**Product Profile**

# ZONOVATE®

Antihemophilic Factor (Recombinant, B-Domain Truncated) turoctocog alfa

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| **TRADE NAME** | ZONOVATE® |
| **PRODUCT COMPOSITION** | Antihemophilic Factor VIII (Recombinant, B-Domain Truncated), turoctocog alfa supplied as a white, lyophilized powder in a single-use vial.<br><br>**Clinically Relevant Nonmedicinal Ingredients:**<br>Content per vial: Sodium chloride*, L-histidine, Sucrose , Polysorbate 80, L-methionine, Calcium chloride dihydrate<br>* The amount of sodium chloride originates from the formulation and from the solvent (0.9% Sodium Chloride Solution) used for reconstitution. |
| **ALTERNATIVES** | **Non-blood product:** |
| | **Blood product:** |
| **DOSAGE** | The recommended dose of ZONOVATE ® for routine prophylaxis is as follows:<br>• For Adults and adolescents (≥ 12 years), 20-50 IU/kg 3 times a weekly or 20-40 IU/kg every other day.<br>• For children (< 12 years), 25-60 IU/kg 3 times a weekly or 25-50 IU/kg every other day.<br><br>**Refer to the Recommended Dose and Dosage Adjustment section of the ZONOVATE® Product Monograph for specific dosage guidelines for each clinical indication** |
| **ADMINSTRATION** | • The recommended infusion rate for ZONOVATE® is 1–2 mL/min. The rate should bedetermined by the patient's comfort level.<br>• Do not mix ZONOVATE® with any other intravenous infusions or medications.<br><br>**Refer to the ZONOVATE ® Product Monograph for detailed information including reconstitution instructions.** |
| **CLINICAL/ DIAGNOSTIC MONITORING** | **Monitoring and Laboratory Tests**<br><br>Patients should be monitored for the development of Factor VIII inhibitors. If the expected plasma levels of Factor VIII activity are not attained, or if bleeding is not controlled with an appropriate dose, an assay should be performed to determine if a Factor VIII inhibitor is present. In patients with high levels of inhibitors, Factor VIII therapy may not be effective and other therapeutic options should be considered. Management of such patients should be directed by physicians with experience in the care of patients with hemophilia and Factor VIII inhibitors.<br><br>When using an in vitro thromboplastin time (aPTT)-based one stage clotting assay for determining Factor VIII activity in blood samples, plasma Factor VIII activity results can be significantly affected by both the type of aPTT reagent and the reference standard used in the assay. Also, there can be significant discrepancies between assay results obtained by aPTTbased one stage clotting assay and the chromogenic assay. This is of importance particularly when changing the laboratory and/or reagents used in the assay.<br><br>**Peri-Operative Considerations**<br><br>ZONOVATE® is indicated in the perioperative management of patients with hemophilia A. Careful control of replacement therapy is important, especially in cases of major surgery or life-threatening hemorrhages. There is limited experience of surgery in pediatric patients. |

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| **CLINICAL INDICATIONS** | • ZONOVATE® (Antihemophilic Factor (Recombinant, B-Domain Truncated)), is indicated for use in adults and children with hemophilia A (congenital Factor VIII deficiency or classic hemophilia) for:<br>  ○ Treatment and control of bleeding episodes<br>  ○ Perioperative management Routine prophylaxis to prevent or reduce the frequency of bleeding episodes<br>• ZONOVATE® is not indicated for the treatment of von Willebrand disease. |
| **SPECIAL CONSIDERATIONS** | **Pediatrics (<18 years of age)**<br>The safety and efficacy of ZONOVATE® have been demonstrated in pediatric patients from 1 to <18 years old Children have a shorter half-life and lower recovery of Factor VIII than adults. Because clearance (based on per kg body weight) has been demonstrated to be higher in the pediatric population, higher or more frequent dosing based on body weight may be needed [see ACTION AND CLINICAL PHARMACOLOGY/ Pharmacokinetics in the ZONOVATE® Product Monograph]<br><br>**Geriatrics (>65 years of age)**<br>Clinical studies of ZONOVATE® did not include patients above 65 to determine whether they respond differently from younger patients. As with any patient receiving ZONOVATE®, dose selection for an elderly patient should be individualized.<br><br>**Pregnant Women**<br>Animal reproduction studies have not been conducted with ZONOVATE®. Based on the rare occurrence of hemophilia A in women, experience regarding the use of Factor VIII during pregnancy is not available. Therefore, ZONOVATE® should only be used during pregnancy ifclearly indicated.<br><br>**Breast-feeding**<br>It is not known whether ZONOVATE® is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ZONOVATE® is administered to anursing woman. |
| **CONTRAINDICATIONS** | Patients who are hypersensitive to this drug or to any ingredient in the formulation (including hamster protein), or component of the container. For a complete listing, see Dosage Forms, Strengths, Composition and Packaging in the ZONOVATE® Product Monograph). |

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| **STORAGE CONDITIONS & SHELF LIFE** | **Prior to Reconstitution**<br>Store in refrigerator (2°C - 8°C). Do not freeze.<br>Keep the vial in the outer carton in order to protect from light.<br>ZONOVATE® vials can be stored in the refrigerator (2°C - 8°C) up to the expiration date stated on the label.<br><br>During the shelf-life, ZONOVATE® may also be stored at room temperature:<br>o up to 30°C for a single period not exceeding 12 months<br>or<br>o up to 40°C for a single period not exceeding 3 months<br><br>Once the product has been taken out of the refrigerator the product must not be returned to the refrigerator. Record the date when the product was removed from the refrigerator in the space provided on the product carton.<br><br>Do not use ZONOVATE® after the end of the specified room temperature storage period at up to 30°C or 40°C, or after the expiration date stated on the carton, whichever occurs earlier.<br><br>**After Reconstitution**<br>Chemical and physical in-use stability have been demonstrated for 24 hours when stored in a refrigerator at 2°C – 8°C, 4 hours when stored at room temperature up to 30°C, and 2 hours when stored between 30°C and 40°C.<br><br>From a microbiological point of view, ZONOVATE® should be used immediately after reconstitution. If the reconstituted product is not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than as stated above, unless reconstitution has taken place in controlled and validated aseptic conditions.<br><br>The reconstituted solution should be stored in the vial, with the vial adapter and the syringe still attached.<br><br>Discard any unused reconstituted product. |
| **REFERENCES** | ZONOVATE® Product Monograph<br>Date of Initial Approval: December 08, 2014<br>Date of Revision: April 14, 2021 |

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The vials in this image may vary from the actual Zonovate vials.