Dosing for Primary Immunodeficiency (PI)

Hizentra is indicated for the treatment of PI in adults and pediatric patients 2 years of age and older.

Initiate therapy with Hizentra 1 week after the last intravenous immunoglobulin (IVIg) infusion
- Before switching to Hizentra, obtain the patient's serum IgG trough level to guide subsequent dose adjustments
- Adjust the dose based on clinical response and serum IgG trough levels

Weekly: Start Hizentra 1 week after last infusion
Initial weekly dose =
\[
\frac{\text{Previous IVIg dose (in grams)}}{\text{No. of weeks between IVIg doses}} \times 1.37
\]
• Biweekly (every 2 weeks): Start Hizentra 1 or 2 weeks after the last IVIg infusion or 1 week after the last weekly SCIg infusion. Administer twice the calculated weekly dose
• Frequent dosing (2 to 7 times per week): Start Hizentra 1 week after the last IVIg or SCIg infusion. Divide the calculated weekly dose by the desired number of times per week

Infusion sites
- The Hizentra dose may be infused into multiple injection sites depending on volume
- Infusion sites should be at least 2 inches apart
- Rotate the actual site of infusion with each administration
- Use up to 8 infusion sites in parallel. More than 1 infusion device can be used simultaneously
- Consider changing one variable at a time (e.g., rate, volume, ancillary supplies, site) to help address local reactions

Volume (as tolerated)
- 1st infusion ≤15 mL/site;
  subsequent infusions ≤25 mL/site

Rate (as tolerated)
- 1st infusion ≤15 mL/site/hr;
  subsequent infusions ≤25 mL/site/hr

PI Dosing Examples
PI patients can self-infuse daily up to every 2 weeks

| Every 2 weeks | Dose: 16 g/80 mL | Infusion sites: 4 | Time per infusion: ~48 min |
| Weekly | Dose: 14 g/70 mL | Infusion sites: 3 | Time per infusion: ~1 hour |
| Every 10 days | Dose: 10 g/50 mL | Infusion sites: 2 | Time per infusion: ~1 hour |
| 2x per week | Dose: 1 g/5 mL | Infusion sites: 1 | Time per infusion: ~12 min |

For more individualized dosing examples, visit Hizentra.com/Personalized-Dosing/PI

Important Safety Information
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.

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 (e.g., 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.

Please see continued Important Safety Information on reverse side and accompanying full prescribing information for Hizentra, including boxed warning.
CIDP Dosing for Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

Hizentra is indicated as maintenance therapy in adults with CIDP.

**Initiate therapy with Hizentra 1 week after the last IVIg infusion**
- Recommended subcutaneous dose is 0.2 g/kg (1 mL/kg) body weight per week
- Administered in 1 or 2 sessions over 1 or 2 consecutive days
  - In the clinical study, after transitioning from IVIg to Hizentra treatment, a dose of 0.4 g/kg (2 mL/kg) body weight per week was also safe and effective to prevent CIDP relapse

**Monitor patient’s clinical response and adjust the duration of therapy based on patient need**
- If CIDP symptoms worsen, consider reinitiating treatment with an IVIg approved for the treatment of CIDP, while discontinuing Hizentra
- If improvement and stabilization are observed during IVIg treatment, consider reinitiating Hizentra at the dose of 0.4 g/kg body weight per week, administered in 2 sessions per week over 1 or 2 consecutive days, while discontinuing IVIg
- If CIDP symptoms worsen on the 0.4 g/kg body weight per week dose, consider reinitiating therapy with an IVIg product approved for treatment of CIDP, while discontinuing Hizentra

**Volume (as tolerated)**
- 1st infusion <20 mL/site; subsequent infusions <50 mL/site

**Rate (as tolerated)**
- 1st infusion <20 mL/site/hr; subsequent infusions <50 mL/site/hr

**Infusion sites**
- The Hizentra dose may be infused into multiple injection sites depending on volume
- Infusion sites should be at least 2 inches apart
- Rotate the actual site of infusion with each administration
- Use up to 8 infusion sites in parallel. More than 1 infusion device can be used simultaneously
- Consider changing one variable at a time (eg, rate, volume, ancillary supplies, site) to help address local reactions

**CIDP Dosing Calculation Examples** (Weight to Grams)

**CIDP patients can self-infuse weekly**

<table>
<thead>
<tr>
<th>Dosing calculation at 0.2 g/kg (1 mL/kg) weekly for a 80 kg patient:</th>
<th>Dosing calculation at 0.4 g/kg (2 mL/kg) weekly for a 80 kg patient:</th>
</tr>
</thead>
<tbody>
<tr>
<td>80 kg x (\frac{1 \text{ mL}}{1 \text{ kg}}) = 80 mL x (\frac{1 \text{ g}}{5 \text{ mL}}) = 16 g</td>
<td>80 kg x (\frac{2 \text{ mL}}{1 \text{ kg}}) = 160 mL x (\frac{1 \text{ g}}{5 \text{ mL}}) = 32 g</td>
</tr>
</tbody>
</table>

**Important Safety Information**

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.

Please see full prescribing information for Hizentra, including boxed warning.