SCIG, she now has the energy to enjoy time with her husband, Ed, and their healthy 2-year-old son, Matthew.

A Lifelong Desire to Care for Others

Annette was known as the “sick kid.” From as far back as she can remember, she was often ill. “My first memories were of my mother shaking amoxicillin powder onto a tablespoon for me to take,” she says. It wasn’t uncommon for her to...
miss 30 days a year of school because of infections.

Being in the hospital and at the doctor’s office so often, Annette became accustomed to being around nurses. “I enjoyed being around nurses,” she explains. “When I was young, parents weren’t allowed to stay with their kids at night in the hospital, and I used to spend time at the nurse’s desk to stay entertained.” Annette says that her mother told her she wanted to be a nurse ever since she was 5 years old. Not surprisingly, considering her own situation, she was interested in pediatrics. And, in high school, she worked as a candy striper and remembers being able to hold the babies.

In 1990, at age 17, she started nursing school at Geisinger Medical Center in Danville, Pa. After graduating, she worked at Altoona Hospital for a year and a half. She then moved to Hershey, where she started working at Penn State Hershey Medical Center in pediatrics, during which time she finished her bachelor’s degree, as well as obtained her master’s degree as a nurse practitioner.

Signs, Signs, Everywhere Signs
Throughout this time, Annette was continually ill and had a chronic cough. “I was sick all the time, and I just attributed it to being around sick kids and the unusual hours that were just draining on me,” she explains. “So, I went into telephone triage to get away from people to see if I would get better. I was still always sick, but it wasn’t impacting me as much, because [the job] wasn’t as labor-intensive.”

When she decided to go back to school for her master’s, she began working in the pediatric outpatient allergy/immunology clinic, where she worked with PIDD patients more regularly. It was at that time when she became really sick and was in the hospital in a telemetry unit, causing her to miss six weeks of work. “That was one of the most scary parts,” Annette says. “I didn’t think I was going to make it through that one, but I did eventually get better. Not being able to breathe well is such an awful feeling.” Annette’s doctors knew she had a bad illness; they just didn’t know what it was. She was first diagnosed with severe acute respiratory syndrome (SARS), and despite being prescribed asthma medication, she wasn’t responding well to it. Her doctors told her she wasn’t taking her medicine correctly. Her response: “I’m an asthma educator, so I know how to take them.”

She continued to be plagued with illness and kept antibiotics at home. Working in an outpatient office, she would treat herself in the back office with nebulizer treatments. It wasn’t until 2006, when she became sick and went to see a different pulmonary doctor, that she was diagnosed. After a work-up, he found she had common variable immune deficiency (CVID).

After being diagnosed, Annette was surprised. Then, she says, “I

Despite the new common bond between her and her patients, Annette knows that because of her lifelong battle with illness, she has always been empathetic to patients and to their issues.
always been empathetic to patients and to their issues. For instance, one of the doctors she worked with was proactive about home schooling, but Annette was just the opposite. “When I was diagnosed and I had newly diagnosed patients that parents were worried about, I would say, ‘As long as you know what to do, there’s nothing you can’t do.’” She wanted them to know that it is important for their kids to go to school and get the socialization skills that they don’t get when home-schooled. Being diagnosed with a 

Today, Annette uses her experiences as a patient and a nurse practitioner to get the word out about PIDD.

PIDD “doesn’t mean you can’t be in crowds and in school; you just have to know how to take care of yourself,” Annette says. “It’s very important to make sure that there is a sense of normalcy so children don’t feel isolated.”

And, she doesn’t empathize only with her patients. Knowing how badly she wanted to be diagnosed herself, she understands how her parents felt. “They felt really bad that they weren’t able to get me diagnosed sooner,” Annette explains. “We lived in a very remote area and they still live there today, and I bet that if anybody there has the same symptoms, they still wouldn’t be diagnosed.”

Unfortunately, it’s hard to turn the tables. “Probably the hardest people to understand and accept [my disease] were my parents,” Annette says. The doctors and nurses all told Annette’s parents that it was in her head — that she just didn’t want to be in school. “When I was diagnosed, my mother said she wanted to call that school nurse and tell her,” she exclaims. Recently, Annette took her mother to the national Immune Deficiency Foundation (IDF) conference in Phoenix, Ariz. “It was really an eye-opener for her,” Annette says. “She never really understood that this is a lifelong thing, and it’s something that can be serious if it’s not monitored and if you don’t take care of yourself.”

Patient, Nurse and Educator
Annette’s illness has shaped her life. Having worked to transition patients from getting intravenous immune globulin (IVIG) treatments to subcutaneous immune globulin (SCIG) treatments, it was easy for her to decide to choose SCIG, which she does weekly. She also attributes the ease of this transition to the friends she has met through IDF and CSL Behring.

Two weeks after her first infusion, she felt so much better that her personal life changed. Before being diagnosed, she was so worn out that she and her husband never did anything; she just wanted to lie on the couch. She also was unable to get pregnant and suffered three miscarriages. “My OB doctor felt that I was too sick — that my body didn’t allow me to maintain any kind of pregnancy because it was all I could do to keep functioning on my own,” Annette explains. Now, she and her husband have a healthy 2-year-old son.

Today, Annette uses her experiences as a patient and a nurse practitioner to get the word out about PIDD and to let people know what they should look for. As the medical science liaison with CSL Behring, she is responsible for working with key opinion leaders on publication planning, research development and other interests. She felt working with CSL Behring was her chance to help make a difference in the PIDD community. “If one person could be diagnosed as a result of learning my story, then I know I am able to make a difference,” Annette explains. “I want to be a role model and make people understand that you can still lead a normal life and follow your hopes and dreams. This is not the end, but a beginning. I may have CVID, but it doesn’t define me.”

She still hears from some of her PIDD patients with whom she was close and who still send her pictures of their kids. “It was a special relationship because I followed them for years,” Annette says. “They saw what I went through, how much better I got and how [treatment] made a difference in my life.”

RONALE TUCKER RHODES is the editor for IG Living magazine.
Imagine having to choose between FEEDING YOUR FAMILY and getting a lifesaving MEDICATION.

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Social Media and Its Effects on the IG Community

Social networking platforms continue to transform the way people in the IG community connect.

By Mark T. Haggard

AN INFORMATION REVOLUTION continues to sweep across the world thanks to social media outlets like Facebook and Twitter. Not only have businesses and organizations reaped the benefits of these networks, so too have individuals — especially those like immune-deficient patients who rely on these networks to connect with others who face the same health issues. And, while each follower of a social media outlet participates for their own reasons, there’s no disputing that individual lives have improved through the sharing of information on the social network.

A Need to Reach Out

Two issues that face many in the immune globulin (IG) community are isolation and the misunderstanding by others around them. Outside of the community, people do not understand the issues that confront us. The classic story is of the person telling someone with primary immunodeficiency (PIDD), “You look great,” while inside the proverbial time bomb is waiting, ready to be detonated by the next pathogen that enters the body. Another issue faced is isolation because of the rarity of our disease. Few people have PIDD. You may find huge gatherings of those with other diseases, but those with immune deficiencies are few and far between.

Only members of our small IG community of PIDD patients and their families know what we are going through. Often, our closest friends and most family members have no idea of the challenges we face. When people ask us how we feel, we are troubled by the double-edged sword of a truthful answer. When we speak honestly, we may be derided as “crazy” or as “complainers.” It is simpler to bite our tongues and lie, telling them that we are doing “fine.”

So with so few of us who can relate to each other, we need a way to get and stay connected, to share our knowledge and to build friendships on common experiences and common concerns.

Social Media’s Many Forms

Along came the social media sites like Facebook and Twitter. But, while these two social media sites have become household names, there exist many other social media forms, including Internet forums, weblogs,
social blogs, microblogging, wikis, podcasts, photographs or pictures, video, rating and social bookmarking. And, there has been rapid growth in the number of U.S. patent applications that cover new technologies related to social media. Today, there are more than 250 published applications.

According to a report by Nielsen (www.nielsen.com/us/en/insights/press-room/2009/time_on_facebook.html): “In the U.S. alone, total minutes spent on social networking sites has increased 83 percent year-over-year. In fact, total minutes spent on Facebook increased nearly 700 percent year-over-year, growing from 1.7 billion minutes in April 2008 to 13.9 billion in April 2009, making it the No. 1 social networking site for the month.” Nielsen lists the top 10 social networking sites as Facebook, Myspace.com, Blogger, Tagged.com, Twitter.com, MyYearbook, LiveJournal, LinkedIn, SlashKey and Gaia Online.

*IG Living* is no stranger to the world of social media. On the *IG Living* website, social networking sites are listed for 15 disorders treated with IG (www.igliving.com/IGTreatedDisorders.aspx). As of this writing, the *IG Living* Facebook page has 965 fans, and by the time this goes to press, it will likely have surpassed the 1,000 mark. Each week, dozens of conversations are initiated about issues relating to chronic illness.

**Benefits of an Online Community**

One of the great things about a social media site is that we can quickly meet other people being treated with IG. Because they know exactly what we are going through, we no longer feel alone. It is the perfect place to vent and be happy at the same time; it is a place where we do not have to worry about being judged. Some go so far as to say that, because it is a place to share our deepest feelings and concerns, it is a place to be truly “loved.”

Beyond making emotional connections online, social media has proven practical for the IG community. It is a place where we can speak to the pioneers who have gone ahead of us who can now pass along invaluable information for our present situation — information about doctors, treatment, billing and any number of things. In turn, we may be someone else’s pioneers. “It’s incredible looking at stories; it’s incredible to look at data,” one user said. “Once you start, people tell others and the stories spread.”

In a similar vein, getting opinions from many sources is likely to produce better options than those produced by the one person to whom you may be talking on the telephone.

But, with the good can also come the bad. The very thing that makes social networking such a useful tool is what can bring about the most grief. A statement posted on a Facebook site is in a public place for anyone to see; even communications that are considered “private” can be made public by an individual with above-average computer skills and malice in their hearts. Once a statement is out, it stays out and cannot be retrieved. So, people should think twice before pressing “send.” Nor are there checks and balances on a public forum; the person professing to be an expert might be passing along information that is out-and-out false. Discretion should be used when taking information from a social networking site. In fact, it is best to run an idea by someone who is a trusted authority in the field, not some hack behind an avatar.

**A Multipronged Platform**

Social media offers numerous benefits for the IG community. It has proven to be a place for individuals to share ideas, to be understood and maybe even to feel loved. It also has grown into a platform to educate the public about the ordeals of those dependent on IG and for advocating on their behalf. Indeed, social networking just may be the path to accessing this life-giving therapy.

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

**How Can You NOT Laugh at a Time Like This? Reclaim Your Health with Humor, Creativity and Grit**

Author: Carla Ulbrich  
Publisher: Tell Me Press LLC, www.tellmepress.com

Singer-songwriter Carla Ulbrich has found laughter to be a lifesaver under the stress of multiple illnesses and constant health “care.” Her book, *How Can You NOT Laugh at a Time Like This?*, is a collection of short, inspiring, funny essays intended to help people thrive and celebrate life despite illness. As Ulbrich tells her story (and shares some songs), she lampoons common fears and prejudices about illness and lambastes the foibles of the medical industry. She offers heartfelt and humorous advice for navigating mainstream and alternative therapies, and she guides partners, families and friends who wish to help their loved ones. Her candid insights, wisecracking commentary, handy lists, hilarious song lyrics and gentle camaraderie will put a smile on the face of anyone who wants to face illness with courage and humor.

**How to Be Sick: A Buddhist-Inspired Guide for the Chronically Ill and Their Caregivers**

Author: Toni Bernhard  
Publisher: Wisdom Publications, www.wisdompubs.org

This instructive and inspiring book is for anyone who is — or who might one day be — sick. And, it can be a gift of guidance, encouragement and uplifting inspiration to family, friends and loved ones struggling with the many terrifying or disheartening life changes that come so close on the heels of a diagnosis of a chronic condition or even life-threatening illness. The author — who became ill while a university law professor in the prime of her career — tells readers how she got sick and, to her and her partner’s bewilderment, stayed that way, and how she had to learn ways to make “being sick” the heart of her spiritual practice.

**On Hope and Healing: For Those Who Have Fallen Through the Medical Cracks**

Author: Neil Nathan, MD  

This new resource book provides the latest information on a variety of illnesses (chronic pain, Lyme disease, chronic fatigue, fibromyalgia) that most family practitioners are unequipped to diagnose or treat effectively. It offers clear, readable explanations for the causes for and cures of today’s onslaught of complex/chronic illnesses. Written in terminology that the average reader can understand, the book can be informative and useful for patients, as well as medical professionals who are currently mistreating or misdiagnosing chronic illness patients.

**Chronic Illness: Impact and Intervention (7th edition)**

Author: Matthew Hansen and Santo Garcia  
Publisher: GBS/CIDP Foundation International, www.gbs-cidp.org

This book’s authors describe the impact and magnitude of chronic illnesses on the U.S. population. It is intended as a resource for nurses caring for patients with chronic illnesses, with information encompassing the needs of not only the patient but also the patient’s family. The focus is on the illness experience as opposed to the disease process. The book is divided into four major topic areas: the impact of the disease, the impact on the client and family, the impact of the health professional, and the impact of the system. Clear, up-to-date information is provided not just on the diseases, but specifically on the perceptions and experiences noted by patients, caregivers and families.
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Managing Chronic Pain

By Kris McFalls

CHRONIC PAIN OFTEN goes hand in hand with chronic illness. And, much like chronic illness, the severity and types of chronic pain are as individual as the patients who experience them. Additionally, how chronic pain is managed directly correlates with the patient’s quality of life.

Combining Alternative Therapies with Traditional Therapies

Often, many chronic pain sufferers find that a combination of traditional and alternative therapies is helpful. Many alternative options are easily available without a doctor’s prescription. But, while the ease of attaining alternative therapies is alluring, these therapies can be dangerous and expensive. So, patients should never start any new treatment without first consulting their physician. Additionally, there are a number of con artists camouflaged as legitimate practitioners who are more than happy to separate desperate patients from their money. Therefore, patients are wise to ask for credentials and to do their homework before agreeing to part with their hard-earned cash.

Often, many chronic pain sufferers find that a combination of traditional and alternative therapies is helpful.

Alternative therapies have been used as therapeutic modalities for centuries. The use of paraffin wax therapy, for instance, can be traced back to the Roman Empire. Today, it is often used by physical therapists, occupational therapists and other specialists to augment the treatment of arthritic pain, stiff joints, certain skin conditions, muscle soreness and fatigue. Paraffin baths and wax refills come in all shapes, sizes and prices, and patients need not spend a lot of money on them.

While some patients find the heat of paraffin wax relieves their stiff and achy joints, others find cold does more to relieve spasms and burning sensations. Ice packs made of gel can be molded comfortably around joints to provide maximum coverage without the sharp, melting edges of ice cubes. There are even form-fitted sleeves to hold cold packs in place for specific joints such as the ankle, shoulder or knee. For those who want the comfort of a gel cold pack but not the cost, one can be made inexpensively at home by combining one part rubbing alcohol with three parts water in double-bagged zip-lock bags.

Heat and cold also can be combined with a transcutaneous electrical nerve stimulation (TENS) unit to control pain. Or, a TENS unit can be used alone. A TENS unit is a small pocket-sized, battery-operated device that uses electrodes placed on the skin over the desired area to deliver mild electrical signals to the nerves. People using a TENS unit feel a mild tingling sensation. Purchase prices for these units can start at about $60 and reach as high as $500. Many lower-priced models will have the options most patients need. And, some insurance companies may even reimburse the rental or purchase price. In any case, a TENS unit usually requires a physician’s prescription.

It is quite common to see a TENS unit used in a rehabilitation setting. But, patients should never begin treatment with one without the supervision of a doctor or therapist. This is because it is important to learn how to properly prepare the skin so that the contact with the electrodes is even. Failing to do so could make this type of therapy very uncomfortable.

Using Prudent Caution

There are many other alternative treatment options that patients find helpful for treating chronic pain, and it may take a combination of alternative and traditional therapies to help give patients a better quality of life. Yet, what works for one patient may not work for another. And, it is wise for patients to exercise a prudent amount of caution when making purchases — especially when purchasing products from a person who is profiting from those purchases.

KRIS MCFALLS is the full-time patient advocate for IG Living magazine.
Carex Health Brands
The new Dual Hot & Cold 2 in 1 Pack has two inserts — a gel pack for the freezer and a microwavable heat pack — that address a wide variety of ailments. The pack features an extra-long elastic strap to comfortably secure the wrap in various positions — knee, wrist, elbow, arm and thigh — for complete mobility. It can be used alone or with physical therapy.
(800) 526-8051; www.carex.com/products/detail/639

ColPaC Supply
ColPaC ice packs come in different sizes, shapes and colors that are universal and can be used on practically any body area, including Neck Ice Packs, Back Ice Packs, Shoulder Ice Packs, Elbow Ice Packs, Wrist Ice Packs, Knee Ice Packs and Ankle Ice Packs. Also available are Eye Ice Packs made to relieve puffy eyes and headaches, as well as for the neck to help treat whiplash, swelling, pinched nerves, stiffness, sprains, neck injuries or other traumas.
(888) 498-8587; www.colpac-supply.com

Homedics
The ParaSpa Plus Paraffin Bath hydrates and soothes skin. The lid locks for safety, a ready light lets users know when wax is ready for use, and it includes three pounds of hypoallergenic wax and 30 liners. No scents or dyes are added.
(800) 466-3342; www.homedics.com

IceWraps
Elasto-Gel therapy products are made with a tough, flexible high-glycerine gel that is covered with a four-way stretch material that allows maximum conformity, hot and cold transfer and comfort. A single Elasto-Gel product can be used for both hot and cold applications. When used for cold therapy, the product will remain flexible even at –20 Fahrenheit. They are microwaveable, will not leak even if punctured and are designed for use in the home or in a healthcare facility.
(800) 650-9727; www.icewraps.net/elasto-gel-brand.html

Performance Health
Biofreeze uses an herb called Ilex, which is extracted from a holly plant in South America, that acts as an instant cold application and helps the gel sink deeper through the skin’s layers. It is designed to be used for physical therapy, massage therapy, arthritis pains, strained muscles, sports injuries, exercise training and patient care, and comes in a 3-ounce roll-on applicator, 4-ounce tube, 4-ounce hands-free tube, 4-ounce cryo-spray, 16-ounce pump, 16-ounce spray, 32-ounce pump, gallon pump waiting room kit, gravity feed dispenser and pain-relieving wipes (24 single-use packs).
(800) 246-3733; www.biofreeze.com

TENS Units
A transcutaneous electrical nerve stimulation (TENS) unit is designed to send mild electrical impulses to certain parts of the body via electrodes that are temporarily attached to the skin. The units require a doctor’s prescription and require supervision by a doctor, physical therapist or occupational therapist.
(866) 237-4013; www.tensunits.com/tens.htm
For a more comprehensive list of resources, visit the Resources page at www.IGLiving.com.

General Resources
These organizations provide information about various disease states, which can be found by conducting a search of the disease state name.
- Advocacy for Patients with Chronic Illness: www.advocacyforpatients.org
- The Alliance for Biotherapeutics (fair access to plasma therapies): www.bioalliance.org
- American 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 Infusion Center Association: www.infusioncenter.net
- National Institutes of Health: www.niams.nih.gov/hi/topics/pemphigus/pemphigus.htm
- National Organization for Rare Disorders (disease-specific support groups and virtual communities for patients and caregivers): www.rarediseases.org
- Office of Rare Diseases Research: rarediseases.info.nih.gov
- Patient Advocate Foundation (patient access to care, maintenance of employment and financial stability): www.patientadvocate.org

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

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

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

Guillain-Barré Syndrome (GBS)
Websites
- GBS/CIDP Foundation International: www.gbs-cidp.org
- The Neuropathy Association: www.neuropathy.org

Online Peer Support
- GBS/CIDP Foundation International Discussion Forums: www.gbs-cidp.org/forums

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

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

Online Peer Support
- Myositis Association Community Forum: www.myositis.org
- Myositis Support Group: www.myositissupportgroup.org

Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus (PANDAS)

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

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
- American Academy of Allergy, Asthma & Immunology: www.aaaai.org
- International Patient Organization for Primary Immunodeficiencies (IPOPI): www.ipopi.org
- Michigan Immunodeficiency Foundation: www.midf.org
Sources

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

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

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

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

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

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

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

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

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

Have something to add to these pages? Please send your suggestions for additions to the IG Living Resource Directory to editor@IGLiving.com.
Hizentra®, Immune Globulin Subcutaneous (Human), 20% Liquid

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

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

4 CONTRAINDICATIONS
Hizentra is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of human immune globulin or to components of Hizentra, such as polysorbate 80. Hizentra is contraindicated in patients with hyperprolinemia because it contains the stabilizer L-proline (see Description [11]).

Hizentra is contraindicated in A-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.

5.3 Reactions Reported to Occur With IGIV Treatment
The following reactions have been reported to occur with IGIV treatment and may occur with IGSC treatment.

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

Periodic monitoring of renal function and urine output is particularly important in patients judged to have a potential increased risk of developing acute renal failure.2 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 products3-5. 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 chylomicronemia, marked high triacylglycerols (triglycerides), or monoclonal gammopathies. For patients judged to be at risk of developing thrombotic events, administer Hizentra at the minimum rate practicable.

Hemolysis
Hizentra can contain blood group antibodies that may act as hemolysins and induce in vivo coating of red blood cells (RBCs) with immunoglobulin, causing a positive direct antiglobulin (Coombs’) test result and hemolysis.6-8 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.9

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.10 TRALI is characterized by decreased respiratory distress, pulmonary edema, hypoxemia, normal left ventricular function, and fever. Typically, it occurs within 1 to 6 hours following transfusion. Patients with TRALI may be managed using oxygen therapy with adequate ventilatory support.

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

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

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

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

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

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

The safety of Hizentra was evaluated in a clinical study for 15 months in subjects with PI who had been treated previously with IGIV every 3 or 4 weeks. The safety analyses included 49 subjects in the intention-to-treat (ITT) population. The ITT population consisted of all subjects who received at least one dose of Hizentra (see Clinical Studies [14]). Subjects were treated with Hizentra at weekly doses ranging from 66 to 331 mg/kg body weight during the wash-in/wash-out period and from 72 to 379 mg/kg during the efficacy period. The 49 subjects received a total of 2264 weekly infusions of Hizentra.

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

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

<table>
<thead>
<tr>
<th>AE (&gt;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>
<tr>
<td>Other AEs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>13 (26.5)</td>
<td>40 (0.18)</td>
</tr>
<tr>
<td>Cough</td>
<td>8 (16.3)</td>
<td>9 (0.04)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>7 (14.3)</td>
<td>8 (0.04)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6 (12.2)</td>
<td>6 (0.03)</td>
</tr>
<tr>
<td>Back pain</td>
<td>5 (10.2)</td>
<td>11 (0.05)</td>
</tr>
<tr>
<td>Nausea</td>
<td>5 (10.2)</td>
<td>5 (0.02)</td>
</tr>
<tr>
<td>Abdominal pain, upper</td>
<td>5 (10.2)</td>
<td>5 (0.02)</td>
</tr>
<tr>
<td>Rash</td>
<td>5 (10.2)</td>
<td>7 (0.03)</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>4 (8.2)</td>
<td>7 (0.03)</td>
</tr>
<tr>
<td>Migraine</td>
<td>4 (8.2)</td>
<td>5 (0.02)</td>
</tr>
<tr>
<td>Pain</td>
<td>4 (8.2)</td>
<td>5 (0.02)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>4 (8.2)</td>
<td>6 (0.03)</td>
</tr>
<tr>
<td>Pharyngolaryngeal pain</td>
<td>4 (8.2)</td>
<td>6 (0.03)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>4 (8.2)</td>
<td>5 (0.02)</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.

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

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

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

<table>
<thead>
<tr>
<th>Adverse Reaction (&gt;2 Subjects)</th>
<th>Number (%) of Subjects (n=49)</th>
<th>Number (Rate†) of Adverse Reactions (n=2264 Infusions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local reactions‡</td>
<td>49 (100)</td>
<td>1338 (0.591)</td>
</tr>
<tr>
<td>Other AEs:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>12 (24.5)</td>
<td>36 (0.16)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3 (6.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Pain</td>
<td>3 (6.1)</td>
<td>4 (0.002)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3 (6.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Confusion</td>
<td>2 (4.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Back pain</td>
<td>2 (4.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Migraine</td>
<td>2 (4.1)</td>
<td>3 (0.001)</td>
</tr>
<tr>
<td>Diahrea</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
<tr>
<td>Abdominal pain, upper</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
<tr>
<td>Nausea</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
<tr>
<td>Rash</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>2 (4.1)</td>
<td>2 (&lt;0.001)</td>
</tr>
</tbody>
</table>

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

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

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

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

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

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

6.2 Postmarketing Experience

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

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

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

To report SUSPECTED ADVERSE REACTIONS, contact CSL Behring Pharmacovigilance at 1-866-915-6938 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

7 DRUG INTERACTIONS

7.1 Live Virus Vaccines

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

7.2 Serological Testing

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

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

8.3 Nursing Mothers

Hizentra has not been evaluated in nursing mothers.

8.4 Pediatric Use

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

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

8.5 Geriatric Use

Of the 49 subjects evaluated in the clinical study of Hizentra, 6 subjects were 65 years of age or older. No overall differences in safety or efficacy were observed between these subjects and younger subjects.

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Make the leap to Hizentra

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

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- Always ready for immediate use

*Based on an equivalent dose in grams.

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

Important Safety Information

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

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

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

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

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

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

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

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

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

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