▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Xenpozyme® (olipudase alfa) – Abbreviated Prescribing Information

Presentation: Xenpozyme® 20 mg (olipudase alfa)**,** powder for concentrate for solution for infusion.
Product composition: Each vial contains 20 mg of olipudase alfa. After reconstitution, each vial contains 4 mg of olipudase alfa per mL. Each vial must be further diluted before use. List of excipients: L-methionine, Sodium phosphate dibasic heptahydrate, Sodium phosphate monobasic monohydrate, Sucrose.
Indication: Xenpozyme is indicated as an enzyme replacement therapy for the treatment of non-Central Nervous System (CNS) manifestations of Acid Sphingomyelinase Deficiency (ASMD) in paediatric and adult patients with type A/B or type B.
Dosage and administration: Xenpozyme treatment should be supervised by a healthcare professional experienced in the management of ASMD or other inherited metabolic disorders. The rapid metabolism of accumulated sphingomyelin (SM) by olipudase alfa generates pro inflammatory breakdown products, which may induce infusion-associated reactions and/or transient liver enzyme elevations. A dose escalation regimen can minimise the majority of these adverse events.
Adult dose escalation phase: The recommended starting dose of Xenpozyme is 0.1 mg/kg* for adults. First dose (Day 1/Week 0) 0.1 mg/kg*. Second dose (Week 2) 0.3 mg/kg*. Third dose (Week 4) 0.3 mg/kg*. Fourth dose (Week 6) 0.6 mg/kg*. Fifth dose (Week 8) 0.6 mg/kg*. Sixth dose (Week 10) 1mg/kg*. Seventh dose (Week 12) 2mg/kg*. Eighth dose (Week 14) 3 mg/kg* (recommended maintenance dose).
Adult maintenance phase: The recommended maintenance dose of Xenpozyme is 3 mg/kg* every 2 weeks. ***Paediatric dose escalation phase***: The recommended starting dose of Xenpozyme is 0.03 mg/kg* for paediatric patients (0 to <18 years old). First dose (Day 1/Week 0) 0.03 mg/kg* Second dose (Week 2) 0.1 mg/kg*. Third dose (Week 4) 0.3 mg/kg*. Fourth dose (Week 6) 0.3 mg/kg*. Fifth dose (Week 8) 0.6 mg/kg*. Sixth dose (Week 10) 0.6 mg/kg*. Seventh dose (Week 12) 1 mg/kg*. Eighth dose (Week 14) 2 mg/kg*. Ninth dose (Week 16) 3 mg/kg* (recommended maintenance dose). ***Paediatric maintenance phase***: The recommended maintenance dose of Xenpozyme is 3 mg/kg* every 2 weeks. *Actual body weight will be used for patients with a BMI ≤ 30. For patients with a BMI > 30, an optimal body weight will be used as described below. ***Patients with BMI> 30***: In adult and paediatric patients with a body mass index (BMI) > 30, the body weight that is used to calculate the dose of Xenpozyme is estimated via the following method (for dose escalation and maintenance phases). Body weight (kg) to be used for dose calculation = 30 × (actual height in m)^2. ***Monitoring of transaminase level***: Transaminase (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) levels should be obtained prior to treatment initiation and monitored during any dose escalation phases. ***Special populations:*** No dose adjustment is recommended for patients over the age of 65. No dose adjustment is recommended in patients with hepatic impairment. No dose adjustment is recommended in patients with renal impairment. ***Method of administration***: Xenpozyme is for intravenous use only. Infusions should be administered in a stepwise manner preferably using an infusion pump. Signs and symptoms of infusion associated reactions (IARs) should be monitored during the infusion. Home infusion under the supervision of a healthcare professional may be considered for patients on maintenance dose and who are tolerating their infusions well, after evaluation and recommendation by the prescribing physician.
Contraindications: Life-threatening hypersensitivity (anaphylactic reaction) to olipudase alfa or to any of the excipients (see product composition).
Special warnings and precautions for use:
Traceability In order to improve the traceability of biological medicinal products, the name and the batch number of the administered medicinal product should be clearly recorded.
Absence of blood-brain barrier transfer Xenpozyme is not expected to cross the blood-brain barrier or modulate the CNS manifestations of the disease.
Infusion associated reactions (IARs) IARs occurred in approximately 58% of patients treated with Xenpozyme in clinical studies, typically between the time of infusion and up to 24 hours after infusion completion. The most frequent IARs were headache, urticaria, pyrexia, nausea and vomiting.
Hypersensitivity/anaphylaxis Hypersensitivity reactions, including anaphylaxis, have been reported in Xenpozyme-treated patients. In clinical studies, hypersensitivity reactions occurred in 7 (17.5%) adult and 9 (45%) paediatric patients including one paediatric patient who experienced anaphylaxis.
Management: Patients should be observed closely during and for an appropriate period of time after the infusion, based on clinical judgement. IARs management should be based on the severity of signs and symptoms and may include temporarily interrupting the Xenpozyme infusion, lowering the infusion rate, and/or appropriate medical treatment. If severe hypersensitivity or anaphylaxis occurs, Xenpozyme should be discontinued immediately, and appropriate medical treatment should be initiated. Patients may be pre-treated with antihistamines, antipyretics, and/or glucocorticoids to prevent or reduce allergic reactions.

Immunogenicity Treatment-emergent antidrug antibodies (ADA) were reported in adult and paediatric patients during the clinical trials. IARs and hypersensitivity reactions may occur independent of the development of ADA. IgE ADA testing may be considered for patients who experienced a severe hypersensitivity reaction to olipudase alfa. While in clinical studies, no loss of efficacy was reported, IgG ADA testing may be considered in case of loss of response to therapy.

Transient transaminases elevation Transient transaminase elevations (ALT or AST) within 24 to 48 hours after infusions were reported during the dose escalation phase with Xenpozyme in clinical studies. Transaminases (ALT and AST) levels should be obtained within 1 month prior to Xenpozyme treatment initiation. During dose escalation or upon resuming treatment following missed doses, transaminases levels should be obtained within 72 hours prior to the next scheduled Xenpozyme infusion. If the pre-infusion transaminase levels are elevated above baseline and >2 times the upper limit of normal (ULN), the Xenpozyme dose can be adjusted (prior dose repeated or reduced) or treatment can be temporarily withheld in accordance with the degree of transaminase elevation. Upon reaching the recommended maintenance dose, transaminase testing can be performed as part of routine clinical management of ASMD.

Sodium content This medicinal product contains 3.02 mg sodium per vial, equivalent to 0.15% of the WHO recommended maximum daily intake of 2 g sodium for an adult or an adolescent, and ≤0. 38% of the maximum acceptable daily intake of sodium for children below 16 years of age.

Interactions: No drug interaction studies have been performed. Because olipudase alfa is a recombinant human protein, no cytochrome P450 mediated drug-drug interactions are expected.

Fertility, pregnancy and lactation: There are no data from the use of olipudase alfa in pregnant women. Studies in animals have shown reproductive toxicity. Xenpozyme is not recommended during pregnancy and in women of childbearing potential not using contraception, unless the potential benefits to the mother outweigh the potential risks, including those to the foetus. It is unknown whether olipudase alfa is excreted in human milk. There is insufficient information on the excretion of olipudase alfa in animal milk. A risk to the newborns/infants cannot be excluded. A decision must be made whether to discontinue breast-feeding or to discontinue Xenpozyme therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman. No human data are available on the effects of olipudase alfa on male and female fertility. Animal data do not indicate direct or indirect harmful effects with respect to fertility.

Effects on ability to drive and use machines: Because hypotension has been reported in clinical studies, Xenpozyme may have minor influence on the ability to drive and use machines.

Undesirable Effects

The pooled safety analysis from 4 clinical studies (in adult and paediatric patients) included a total of 60 patients (40 adult and 20 paediatric patients) treated with Xenpozyme at doses up to 3 mg/kg every 2 weeks. The very common (≥/=10%) and common (≥/=1% to <10%) adverse reactions reported are listed below.

Very common (≥10%): headache, nausea, abdominal pain, vomiting, urticaria, pruritus, myalgia, pyrexia, C-reactive protein increased.

Common (≥1% to <10%): anaphylaxis and hypersensitivity, ocular hyperaemia, ocular discomfort, eye pruritus, palpitations, tachycardia, hypotension, hot flush, flushing, pharyngeal oedema, pharyngeal swelling, throat tightness, wheezing, larynx irritation, dyspnoea, throat irritation, diarrhoea, abdominal pain upper, abdominal discomfort, gastrointestinal pain, hepatic pain, angioedema, fixed eruption, rash, rash papular, rash macular, rash maculopapular, rash erythematous, rash pruritic, rash morbilliform, papule, macule, erythema, bone pain, arthralgia, back pain, pain, chills, catheter site pain, catheter site related reaction, catheter site pruritus, catheter site swelling, fatigue, asthenia, alanine aminotransferase increased, aspartate aminotransferase increased, serum ferritin increased, C-reactive protein abnormal, body temperature increased.

Except for a higher incidence of hypersensitivity-related IARs in paediatric patients compared to adults, the safety profile of Xenpozyme in paediatric and adult patients was similar. Overall, the pattern of adverse events observed in adult and paediatric patients in longer term use was consistent with that observed during the first year of treatment. Health care professionals are asked to report any suspected adverse reactions via the national reporting system.

LEGAL CLASSIFICATION: POM (Prescription Only Medicine).

Marketing authorisation holder: Genzyme Europe B.V., Paasheuvelweg 25, 1105 BP Amsterdam, The Netherlands**. Date of last review:** September 2022.

Abbreviated Prescribing Information based on the EU SmPC as of June 2022.

Before prescribing the product always refer to your full local prescribing information as this information may vary from country to country.