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SCIENCE MEDICINES HEALTH

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Xenpozyme (*olipudase alfa*)

An overview of Xenpozyme and why it is authorised in the EU

What is Xenpozyme and what is it used for?

Xenpozyme is a medicine for treating patients with acid sphingomyelinase deficiency (ASMD), a genetic condition, historically known as Niemann-Pick disease type A, A/B and B. There are three types of Niemann-Pick disease (A, B and C), with different genetic causes and different symptoms. Xenpozyme is used to treat patients with type A/B or type B. It is intended to treat the symptoms of ASMD that are not related to the brain.

Niemann-Pick disease is rare, and Xenpozyme was designated an 'orphan medicine' (a medicine used in rare diseases) on 5 December 2016. Further information on the orphan designation can be found here: ema.europa.eu/medicines/human/orphan-designations/eu-3-01-056.

Xenpozyme contains the active substance olipudase alfa.

How is Xenpozyme used?

Xenpozyme can only be obtained with a prescription and treatment should be supervised by a healthcare professional experienced in the management of ASMD or other inherited metabolic disorders. Xenpozyme should be administered by a healthcare professional with access to appropriate medical support to manage potential severe reactions such as hypersensitivity (allergic) reactions affecting the whole body (see risks section below).

Xenpozyme is given by infusion (drip) into a vein every two weeks. The recommended dose depends on the patient's weight. The treatment starts with a low dose that is gradually increased until the recommended dose is reached, usually after 14 to 16 weeks. Depending on the dose, the duration of the infusion ranges between 18 and 220 minutes (almost 3.7 hours).

For more information about using Xenpozyme, see the package leaflet or contact your doctor or pharmacist.

How does Xenpozyme work?

Because of a genetic mutation, patients with ASMD type A, A/B and B lack a functioning enzyme, acid sphingomyelinase, which is found in lysosomes (parts of the body's cells that break down nutrients and other materials) and is needed to break down certain fats. The resulting build-up of fats changes the

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way cells work and causes them to die, affecting normal functioning of tissues and organs, including the liver, spleen, lungs, heart and brain.

The active substance in Xenpozyme, olipudase alfa, is a copy of the normal acid sphingomyelinase enzyme. It is expected to replace the patients' faulty enzyme and thereby reduce the build-up of fats within lysosomes and relieve some of the symptoms of the disease. It is not, however, expected to improve symptoms affecting the brain as the medicine is unable to cross the blood-brain barrier which separates the blood from brain tissue.

What benefits of Xenpozyme have been shown in studies?

Xenpozyme was shown to improve lung function and reduce spleen volume both in adults and in children.

In a main study conducted in 36 adults with ASMD type B or type A/B, improvement in lung function was measured by looking at the change in diffusing capacity of the lungs for carbon monoxide (DLco), a type of gas used in small quantities to measure how much oxygen travels from the lungs to the blood. After one year of treatment, the increase in DLco was greater in the group of patients who received Xenpozyme (22% increase on average) compared with the group who received placebo, a dummy treatment (3% increase on average). Based on other lung-related conditions, a greater than 15% increase is considered a meaningful improvement.

In addition, after one year of treatment, spleen volume in patients receiving Xenpozyme reduced on average by 39%, while it increased by 0.5% on average in patients receiving placebo. Based on Gaucher's disease (another genetic disease where fats build up in the spleen and other organs), a greater than 30% reduction in spleen volume is considered clinically meaningful.

A second main study was conducted in 20 patients under 18 years of age (4 adolescents, 9 children, 7 infants/young children) who all received Xenpozyme. The medicine appeared to work in the same way and have the same effects in children and adults. Improvements in lung function and spleen volume were also observed, with an average increase in DLco of 33% and reduction in spleen volume of 49% after one year of treatment.

What are the risks associated with Xenpozyme?

The most common side effects with Xenpozyme (which may affect more than 1 in 10 people) are headache, fever, itching, urticaria (itchy rash), nausea (feeling sick), vomiting, abdominal (belly) pain, muscle pain and increased blood level of C-reactive protein (a marker of inflammation). In clinical trials, infusion-associated reactions, including hypersensitivity (allergic reactions), occurred in more than 1 in 2 adults and in around 2 in 3 children.

Serious side effects that were reported during the clinical trials are extrasystoles (additional heartbeats that interrupt the normal heart rhythm) in a patient who already had damage to the heart muscle. Anaphylactic reaction (sudden, severe allergic reaction) and severe cases of urticaria, rash, hypersensitivity and increased blood level of alanine aminotransferase (a liver enzyme) were reported in children. Serious hypersensitivity reactions linked to the infusion were more common in children than in adults.

For the full list of side effects and restrictions of Xenpozyme, see the package leaflet.

Why is Xenpozyme authorised in the EU?

There are very limited treatment options for patients with ASMD. Xenpozyme has been shown to provide clinically meaningful benefits to patients with ASMD type B or type A/B, improving lung function and reducing spleen volume. In terms of safety, Xenpozyme's side effects are generally mild to moderate. More serious side effects, in particular severe allergic reactions, can occur but are considered manageable with the risk minimisation measures in place. The European Medicines Agency decided that Xenpozyme's benefits are greater than its risks and it can be authorised for use in the EU.

What measures are being taken to ensure the safe and effective use of Xenpozyme?

The company that markets Xenpozyme is requested to distribute educational materials to healthcare professionals, patients or caregivers to help manage the risk of serious side effects, particularly severe allergic reactions linked to the infusion. These include information on the signs and symptoms to watch out for and recommended actions if side effects occur.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Xenpozyme have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Xenpozyme are continuously monitored. Suspected side effects reported with Xenpozyme are carefully evaluated and any necessary action taken to protect patients.

Other information about Xenpozyme

Xenpozyme received a marketing authorisation valid throughout the EU on 24 June 2022.

Further information on Xenpozyme can be found on the Agency's website:
ema.europa.eu/medicines/human/EPAR/xenpozyme.

This overview was last updated in 07-2022.