CSL Behring

Hizentra®

Immune Globulin Subcutaneous (Human), 20% Liquid

Explore the value of CSL Behring's leading SCIg therapy

Indications

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.

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Healthcare Systems

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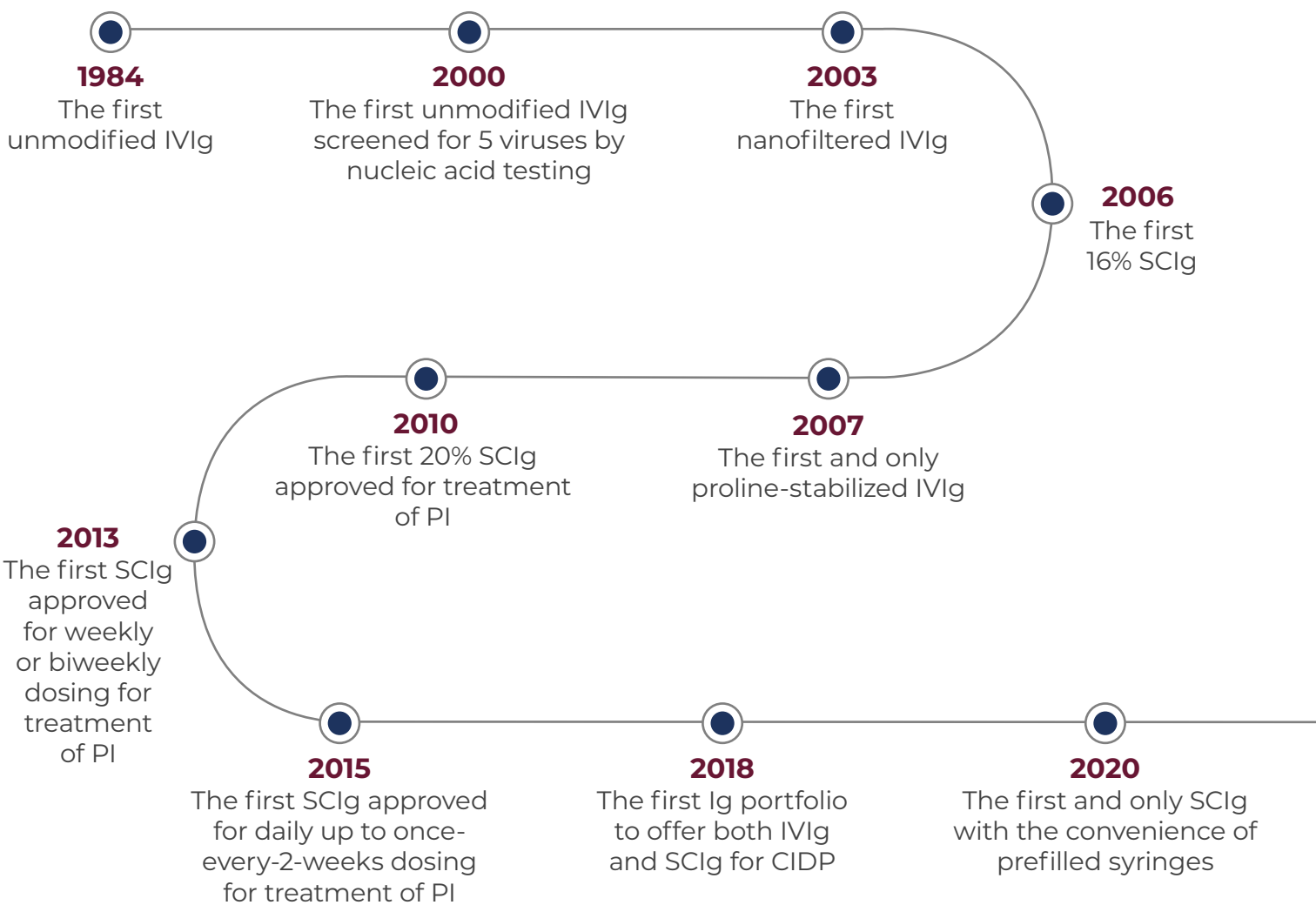
Leading the way in the Ig marketplace

With more than 60 years of experience in the research, development, manufacturing, and distribution of innovative plasma-derived therapies, CSL Behring is no stranger to being first

CSL Behring Ig therapies—timeline of FDA approval



FDA=US Food and Drug Administration; Ig=immunoglobulin; IVIg=intravenous immunoglobulin; PI=primary immunodeficiency; SCIg=subcutaneous immunoglobulin.

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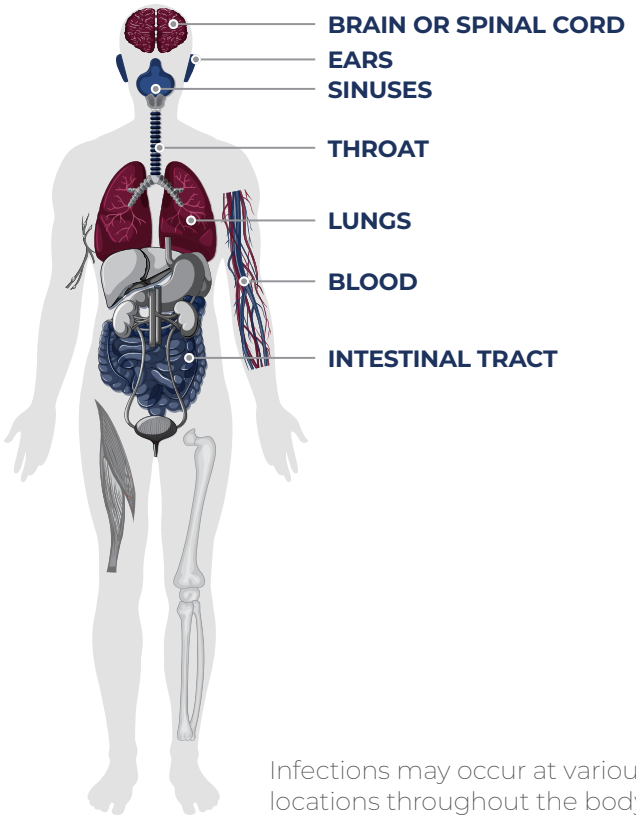
About primary immunodeficiency (PI)



Infections may occur at various locations throughout the body.

PI includes numerous rare, chronic disorders that increase the risk of persistent infections

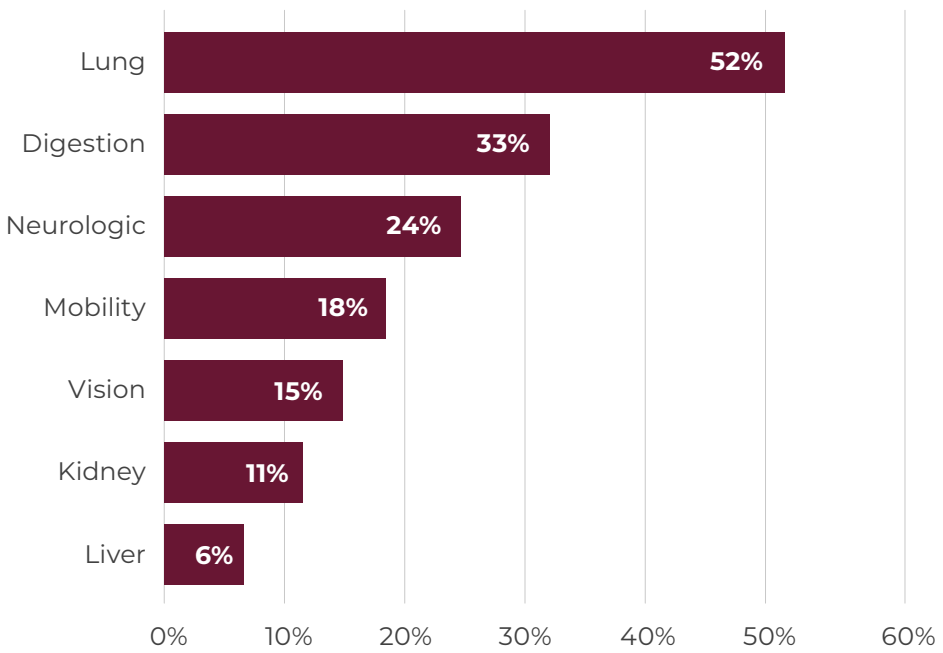
- PI is caused by a variety of genetic defects in which part of the body's immune system is missing or impaired[1]
- Untreated patients are at increased risk of severe, persistent, and recurrent infection[1,2]

There are more than 485 different forms of primary immune deficiency diseases affecting approximately 500,000 people in the United States.[3,4]

Serious infections prior to PI diagnosis led to permanent functional impairment[5]

- Irreversible organ damage may result from severe and repeated infections, often prior to diagnosis

Permanent impairments prior to diagnosis



Early diagnosis of PI and treatment with Ig can help prevent permanent organ damage

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About PI (continued)

Early diagnosis of PI can help reduce healthcare utilization costs[6]

Condition	Pre-Dx average no. of episodes	Pre-Dx cost per episode	Pre-Dx annual cost	Post-Dx average no. of episodes	Post-Dx cost per episode	Post-Dx annual cost	Post-Dx average annual savings
Persistent otitis media	4.2	$528	$2217	1.6	$528	$845	
Serious sinus and upper respiratory infections	4.6	$1125	$5175	2.1	$1125	$2362	
Viral infections	3.7	$1275	$4717	1.4	$1275	$1785	
Acute bronchitis	3.1	$1700	$5270	0.8	$1700	$1360	
Bacterial pneumonia	2.8	$3552	$9945	0.6	$3552	$2131	
COPD and bronchiectasis	4.3	$3165	$13,609	1.4	$3165	$4431	
Hospitalization days	19.8	$2480	$49,104	3.1	$2480	$7688	
Physician/ED visits	70.8	$180	$12,744	11.7	$180	$2106	
Days on antibiotics	166.2	$10	$1662	72.8	$10	$728	
School/workdays missed	33.9	$195	$6610	8.9	$195	$1735	
Total cost annually per patient (without IgG)			$111,053			$25,171	$85,882 PPPY without IgG
Average annual cost of IgG						$30,000	
Total cost annually including 100% on IgG							**$55,882 PPPY with IgG**

COPD=chronic obstructive pulmonary disease; Dx=diagnosis; ED=emergency department; IgG=immunoglobulin G; PPPY=per patient per year.

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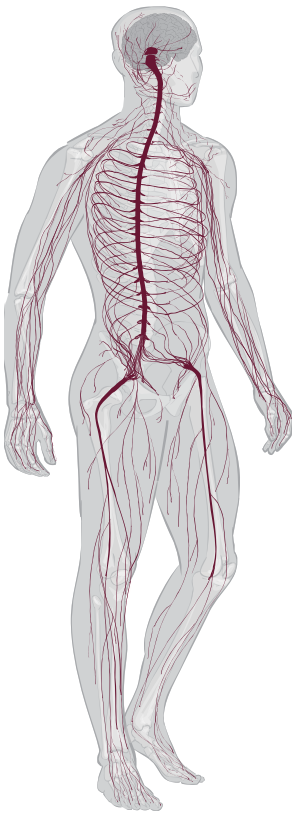
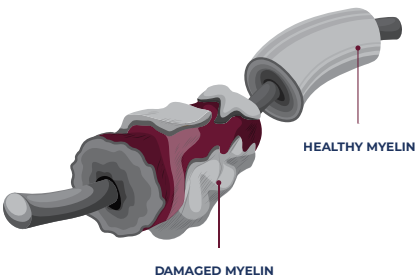
About chronic inflammatory demyelinating polyneuropathy (CIDP)





CIDP is a rare, progressive, and disabling autoimmune disease

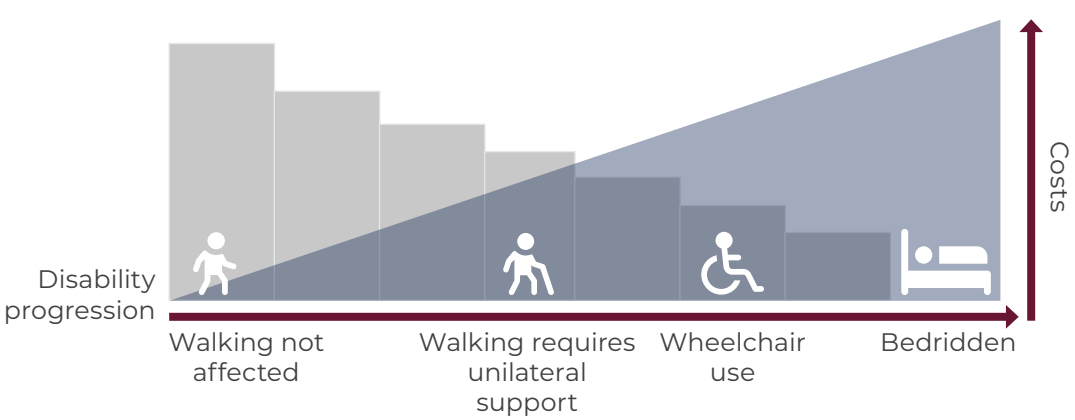
- CIDP is an autoimmune disease of the peripheral nervous system, with an estimated prevalence of 1 to 9 per 100,000 individuals[7-9]
- The immune system attacks and destroys myelin, a material that protects the nerve fibers (axons), which transmit electrical signals throughout the body[10,11]
- Myelin damage results in signaling impairment, leading to loss of strength and sensation in the arms and legs[7,8,10,11]

CIDP affects the peripheral nervous system—
all nerves that connect the spinal cord and brain with other tissues and organs in the body[12]

Early treatment is critical to limiting damage to the myelin sheath and axons[11]

CIDP can lead to increasing functional impairment and related costs

- CIDP is characterized by progressive muscle weakness and sensory and motor disturbances, leading to difficulty walking and using the arms and legs[7]
- Increased functional impairment may be associated with increasing health-related costs (eg, need for additional support services)[13]



Most patients respond to treatment, but if left untreated, 30% of patients will progress to wheelchair dependence.[14]

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Hizentra for the treatment of PI and CIDP

Market highlights

- #1 prescribed Ig for PI and the only 20% SCIg approved for CIDP[15]
- Proven experience since 2010 and more than 14.9 million exposures worldwide[15]*
- Market share leader in new starts and switches† and holds ~58% of the SCIg market share[16]‡

How supplied

- Available in 1 g, 2 g, 4 g, and 10 g prefilled syringes

Hizentra is the SCIg with the longest record of proven safety and efficacy in patients with PI

Efficacy and tolerability were confirmed in a US phase 3 trial[17§‖]

- Zero serious bacterial infections (SBIs) per subject year, annualized rate¶
- 2.76 infections (any kind) per subject year, annualized rate
- Zero serious adverse reactions
  - Two subjects withdrew from the study due to adverse reactions

Sustained protection was demonstrated in a long-term US extension study (1.7 years)[18]

- 0.06# SBIs per subject year, annualized rate¶
- 2.38 infections (any kind) per subject year, annualized rate
- Zero treatment-related serious adverse reactions
  - Zero subjects discontinued because of treatment-related adverse reactions

*Estimate based on Hizentra grams sold worldwide, across all indications, from 2010 through March 2024.
†Market share data January 2020 through December 2023.
‡Based on volume share of SCIg brands through December 2023.
§Demonstrated in patients aged 5 to 72 years in the 12-month US phase 3 trial with Hizentra weekly (n=38).
‖Hizentra was initiated at a weekly dose of 153% of the previous weekly-equivalent IVIg dose in the US study.
¶SBIs were defined as bacterial pneumonia, bacteremia/septicemia, osteomyelitis/septic arthritis, bacterial meningitis, and visceral abscess.
#During the US extension study, 2 SBIs (bacterial pneumonia) in 2 subjects were reported, giving an annualized rate of 0.06 infections per subject (n=21).

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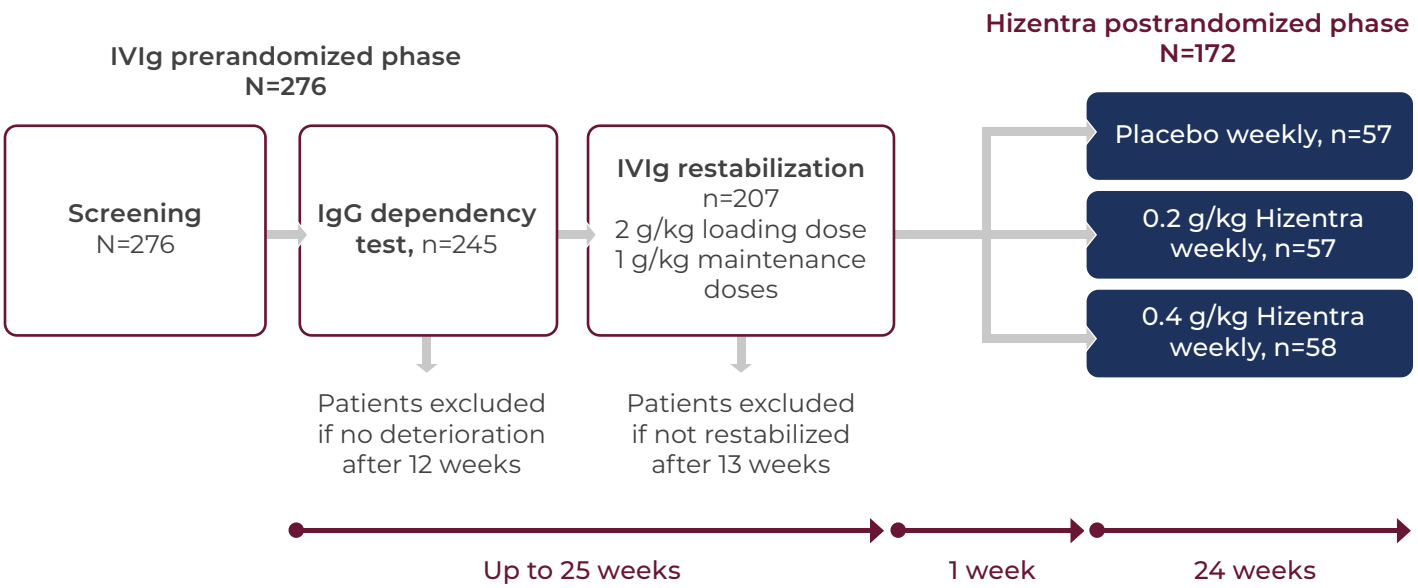
PATH study design

Hizentra was evaluated in the largest Ig study in CIDP: Polyneuropathy and Treatment with Hizentra (PATH)

Primary endpoint: The proportion of patients who had a CIDP relapse or were withdrawn from the study for any reason during the 24-week subcutaneous treatment period.[19]



In the PATH study, relapse or withdrawal was significantly reduced with Hizentra vs placebo

- Relapse or withdrawal rate: 38.6% Hizentra 0.2 g/kg, 32.8% Hizentra 0.4 g/kg vs 63.2% placebo (*P*=0.007, *P*<0.001, respectively)[19]
- 93% of Hizentra infusions were free of any reported adverse reactions (N=4225)[19,20]*
- 3.6x lower rate of systemic adverse reactions per infusion when switched from IVIg to Hizentra[19,20]*

*Including adverse reactions during the open-label extension study.

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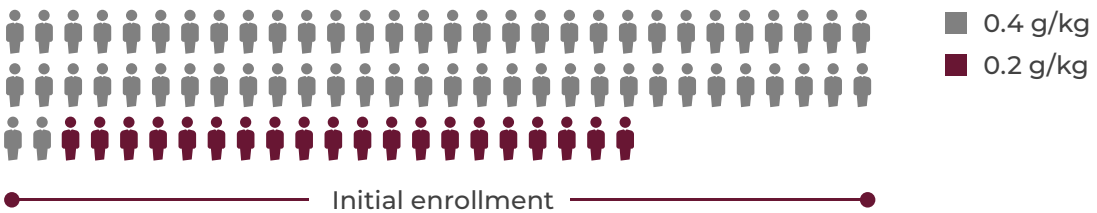
PATH open-label extension study

The PATH extension study supported a label change with simplified dosing adjustments[20]

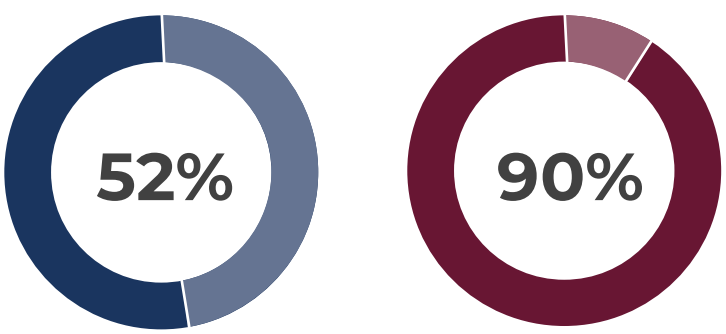
The PATH extension study demonstrated dosage adjustments between 2 safe and effective doses to prevent CIDP relapse. The 48-week, open-label, prospective extension study for PATH enrolled 82 patients, with 62 patients starting on 0.4 g/kg weekly infusion of Hizentra and 20 patients starting on 0.2 g/kg weekly.

- If clinically stable, patients on 0.4 g/kg were switched to 0.2 g/kg after 24 weeks
- If relapse* occurred while on the 0.2 g/kg dose, 0.4 g/kg was either initiated or reinitiated



Most patients remained relapse free on either dosing option[20]

Relapse-free rates by dose (%)†



0.2 g/kg Hizentra (n=73)

0.4 g/kg Hizentra (n=72)

In the open-label extension study to PATH, 92% of patients who relapsed on the low dose after switching from the high dose recovered within 4 weeks after reinitiating on the high dose (n=26).

- The most common adverse reactions reported during the extension study included local site reactions, infections, fatigue, back pain, headache, dizziness, and nausea
- 18 (22%) patients reported 40 location reactions; 1 patient reported 3 causally related severe local reactions
- The majority of adverse reactions were either mild (62%) or moderate (29%)

Safety findings were consistent with the established safety profile for Hizentra.

*CIDP relapse defined as a ≥1-point increase in adjusted Inflammatory Neuropathy Cause and Treatment (INCAT) score compared with baseline.
†Approximately 68% of patients who completed the PATH study without relapse were able to remain relapse free after dose reduction to 0.2 g/kg. Statistical tests comparing relapse rates between the 2 doses were not conducted.

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Hizentra Connect℠ is a comprehensive resource center for healthcare providers and patients[21]

Hizentra Connect℠
Connecting Patients to Therapy

1-877-355-4447
Monday through Friday, 8 AM to 8 PM ET

Copay Support Program

Helps eligible people with commercial insurance by assisting with out-of-pocket (OOP) expenses for Hizentra. Most people with commercial insurance pay $0 OOP*

Patient assistance program

Provides access to therapies for qualified patients who are uninsured or underinsured

Free trial

Provides a 1-month supply of product, infusion equipment, and training at no cost to the patient

Free in-home visits by a trained nurse who will teach patients how to infuse Hizentra

Seamless process, from trial to follow-up therapy notes provided to the doctor's office and the patient's pharmacy

Continued treatment

Only CSL Behring offers an Ig product loyalty program in which people receive a point for every month of continuous product use†

Points can be redeemed for free product should there be a lapse in third-party private health insurance (3 points for a 1-month supply of CSL Behring therapy)

Voice2Voice®

A unique program that connects PI and CIDP patients and caregivers with people who have direct experience with Hizentra therapy

Offers peer-to-peer support, resources, and encouragement‡

Reimbursement support

Prior authorization, appeals, and connection to CSL Behring's HUB

*Subject to terms and conditions of the Copay Support Program available at https://www.csl.com/patients-public-health/patient-support-and-organizations/csl-behring-usa-support-and-assistance-programs.
†Enrollment required. Subject to terms and conditions. For the CSL Behring Assurance℠ program, visit https://www.csl.com/patients-public-health/patient-support-and-organizations/csl-behring-usa-support-and-assistance-programs.
‡Voice2Voice advocates are not healthcare professionals or medical experts. For medical questions, patients should contact their healthcare providers. Voice2Voice advocates are compensated by CSL Behring LLC for their time and/or expenses.

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Hizentra is covered under Medicare Part B for both PI and CIDP*

Medicare coverage

Convenience of self-infused Hizentra covered under the same benefit category as IVIg†

Lower patient OOP cost than with Part D (coverage includes infusion pump, ancillary supplies, medication, and nurse training)

No prior authorization required‡

OOP=out of pocket
*100% coverage for those with Medicare Part B and a Medigap plan after Part B annual deductible is met.
†Coverage of IVIg when administered in a clinical setting.
‡Chart notes must be up to date and include diagnostic criteria.

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Important Safety Information

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.

Hizentra is contraindicated in patients with a history of anaphylactic or severe systemic reaction to human immune globulin (Ig) or components of Hizentra (eg, polysorbate 80), as well as in patients with immunoglobulin A deficiency with antibodies against IgA and a history of hypersensitivity. Because Hizentra contains L-proline as stabilizer, use in patients with hyperprolinemia is contraindicated.

IgA-deficient patients with anti-IgA antibodies are at greater risk of severe hypersensitivity and anaphylactic reactions. Thrombosis may occur following treatment with Ig products, including Hizentra.

Monitor patients for aseptic meningitis syndrome (AMS), which may occur following treatment with Ig products, including Hizentra. In patients at risk of acute renal failure, monitor renal function, including blood urea nitrogen, serum creatinine and urine output. In addition, monitor patients for clinical signs of hemolysis or pulmonary adverse reactions (eg, transfusion-related acute lung injury [TRALI]).

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

The passive transfer of antibodies can interfere with response to live virus vaccines and lead to misinterpretation of serologic test results.

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

The importance of early diagnosis and treatment in PI and CIDP

- Early diagnosis and treatment are critical for rare diseases like PI and CIDP. The sooner an accurate diagnosis can be made, the sooner appropriate treatment can be initiated
- For both PI and CIDP, the risk of permanent functional impairment, with associated healthcare utilization costs, highlights the importance of early diagnosis and management with Ig therapy[5,6,13]

Ensure your eligible members have access to Hizentra

Learn more at marketaccess.cslbehring.com

References: 1. What is PI? Immune Deficiency Foundation. Accessed June 24, 2024. https://primaryimmune.org/understanding-primary-immunodeficiency/what-is-pi **2.** About primary immunodeficiency (PI). Centers for Disease Control and Prevention. May 15, 2024. Accessed June 24, 2024. https://www.cdc.gov/primary-immunodeficiency/about/ **3.** Tangye SG, Al-Herz W, Bousfiha A, et al. Human inborn errors of immunity: 2022 update on the classification from the International Union of Immunological Societies Expert Committee. *J Clin Immunol.* 2022;42(7):1473-1507. doi:10.1007/s10875-022-01289-3 **4.** Primary immune deficiency diseases (PIDDs). National Institute of Allergy and Infectious Disease. Accessed June 24, 2024. https://www.niaid.nih.gov/diseases-conditions/primary-immune-deficiency-diseases-pidds **5.** IDF 2023 National Patient Survey. Immune Deficiency Foundation. April 24, 2024. Accessed July 23, 2024. https://primaryimmune.org/sites/default/files/IDF-2023-Patient-Survey-Full-Analysis-Protocol-IRB.pdf **6.** Modell V, Orange JS, Quinn J, Modell F. Global report on primary immunodeficiencies: 2018 update from the Jeffrey Modell Centers Network on disease classification, regional trends, treatment modalities, and physician reported outcomes. *Immunol Res.* 2018;66(3):367-380. doi:10.1007/s12026-018-8996-5 **7.** Dalakas MC. Advances in the diagnosis, pathogenesis and treatment of CIDP. *Nat Rev Neurol.* 2011;7(9):507-517. doi:10.1038/nrneurol.2011.121 **8.** Mathey EK, Park SB, Hughes RAC, et al. Chronic inflammatory demyelinating polyradiculoneuropathy: from pathology to phenotype. *J Neurol Neurosurg Psychiatry.* 2015;86(9):973-985. doi:10.1136/jnnp-2014-309697 **9.** European Academy of Neurology/Peripheral Nerve Society guideline on diagnosis and treatment of chronic inflammatory demyelinating polyradiculoneuropathy: Report of a joint Task Force-Second revision. *J Peripher Nerv Syst.* 2022;27(1):94. doi:10.1111/jns.12479 **10.** Myelin. MedlinePlus. Updated April 27, 2023. Accessed June 17, 2024. https://medlineplus.gov/ency/article/002261.htm **11.** Koski CL, Koehlinger K. *CIDP: Chronic Inflammatory Demyelinating Polyneuropathy.* GBS/CIDP Foundation International. May 2012. Accessed June 24, 2024. https://www.gbs-cidp.org/wp-content/uploads/2012/05/CIDP-Booklet.pdf **12.** Amaral DG, Strick PL. The organization of the central nervous system. In: Kandel ER, Schwartz JH, Jessell TM, Siegelbaum SA, Hudspeth AJ, Mack S, eds. *Principles of Neural Science, Fifth Edition.* McGraw-Hill Education; 2014:337-355. Accessed June 25, 2024. https://neurology.mhmedical.com/content.aspx?bookid=1049&sectionid=59138139 **13.** *CHRONIC Care Act*: Making the Case for Non-Medical Services and Supports in Medicare Advantage Supplemental Benefits. Anne Tumlinson Innovations. November 2018. Accessed March 9, 2021. https://atiadvisory.com/wp-content/uploads/2018/11/Anne-Tumlinson-Innovations_Chronic-Care-Act-Data-Brief_Nov-2018.pdf **14.** CIDP. GBS/CIDP Foundation International. Accessed July 14, 2024. https://www.gbs-cidp.org/cidp/ **15.** Data on file. Available from CSL Behring as DOF HIZ-005. **16.** Data on file. Available from CSL Behring as DOF HIZ-011. **17.** Hagan JB, Fasano MB, Spector S, et al. Efficacy and safety of a new 20% immunoglobulin preparation for subcutaneous administration, IgPro20, in patients with primary immunodeficiency. *J Clin Immunol.* 2010;30(5):734-745. doi:10.1007/s10875-010-9423-4 **18.** Jolles S, Borte M, Nelson RP Jr, et al. Long-term efficacy, safety, and tolerability of Hizentra® for treatment of primary immunodeficiency disease. *Clin Immunol.* 2014;150(2):161-169. doi:10.1016/j.clim.2013.10.008 **19.** van Schaik IN, Bril V, van Geloven N, et al; PATH study group. Subcutaneous immunoglobulin for maintenance treatment in chronic inflammatory demyelinating polyneuropathy (PATH): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Neurol.* 2018;17(1):35-46. doi:10.1016/S1474-4422(17)30378-2 **20.** van Schaik IN, Mielke O, Bril V, et al; PATH study group. Long-term safety and efficacy of subcutaneous immunoglobulin IgPro20 in CIDP: PATH extension study. *Neurol Neuroimmunol Neuroinflamm.* 2019;6(5):e590. doi:10.1212/NXI.0000000000000590 **21.** Comprehensive support from the start with Hizentra Connect℠. CSL Behring. Accessed July 22, 2024. https://www.hizentra.com/hcp/hizentra-connect-support

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