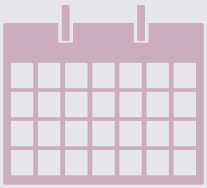
Hizentra®
Immune Globulin Subcutaneous (Human) 20% Liquid

Optimizing the Transition to Hizentra for CIDP Patients

Chronic Inflammatory Demyelinating Polyneuropathy

Consider this information when starting Hizentra therapy

Initiate therapy with Hizentra 1 week after the last IVIg infusion



Monitor your patients and adjust dosing as needed

- In the PATH study,* both 0.2 g/kg and 0.4 g/kg doses were found to be safe and effective. Patients who relapsed were restabilized with IVIg
- During an Open-Label Extension (OLE) study,* patients who relapsed on 0.2 g/kg were titrated to 0.4 g/kg without IVIg restablization

*See inside for additional details on both the PATH and OLE studies.

Proactively Optimize Infusion

- Volume and rate can be adjusted after initial infusion as tolerated, which may decrease infusion time and number of sites
- Consider changing one variable at a time (eg, rate, volume, ancillary supplies, site) to help achieve ideal treatment for your patient
- In PATH, site reactions were common and were reported to decrease over time

Administration Parameters

	Infusion parameters†	1st infusion	Subsequent infusions
CIDP Weekly	Volume (mL/site)	≤20	≤50
	Rate (mL/hr/site)	≤20	≤50

†As Tolerated.

Indication

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.

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.

Important Safety Information continues on back cover. Please see full prescribing information for Hizentra, including boxed warning, attached.

Polyneuropathy and Treatment With Hizentra (PATH)

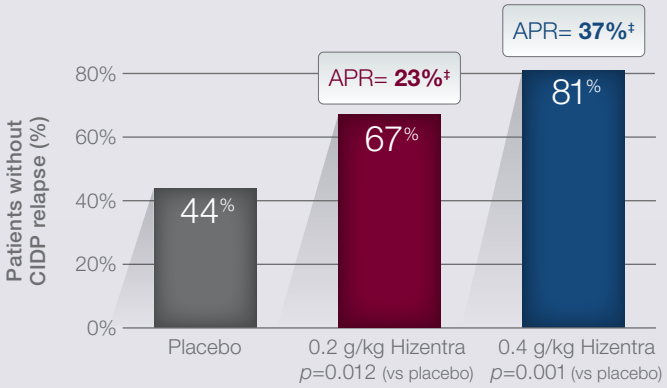
Pivotal Study

- PATH is the largest CIDP study to date (n=172)
  - Randomized, multicenter, double-blind, placebo-controlled, parallel-group, phase III study of Hizentra, a subcutaneous immunoglobulin (SCIg) for maintenance therapy in adults with CIDP
- Evaluated the efficacy, safety and tolerability of 0.2 g/kg/week (low dose) and 0.4 g/kg/week (high dose) of Hizentra vs placebo (randomized 1:1:1) as maintenance therapy for 6 months after stabilization with intravenous immunoglobulin (IVIg)

Efficacy

- 38.6% of low-dose and 32.8% of high-dose Hizentra-treated subjects relapsed* or were within from the study, compared with 63.2% of placebo subjects (p=0.007 and p<0.001, respectively)
  - There was no statistically significant difference between the two HIzentra doses
- A sensitivity analysis only considering relapse showed 81% and 67% of Hizentra-treated subjects remained relapse-free (0.4 g/kg and 0.2 g/kg, respectively); 44% of placebo subjects remained relapse-free for up to 24 weeks

Patients without CIDP relapse based on relapse sensitivity analysis[1†]



Safety

- All reported local reactions were either mild (did not interfere with routine activities [94.5%]) or moderate (interfered somewhat with routine activities and may have warranted intervention [5.5%]) in intensity and the frequency tended to decrease over time. No subject withdrew because of local reaction
- 93% of the 4,225 Hizentra infusions were free of any adverse reactions
- Adverse events occurring in >5% of Hizentra-treated subjects included local reactions, headache, nasopharyngitis, fatigue, upper respiratory tract infection, fall, back pain, arthralgia, and pain in extremity

*CIDP relapse was defined as a ≥1 point increase in adjusted Inflammatory Neuropathy Cause and Treatment [INCAT] score compared with baseline.
†Data shown only consider CIDP relapse based on the adjusted INCAT score (relapse sensitivity analysis). All patients who withdrew for reasons other than relapse were assumed not to have had a relapse.
‡ARR=Absolute Risk Reduction in risk of relapse compared to placebo.

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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.

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Polyneuropathy and Treatment With Hizentra (PATH)

Open-Label Extension Study

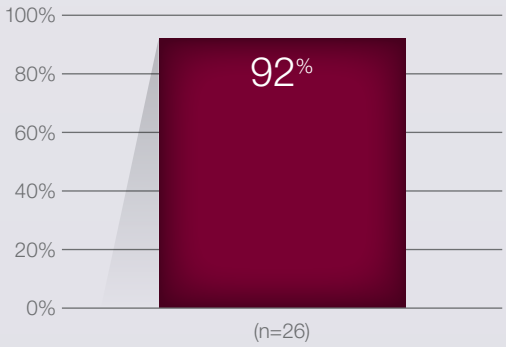
In the PATH OLE study, adjustable Hizentra dosing regimen demonstrated protection from CIDP relapse during the 48-week study.

- 62 patients were started on 0.4g/kg weekly and 20 patients were started on 0.2g/kg weekly
- Patients on 0.4 g/kg were switched to 0.2 g/kg after 24 weeks if clinically stable
- Patients who relapsed while on 0.2g/kg dose, initiated or re-initiated a dose of 0.4g/kg
- Patients who relapsed on 0.4 g/kg could remain on that dose and had to successfully recover within 4 weeks or were discontinued

Efficacy

- Of the 72 patients who received 0.4 g/kg at some time during the study, 90% remained relapse-free while on the 0.4 g/kg dose
- Of the 73 patients who received the 0.2 g/kg at some time during the study, 52% remained relapse-free while on the 0.2 g/kg dose
- Statistical tests comparing relapse rates between the two doses were not conducted
- Approximately 68% (19/28) of the extension study patients who previously completed the PATH study without relapse were able to remain relapse-free after dose reduction to 0.2 g/kg
- Of the 62 patients started on the high dose, 52 patients switched to the low dose at week 24 per protocol:
  - 50% (26 of 52) of those patients relapsed on the low dose
  - 92% (24 of 26) of those who relapsed recovered within 4 weeks after reinitiating on the high dose (see graph at right)

Percent of patients who relapsed on 0.2 g/kg, then recovered within 4 weeks after reinitiating on 0.4 g/kg



Safety

- Overall, safety findings in the extension study were consistent with those from the PATH study and the already known safety profile for Hizentra

Important Safety Information

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.

Please see enclosed full prescribing information for Hizentra.

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.

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Dosing Chart

Weight		Dose	Total weekly volume	# sites*	Time per infusion*
Pounds (lbs)	Kilograms (kgs)				
132 lb	60 kg	0.2 g/kg	60 mL	2	~1 hour
		0.4 g/kg	120 mL	3	
176 lb	80 kg	0.2 g/kg	80 mL	2	
		0.4 g/kg	160 mL	4	
198 lb	90 kg	0.2 g/kg	90 mL	2	
		0.4 g/kg	180 mL	4	

Personalize treatment for your patients with our dosing calculator at **Hizentra.com**

*As tolerated; the number of sites and time per infusion is based on subsequent infusions.

References: 1. van Schaik IN, Bril V, van Geloven N, et al. Subcutaneous immunoglobulin for maintenance treatment in chronic inflammatory demyelinating polyneuropathy (PATH): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Neurol*. 2017;17(1):35-46. **2.** van Schaik IN, Mielke O, Bril V, et al. Long-term safety and efficacy of subcutaneous immunoglobulin IgPro20 in CIDP. *Neurol Neuroimmunol Neuroinflamm*. 2019;6:e590.

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