



## **CSL Behring Receives FDA Approval of Hizentra™, First 20 Percent Subcutaneous Immunoglobulin Therapy**

*New high concentration, at-home therapy offers convenience to patients managing primary immunodeficiency – a rare and serious disorder affecting millions worldwide*

**King of Prussia, Pa.—March 4, 2010—**[CSL Behring](#) announced today that the U.S. Food and Drug Administration (FDA) has granted marketing approval for Hizentra™, Immune Globulin Subcutaneous (Human), 20% Liquid, for treating patients diagnosed with primary immunodeficiency (PI). A once weekly immunoglobulin (Ig) replacement therapy, [Hizentra](#) provides effective protection against infection by maintaining a steady and normal level of immunoglobulin in the body. Primary immunodeficiencies constitute a group of disorders, usually genetic, that cause a malfunction in all or part of the immune system, thereby rendering the patient unable to fight off infections caused by everyday germs.<sup>1</sup>

*Hizentra* is the first 20 percent subcutaneous immunoglobulin (SCIg) approved in the U.S. by the FDA. This high-concentration product is stabilized with L-proline, a naturally-occurring amino acid. L-proline allows *Hizentra* to be stored at room temperature (up to 25°C [77°F]). Because no refrigeration is necessary, *Hizentra* is ready to use, offering patients and physicians convenience and portability. *Hizentra* can be safely self-administered by PI patients under a physician's care.

"As the first SCIg treatment with a 20 percent concentration of immunoglobulin, *Hizentra* represents an effective, convenient choice of at-home Ig therapy that will allow people with PI to schedule treatment around their busy lives instead of scheduling their lives around treatment," said [Robert Lefebvre](#), Vice President and General Manager, U.S. Commercial Operations at CSL Behring. "*Hizentra* is an important new addition to the rapidly growing CSL Behring product portfolio, and further demonstrates our long-standing commitment to the PI and rare disease communities."

## CSL Behring

"With its high concentration, *Hizentra* is a welcome new SCIg treatment option for patients managing primary immunodeficiencies," said John Sleasman, M.D., Professor and Chief of the Division of Allergy, Immunology and Rheumatology at the University of South Florida College of Medicine, Department of Pediatrics, and one of the investigators on CSL Behring's clinical study of *Hizentra*. "*Hizentra*'s ready-to-use attribute will allow patients to infuse the product where and when it suits them, and physicians now have another product to select to best meet the individual needs of their patients."

For patients with primary immunodeficiencies, immunoglobulin replacement therapy with a product like *Hizentra* can help treat existing or chronic infections and prevent new infections from occurring. No single treatment works for every type of PI, but infusions of replacement antibodies (immunoglobulins) can help supplement the immune system to prevent infection in nearly three-quarters of PI cases that are due to antibody deficiencies.<sup>2</sup>

Immunoglobulin, or Ig, is a blood component that has become standard immune replacement therapy for most people living with PI, and nearly 70 percent of PI patients receive Ig replacement therapy. Since the 1980s, the first-line therapy for most PI patients has been intravenous immunoglobulin (IVIg), in which immunoglobulin is delivered through a needle into the vein.<sup>3</sup> Many patients, however, cannot easily tolerate intravenous infusions due to serious side effects or poor veins.<sup>4</sup> *Hizentra* allows patients to use a small, portable pump to self-administer their weekly infusions by injection under the skin (subcutaneous administration).

*Hizentra* is part of CSL Behring's Ig franchise, which also includes both the [first FDA-approved subcutaneous Ig treatment](#) and the [first proline-stabilized IVIg therapy](#). *Hizentra*, also stabilized with proline, will be manufactured at CSL Behring's new state-of-the-art facility, located at its center of excellence for immunoglobulins in Bern, Switzerland. This new manufacturing facility, which uses advanced technologies to ensure product safety and steady supply production, represents CSL Behring's long-term commitment to global Ig markets.

### **Clinical Studies**

The FDA approval of *Hizentra* was based on results from a prospective, open-label, multicenter, single-arm, clinical study conducted in the United States, evaluating the efficacy, tolerability, and safety of *Hizentra* in adult and pediatric subjects with PI. In this

**CSL Behring** study, subjects previously receiving IVIg treatments every three or four weeks were switched to weekly subcutaneous administration of *Hizentra* for 15 months (a three-month wash-in/wash-out period followed by a 12-month efficacy period). The efficacy of *Hizentra* was analyzed in 38 subjects who received at least one infusion after the wash-in/wash-out period.

### **Important Safety Information**

*Hizentra*<sup>™</sup>, Immune Globulin Subcutaneous (Human), is indicated for the treatment of patients with primary immunodeficiency (PI).

*Hizentra* is contraindicated in individuals with a history of anaphylactic or severe systemic response to immune globulin preparations or components of *Hizentra*, and in persons with selective immunoglobulin A deficiency who have known antibody against IgA and a history of hypersensitivity. If anaphylactic reactions are suspected, administration should be discontinued immediately and the patient treated as medically appropriate. Because *Hizentra* contains the stabilizer L-proline, it is also contraindicated in patients with hyperprolinemia.

*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 eliminated completely.

The most common drug-related adverse reactions, observed in 5 percent or more of subjects in the clinical study, were local injection-site reactions, headache, vomiting, pain, and fatigue.

Monitor patients for reactions associated with IVIg treatment that might occur with *Hizentra*, including renal dysfunction/failure, thrombotic events, aseptic meningitis syndrome (AMS), hemolysis and transfusion-related acute lung injury (TRALI).

For more information, including full prescribing information, visit [www.hizentra.com](http://www.hizentra.com).

### **About Primary Immunodeficiencies**

Nearly 100 types of PIs exist.<sup>5</sup> For individuals with PI, many of them children, infections may not improve as expected with usual treatments and may keep returning. As a result, patients may face repeated rounds of antibiotics or hospitalization for treatment. Repeated

**CSL Behring** infections can lead to organ damage, which over time can become life-threatening. Some infections, such as meningitis, may even result in death.<sup>6</sup>

Collectively, PIs affect an estimated 10 million people worldwide,<sup>7</sup> and the incidence is estimated to be 1 in 10,000.<sup>8</sup> Due to the X-linked inheritance in many PI syndromes, more males are affected than females.<sup>9</sup> For more information on PI, please visit [www.cslbehring.com](http://www.cslbehring.com) or contact the leading PI patient advocate groups in the U.S., the [Immune Deficiency Foundation](#) and the [Jeffrey Modell Foundation](#).

### **About CSL Behring**

CSL Behring is a leader in the plasma protein therapeutics industry. Committed to saving lives and improving the quality of life for people with rare and serious diseases, the company manufactures and markets a range of plasma-derived and recombinant therapies worldwide. CSL Behring therapies are indicated for the treatment of coagulation disorders including hemophilia and von Willebrand disease, primary immune deficiencies and inherited respiratory disease. The company's products are also used in cardiac surgery, organ transplantation, burn treatment and to prevent hemolytic diseases in newborns. CSL Behring operates one of the world's largest plasma collection networks, [CSL Plasma](#). CSL Behring is a subsidiary of [CSL Limited](#) (ASX:CSL), a biopharmaceutical company headquartered in Melbourne, Australia. For more information, visit [www.cslbehring.com](http://www.cslbehring.com).

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<sup>1</sup> Lindegren ML, Kobrynski L, Rasmussen SA, et al. Applying Public Health Strategies to Primary Immunodeficiency Diseases: A Potential Approach to Genetic Disorders. MMWR. 2004; 53(RR-1):1-29.

<sup>2</sup> Primary Immune Deficiency Diseases in America. The First National Survey of Patients and Specialists. Available at:

[www.primaryimmune.org/publications/surveys/First\\_National\\_Survey\\_of\\_Patients\\_and\\_Specialists\\_\(1995\).pdf](http://www.primaryimmune.org/publications/surveys/First_National_Survey_of_Patients_and_Specialists_(1995).pdf). Accessed December 2009.

<sup>3</sup> Buckley RH, Schiff RI. The Use of Intravenous Immune Globulin in Immunodeficiency Diseases. N Engl J Med. 1991;325(2):110-7.

<sup>4</sup> Berger M. Subcutaneous Immunoglobulin Replacement in Primary Immunodeficiencies. Clin Immunol. 2004; 112(1):1-7.

<sup>5</sup> About Primary Immune Deficiencies. What is a Primary Immune Deficiency Disease? Immune Deficiency Foundation Website. Available at: [http://www.primaryimmune.org/about\\_pi/about\\_pi.htm](http://www.primaryimmune.org/about_pi/about_pi.htm). Accessed December 2009.

<sup>6</sup> Primary Immunodeficiency. National Institute of Child Health & Human Development Web site. Available at: [http://www.nichd.nih.gov/health/topics/Primary\\_Immunodeficiency.cfm](http://www.nichd.nih.gov/health/topics/Primary_Immunodeficiency.cfm). Accessed December 2005.

<sup>7</sup> Jeffrey Modell Foundation. Primary Immunodeficiency Resource Center. Available on <http://www.info4pi.org/aboutPI/>, last accessed September 2009.

<sup>8</sup> Dube D; The challenge of immunodeficiency disorders. Postgraduate Medicine 2002.

<sup>9</sup> Patient UK. Immunodeficiency (Primary and Secondary). Available on [http://www.patient.co.uk/doctor/Immunodeficiency-\(Primary-and-Secondary\).htm](http://www.patient.co.uk/doctor/Immunodeficiency-(Primary-and-Secondary).htm). Accessed September 2009.