Package leaflet: Information for the patient

Xenpozyme 20 mg powder for concentrate for solution for infusion

olipudase alfa

Is this leaflet hard to see or read? Phone 0800 035 2525 for help

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Xenpozyme is and what it is used for

What Xenpozyme is
Xenpozyme contains an enzyme called olipudase alfa.

What Xenpozyme is used for
Xenpozyme is used to treat an inherited disorder called acid sphingomyelinase deficiency (ASMD). It is used in children and adults with ASMD types A/B or B to treat the signs and symptoms of ASMD not related to the brain.

How Xenpozyme works
Patients with ASMD lack a properly working version of the enzyme acid sphingomyelinase. This results in build-up of a substance called sphingomyelin, which damages organs such as spleen, liver, heart, lungs and blood. Olipudase alfa acts in the same way as the natural enzyme would, and so acts as a replacement, reducing the build-up of sphingomyelin in the organs and treating the signs and symptoms.

2. What you need to know before you are given Xenpozyme

You must not be given Xenpozyme
- If you have experienced life-threatening allergic (anaphylactic) reactions to olipudase alfa (see section 'Warnings and precautions' below) or any of the other ingredients of this medicine (listed in section 6).

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Warnings and precautions
You may have side effects called infusion-associated reactions (IARs) that may be caused by the infusion (drip) of the medicine. They may occur while you are being given Xenpozyme or within 24 hours after the infusion.

They may include allergic reactions (see section 4) and symptoms such as headache, a raised, itchy rash (hives), fever, nausea, vomiting and itchy skin.

If you think you are having an IAR, **tell your doctor straight away.**
If you have a severe allergic reaction during your infusion your doctor will stop your infusion and provide appropriate medical treatment. Your doctor will make a judgement about the risks and benefits of giving you further doses of Xenpozyme.

If you have a mild or moderate IAR, your doctor or nurse may temporarily stop the infusion, lower the infusion rate, and/or reduce the dose.

Your doctor may also give (or have given) you other medicines to prevent or manage allergic reactions.

Your doctor will order blood tests to check how well your liver is working (by measuring levels of your liver enzymes) before starting the treatment, and then at regular intervals as the doses are adjusted (see section 3).

Other medicines and Xenpozyme
Tell your doctor or nurse if you are using, have recently used, or might use any other medicines.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, ask your doctor or nurse for advice before using this medicine.

There is no experience with the use of Xenpozyme in pregnant women. Xenpozyme may be harmful to unborn children when taken by a woman during pregnancy. Xenpozyme should only be used during pregnancy if clearly necessary. Women who are able to become pregnant should use effective contraception during treatment and for 14 days after the last dose if Xenpozyme is discontinued.

It is not known whether Xenpozyme passes into human breast milk. Xenpozyme was detected in animal milk. Tell your doctor if you are breast-feeding or plan to do so. Your doctor will then help you decide whether to stop breast-feeding, or whether to stop taking Xenpozyme, considering the benefit of breast-feeding the baby and the benefit of Xenpozyme to the mother.

Driving and using machines
Xenpozyme may have a minor influence on the ability to drive and use machines because you may experience low blood pressure (which may make you feel faint).

Xenpozyme contains sodium
This medicine contains 3.02 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 0.15% of the recommended maximum daily dietary intake of 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.

3. How Xenpozyme is given

Xenpozyme will be given to you as a drip (infusion) under the supervision of a healthcare professional who is experienced in the treatment of ASMD or other metabolic diseases.

The dose you receive is based on your body weight and will be given to you every two weeks. Treatment starts with a low dose of the medicine, which is gradually increased.
Infusion usually lasts around 3 to 4 hours but may be shorter or longer based on your doctor's judgement, and may be shorter during the period whilst your dose is being increased.

Adult patients
The recommended starting dose of Xenpozyme is 0.1 mg for each kg of body weight. This is increased in a planned way with each subsequent dose, until the recommended dose of 3 mg for each kg of body weight every 2 weeks is reached. It typically takes up to 14 weeks to reach the recommended dose but may be longer based on your doctor's judgement.

Children
The recommended starting dose of Xenpozyme is 0.03 mg for each kg of body weight. The subsequent doses should be increased in a planned way up to the recommended dose of 3 mg for each kg of body weight every 2 weeks. It typically takes up to 16 weeks to reach the recommended dose but may be longer based on your doctor's judgement.

Home infusion
Your doctor may consider home infusion of Xenpozyme if you are on stable dose and tolerating your infusions well. This decision to move to home infusion should be made after evaluation and recommendation by your doctor. If you get a side effect during an infusion of Xenpozyme, the person giving your home infusion may stop the infusion and start appropriate medical treatment.

Instructions for proper use
Xenpozyme is given by intravenous infusion (a drip into a vein). It is supplied as a powder that will be mixed with sterile water before it is given.

If you are given more Xenpozyme than you should
Tell your doctor immediately, if you suspect a change from your routine infusion.

If you miss a Xenpozyme infusion
It is important to have your infusion every 2 weeks. An infusion is considered missed if not given within 3 days from the scheduled infusion. Depending on the number of missed doses, your doctor may have to restart from a lower dose.

The following information is intended for healthcare professionals only:

Preparation of the dosing solution
The powder for concentrate for solution for infusion must be reconstituted with sterile water for injection, diluted with sodium chloride 9 mg/mL (0.9%) solution for injection and then administered by intravenous infusion.
The reconstitution and dilution steps must be completed under aseptic conditions. Filtering devices should not be used at any time during the preparation of the infusion solution. Avoid foaming during reconstitution and dilution steps.

1) Determine the number of vials to be reconstituted based on the individual patient's weight and the prescribed dose.
   Patient weight (kg) × dose (mg/kg) = patient dose (in mg). Patient dose (in mg) divided by 20 mg/vial = number of vials to reconstitute. If the number of vials includes a fraction, round up to the next whole number.
2) Remove the required number of vials from refrigeration and set aside for approximately 20 to 30 minutes to allow them to reach room temperature.
3) Reconstitute each vial by injecting 5.1 mL of sterile water for injection into the vial using a slow drop-wise addition technique to the inside wall of the vial.
4) Tilt and roll each vial gently. Each vial will yield a 4 mg/mL clear, colorless solution.
5) Visually inspect the reconstituted solution in the vials for particulate matter and discoloration. Xenpozyme solution should be clear and colorless. Any vials exhibiting opaque particles or discoloration should not be used.
6) Withdraw the volume of reconstituted solution, corresponding to the prescribed dose, from the appropriate number of vials and dilute with sodium chloride 9 mg/mL (0.9%) solution for injection, in a syringe or infusion bag depending on the volume of infusion (see Table 1 for the recommended total infusion volume based on patients age and/or weight).

If you have missed an infusion or are unable to attend a scheduled appointment, please contact your doctor right away.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Infusion-associated reactions (IARs) have been seen while patients were being given the medicine or within 24 hours after the infusion.

The most serious side effects may include sudden severe allergic reactions, raised, itchy rash (hives), rash, increased liver enzymes and irregular heartbeat.

You must tell your doctor immediately if you get an IAR or an allergic reaction.
If you have an infusion reaction you may be given additional medicines to treat or help prevent future reactions. If the infusion reaction is severe, your doctor may stop the infusion of Xenpozyme and start giving appropriate medical treatment.

Very common (may affect more than 1 in 10 people):
- Headache
- Fever – body temperature increased
- Raised, itchy rash (hives)
- Nausea
- Vomiting
- Abdominal (belly) pain
- Muscle aches
- Itchy skin
- Increased blood test for inflammation

Common (may affect up to 1 in 10 people):
- Rash (different types of rash sometimes with itch)
- Pain in upper belly
- Fatigue
- Abnormal blood test for liver function
- Diarrhoea
- Reddening of the skin
- Joint pain
- Back pain
- Chills
- Difficulty breathing
- Abdominal discomfort
- Bone pain
- Pain
- Low blood pressure
- Forceful heartbeat that may be rapid or irregular
- Fast heartbeat
- Liver pain
- Severe allergic reactions
- Feeling very warm
- Throat and voice box irritation
- Throat tightness and swelling
- Wheezing
- Skin lesions (such as solid elevated or red flat lesions)
- Rapid swelling under the skin in areas such as the face, throat, arms and legs which can be life threatening if throat swelling blocks the airway
- Stomach pain
- Itchy or red eyes
- Eye discomfort
- Weakness
- Abnormal blood test for inflammation
- Catheter site-related reactions including pain, itching, or swelling

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Xenpozyme

Keep this medicine out of the sight and reach of children.

Do not use Xenpozyme after the expiry date stated on the label and the carton. The expiry date refers to the last day of the month.

Store in refrigerator between 2°C to 8°C.

After dilution, immediate use is recommended.

If not used immediately, the reconstituted solution may be stored for up to 24 hours at 2°C to 8°C or up to 12 hours at room temperature (up to 25°C).

After dilution, the solution can be stored for up to 24 hours at 2-8°C followed by 12 hours (including infusion time) at room temperature.

Do not throw away any medicines via wastewater or household waste. Ask your doctor or nurse how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Xenpozyme contains
- The active substance is olipudase alfa. One vial contains 20 mg of olipudase alfa.
- Other ingredients are
  - L-methionine
  - Sodium phosphate dibasic heptahydrate
  - Sodium phosphate monobasic monohydrate
  - Sucrose

  see section 2 Xenpozyme contains sodium

What Xenpozyme looks like and contents of the pack
Xenpozyme is a powder for concentrate for solution for infusion in a vial (20 mg/vial).
The powder is white to off-white lyophilised powder. After mixing with sterile water, it is a clear, colorless solution. The solution must be further diluted before infusion.

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Manufacturer
Genzyme Ireland Limited, IDA Industrial Park, Old Kilmeaden Road, Waterford, Ireland

This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, ask your doctor, nurse or pharmacist.

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Table 1: Recommended infusion volumes

	Body weight ≥ 3 kg to < 10 kg	Body weight ≥ 10 kg to < 20 kg	Body weight ≥ 20 kg (paediatric patients < 18 years)	Adult patients (≥ 18 years)
Dose (mg/kg)	Total infusion volume (mL)	Total infusion volume (mL)	Total infusion volume (mL)	Total infusion volume (mL)
0.03	Variable volume will vary based on body weight	Variable volume will vary based on body weight	5	NA
0.1	Variable volume will vary based on body weight	5	10	20
0.3	5	10	20	100
0.6	10	20	50	100
1.0	20	50	100	100
2.0	50	75	200	100
3.0	50	100	250	100

- For variable final volumes of infusion based on body weight in paediatric patients (see Table 1):
  - Prepare an infusion solution at 0.1 mg/mL by adding 0.25 mL (1 mg) of the reconstituted solution prepared in step 3) and 9.75 mL of sodium chloride 9 mg/mL (0.9%) solution for injection in an empty 10 mL syringe.
  - Calculate the volume (mL) required to obtain the patient dose (mg).

  Example: 0.3 mg ÷ 0.1 mg/mL = 3 mL
- Dilution instructions for 5 mL ≤ total volume ≤ 20 mL using a syringe:
  - Inject the required volume of reconstituted solution slowly to the inside wall of the empty syringe.
  - Add slowly the sufficient quantity of sodium chloride 9 mg/mL (0.9%) solution for injection to obtain the required total infusion volume (avoid foaming within the syringe).
- Dilution instructions for a total volume ≥ 50 mL using an infusion bag:
  - Empty infusion bag:
    - Inject slowly the required volume of reconstituted solution from step 3) in the appropriate size sterile infusion bag.
    - Add slowly the sufficient quantity of sodium chloride 9 mg/mL (0.9%) solution for injection to obtain the required total infusion volume (avoid foaming within the bag).
  - Pre-filled infusion bag:
    - Withdraw from the infusion bag pre-filled with sodium chloride 9 mg/mL (0.9%) solution for injection the volume of normal saline to obtain a final volume as specified in Table 1.
    - Add slowly the required volume of the reconstituted solution from step 3) into the infusion bag (avoid foaming within the bag).

7) Gently invert the syringe or the infusion bag to mix. Do not shake. Because this is a protein solution, slight flocculation (described as thin translucent fibers) occurs occasionally after dilution.
8) The diluted solution must be filtered through an in-line low protein-binding 0.2 µm filter during administration.
9) After the infusion is complete, the infusion line should be flushed with sodium chloride 9 mg/mL (0.9%) solution for injection using the same infusion rate as the one used for the last part of the infusion.