

IG Treatment

Choosing a Delivery Method and Site Location



As the number of approved IG products continues to evolve, so have delivery methods and infusion site options. Here are some tips for helping patients decide which are best for them.

By Abbie Cornett

TODAY, PATIENTS TREATED with immune globulin (IG) replacement therapy have options about how and where they receive treatment. Historically, this hasn't always been the case. It's been almost 70 years since a medical discovery changed the way many primary immunodeficiency diseases (PIs) and autoimmune diseases (ADs) are treated. This breakthrough occurred when Ogden Bruton, MD, chief of pediatrics at Walter Reed Army Hospital, successfully treated an 8-year-old boy with regular intramuscular (IM) injections of human plasma-derived IG. The boy had agammaglobulinemia characterized by low immunoglobulin (IgG) levels

and repeated pneumonia. The new treatment resulted in increased serum IgG levels and an impressive reduction in the number of serious bacterial infections. While few appreciated its implications at the time, Bruton's success was expanded on and IMIG dosages became the standard of care for PI.²

Yet, despite the initial success of IMIG, these injections could only be given in limited amounts and were extremely painful. Thus, it was recognized patients needed a new method of receiving large doses of IG at one time. Fortunately, in the early 1980s, researchers developed the intravenous (IV) delivery method, which led to a rapid

increase in the amount of IG prescribed and the number of diseases it was approved to treat. Then, in the mid-2000s, the subcutaneous (SC) delivery method was developed, allowing for more frequent IG dosing and greater convenience in dosing schedules.

Today, IVIG can be administered at home and in a clinical setting, whereas SCIG is administered only in the home. Together, patients and their physicians should decide which product and delivery method are best for them and, if choosing the IV delivery method, in what setting it will be administered.

What IG Treats

IG was originally used as antibody replacement therapy in patients with PI to supplement the immune system. Since then, its use has expanded considerably to include treating and preventing various other conditions.³ Currently, IG is approved by the U.S. Food and Drug Administration (FDA) to treat:⁴

- Chronic inflammatory demyelinating polyneuropathy
- Chronic lymphocytic leukemia
- Immune thrombocytopenic purpura
- Infections following bone marrow transplants
- Kawasaki disease
- Multifocal motor neuropathy
- PI

IG is also routinely used to treat a variety of ADs and neurological diseases that are not approved by FDA, including but not limited to:⁴

- Guillain-Barré syndrome
- Lupus
- Multifocal motor neuropathy
- Polymyositis and dermatomyositis
- Multiple sclerosis
- Myasthenia gravis

A Historical Review

Because of the risk of adverse side effects, IVIG treatments were once administered only in hospitals as a safety precaution. However, expenses of these procedures soon became a major factor for insurance companies, and they began looking for less-costly alternatives to hospital infusions. In response, marketed IG products evolved rapidly to meet this need. These new IG products gave patients and clinicians additional safe IVIG and SCIG therapeutic options,⁵ which could be administered in a variety of settings, including the home, hospital, outpatient clinic and doctor office.

Site-of-Care Considerations

When making a decision about an infusion setting, it is important to remember the administration of IVIG is a complex undertaking. Providers and patients need to take multiple factors into account. First, providers need to decide which IG product is best suited to the patient to minimize adverse side effects from therapy. Therefore, each patient's clinical characteristics must be considered when selecting an IG product.⁶ Second, when choosing an IVIG product, providers need to identify which patients need a higher level of care of a clinical setting, and which patients are more suited to receive treatment at home. Further, patients need to decide which option best fits their lifestyle, as well as any insurance coverage limitations.

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Clinical Setting Considerations

For IVIG infusions, doctors may select a clinical setting if they feel additional medical supervision is warranted. In some instances, supervision may be needed because patients have experienced adverse side effects such as anaphylactic reactions, hypotension, seizures, pulmonary edema or aseptic meningitis. Other risk factors may include a health history of diabetes, age (65 years or older), coronary artery disease, hypertension, hyperviscosity disorder (including multiple myeloma, macroglobulinemia and polycythemia), thrombotic events and peripheral vascular disease.⁷

Beyond safety reasons, infusing in a clinical setting allows patients to have more interaction with doctors and nurses who can monitor their health. This oversight is particularly important for patients with comorbidities and those who have been chronically ill for a long time and may fail to notice signs of infection or a declining disease state.

Hizentra®

Immune Globulin Subcutaneous
(Human) 20% Liquid

1st and only Self-administered Ig for CIPD Maintenance

#1 Ig Prescribed for PI

**My Life,
My Way
With
Hizentra**

Hizentra is an Ig* therapy that provides proven protection for PI and CIPD with the convenience of self-administration, so you can focus on everyday living

*Ig=immunoglobulin

Important Safety Information

WARNING: Thrombosis (blood clots) can occur with immune globulin products, including Hizentra. Risk factors can include: advanced age, prolonged immobilization, a history of blood clotting or hyperviscosity (blood thickness), use of estrogens, installed vascular catheters, and cardiovascular risk factors.

If you are at high risk of blood clots, your doctor will prescribe Hizentra at the minimum dose and infusion rate practicable and will monitor for signs of clotting events and hyperviscosity. Always drink sufficient fluids before infusing Hizentra.

See your doctor for a full explanation, and the full prescribing information for complete boxed warning.

Hizentra is a prescription medicine used to treat:

- Primary immune deficiency (PI) in patients 2 years and older
- Chronic inflammatory demyelinating polyneuropathy (CIPD) in adults

Treatment with Hizentra might not be possible if your doctor determines you have hyperprolinemia (too much proline in the blood), or are

IgA-deficient with antibodies to IgA and a history of hypersensitivity. Tell your doctor if you have previously had a severe allergic reaction (including anaphylaxis) to the administration of human immune globulin. Tell your doctor right away or go to the emergency room if you have hives, trouble breathing, wheezing, dizziness, or fainting. These could be signs of a bad allergic reaction.

Inform your doctor of any medications you are taking, as well as any medical conditions you may have had, especially if you have a history of diseases related to the heart or blood vessels, or have been immobile for some time. Inform your physician if you are pregnant or nursing, or plan to become pregnant.

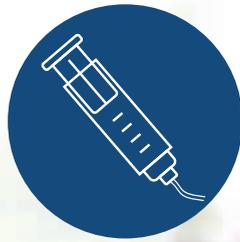
Infuse Hizentra under your skin *only*; do not inject into a blood vessel. Self-administer Hizentra only after having been taught to do so by your doctor or other healthcare professional, and having received dosing instructions for treating your condition.

Why Choose Hizentra?



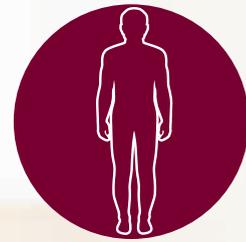
Choose where you infuse

Self-administration with Hizentra means you and your doctor can decide where you can infuse. Convenient dosing routines mean you won't have to adjust or cancel your plans due to IV infusion appointments.



No IV infusions

IV infusions can be challenging for people who have hard-to-find or damaged veins. Hizentra allows you to infuse just under the skin, not into a vein, after training from your doctor.



Proven safety

Hizentra has an established safety profile and demonstrated tolerability. In clinical trials, the most common side effects were redness, swelling, itching, and/or bruising at the infusion site; headache, chest, joint or back pain; diarrhea; tiredness; cough; rash; itching; fever, nausea, and vomiting. These are not the only side effects possible.

Discover all the benefits Hizentra has to offer at Hizentra.com

Immediately report to your physician any of the following symptoms, which could be signs of serious adverse reactions to Hizentra:

- Reduced urination, sudden weight gain, or swelling in your legs (possible signs of a kidney problem).
- Pain and/or swelling or discoloration of an arm or leg, unexplained shortness of breath, chest pain or discomfort that worsens on deep breathing, unexplained rapid pulse, or numbness/weakness on one side of the body (possible signs of a blood clot).
- Bad headache with nausea; vomiting; stiff neck; fever; and sensitivity to light (possible signs of meningitis).
- Brown or red urine; rapid heart rate; yellowing of the skin or eyes; chest pains or breathing trouble; fever over 100°F (possible symptoms of other conditions that require prompt treatment).

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

The most common side effects in the clinical trials for Hizentra include redness, swelling, itching, and/or bruising at the infusion site; headache; chest, joint or back pain; diarrhea; tiredness; cough; rash; itching; fever, nausea, and vomiting. These are not the only side effects possible. Tell your doctor about any side effect that bothers you or does not go away.

Before receiving any vaccine, tell immunizing physician if you have had recent therapy with Hizentra, as effectiveness of the vaccine could be compromised.

Please see brief summary of full prescribing information for Hizentra on adjacent page. For full prescribing information, including boxed warning and patient product information, please visit Hizentra.com.

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.

IgIQ: Support Programs to Help You Get Started

Call IgIQ to find out about programs such as:



Free 1-month supply of Hizentra and free at-home nurse visits



Most patients with commercial insurance pay \$0 out-of-pocket*



Protection if you lose insurance*



Your single source for Ig solutions

1-877-355-IGIQ (4447)

*Other terms and conditions apply. Call IgIQ to learn more.

HIZENTRA®, Immune Globulin Subcutaneous (Human), 20% Liquid
Initial U.S. Approval: 2010

BRIEF SUMMARY OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use HIZENTRA safely and effectively. See full prescribing information for HIZENTRA.

WARNING: THROMBOSIS

See full prescribing information for complete boxed warning.

- **Thrombosis may occur with immune globulin products, including HIZENTRA. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, hyperviscosity, and cardiovascular risk factors.**
- **For patients at risk of thrombosis, administer HIZENTRA at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.**

INDICATIONS AND USAGE

HIZENTRA is indicated for:

*Treatment of primary immunodeficiency (PI) in adults and pediatric patients 2 years and older.

* Maintenance therapy in adults with chronic inflammatory demyelinating polyneuropathy (CIDP) to prevent relapse of neuromuscular disability and impairment.

-Limitation of Use: Maintenance therapy in CIDP has been systematically studied for 6 months and for a further 12 months in a follow-up study. Continued maintenance beyond these periods should be individualized based on patient response and need for continued therapy.

For subcutaneous infusion only.

DOSAGE FORMS AND STRENGTHS

0.2 g per mL (20%) protein solution for subcutaneous injection

CONTRAINDICATIONS

- Anaphylactic or severe systemic reaction to human immune globulin or components of HIZENTRA, such as polysorbate 80
- Hyperprolinemia (type I or II) (HIZENTRA contains the stabilizer L-proline)
- IgA-deficient patients with antibodies against IgA and a history of hypersensitivity

WARNINGS AND PRECAUTIONS

- IgA-deficient patients with anti-IgA antibodies are at greater risk of severe hypersensitivity and anaphylactic reactions.
- Thrombosis may occur following treatment with immune globulin products, including HIZENTRA.
- Aseptic meningitis syndrome has been reported with IGIV or IGSC, including HIZENTRA treatment.
- Monitor renal function, including blood urea nitrogen, serum creatinine, and urine output in patients at risk of acute renal failure.
- Monitor for clinical signs and symptoms of hemolysis.
- Monitor for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI])
- HIZENTRA is made from human plasma and may contain infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

ADVERSE REACTIONS

The most common adverse reactions observed in ≥5% of study subjects were local infusion site reactions, headache, diarrhea, fatigue, back pain, nausea, pain in extremity, cough, upper respiratory tract infection, rash, pruritus, vomiting, abdominal pain (upper), migraine, arthralgia, pain, fall and nasopharyngitis.

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

DRUG INTERACTIONS

The passive transfer of antibodies may interfere with the response to live virus vaccines, and lead to misinterpretation of the results of serological testing.

Based on March 2018 revision

Yet, there are drawbacks to clinical settings as well. One is increased exposure to infection. A study that compared rates of pneumonia and bronchitis in PI patients found those who received IVIG therapy in the home demonstrated significantly lower rates of infection than those treated in outpatient hospitals.^{8,9} Infusing in a clinical setting also costs significantly more and can have quality-of-life implications. Because of scheduling requirements, patients frequently miss work or school, and their ability to travel is limited.

Home-Based Infusions

Home-based infusions may be beneficial to patients for many reasons. Unlike the clinical setting, home-based care offers many quality-of-life advantages such as convenience, privacy and flexibility. When patients receive services in their homes, they have greater control over their living activities and enhanced options for the resumption of normal activities, including work, school and travel. And, because patients are able to schedule treatments around their lives, they have better adherence to medications and better overall outcomes. Another significant advantage of home-based therapy, as mentioned previously, is reduced exposure to pathogens, which can greatly lower the risk of infections for patients.

When infusing at home, patients can choose either IVIG or SCIG. In the past, IVIG outside the clinical setting was discouraged because of the risk of adverse reactions. Currently, those concerns have been alleviated with increased safety and training for home care nurses, so IVIG has seen a substantial shift to home-based therapy.

SCIG infusions, which have become increasingly popular in recent years, are given by slowly injecting purified IG into fatty tissue just underneath the skin with the use of a mechanical infusion pump. SCIG is a good option for patients who have experienced serious side effects with IVIG. Common injection site reactions to SCIG include redness, swelling and itching, which are usually mild and go away after a day or two. In many cases, these reactions are generally worse with the first few infusions and diminish over time. Adverse reactions to SCIG are rare and usually mild, but can include headaches, feeling hot, nausea, diarrhea, sore throat, rash, increased cough and back pain. Extremely rare are serious side effects such as allergic reactions, kidney problems or blood clots.⁸

When comparing a clinical site to home care, cost must also be considered. Infusing at home is much less expensive. One observational study conducted in 2014 noted a statistically significant difference when patients were switched from outpatient hospital care to home care, with the median price reduced from \$6,916 to \$4,188.¹⁰ These savings are considerable for insurance companies, healthcare providers and patients.

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Options Are Greatly Expanded

IG therapy has come a long way since its first use in the 1950s. Today's IG products are safer than ever, treating a host of diseases and offering patients new routes of administration and treatment sites. Patients and physicians should discuss which product is best for them and where to infuse by taking many factors into account, including the patients' overall health, past adverse reactions and patient preference. ■

ABBIE CORNETT is the patient advocate for *IG Living* magazine.

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