PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Nexviazyme

Powder for concentrate for solution for infusion

Active ingredient and its quantity

One vial contains: 100 mg of avalglucosidase alfa. After reconstitution, the solution contains 10 mg/ml avalglucosidase alfa and after dilution the concentration varies from 0.5 mg/ml to 4 mg/ml.

Inactive and allergenic ingredients: see section 6 "Further Information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for the treatment of your aliment. Do not pass it on to others. It may harm them, even if it seems to you that their aliment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Nexviazyme is used for long-term enzyme replacement therapy for patients with Pompe disease.

Therapeutic group: Nexviazyme contains an enzyme called avalglucosidase alfa – it is a copy of the natural enzyme called acid alpha-glucosidase (GAA) that is lacking in people with Pompe disease.

People with Pompe disease have low levels of the enzyme acid alpha-glucosidase (GAA). This enzyme helps control levels of glycogen (a type of carbohydrate) in the body. Glycogen provides the body with energy, but in Pompe disease high levels of glycogen build-up in different muscles and damages them. The medicine replaces the missing enzyme so the body can reduce the build-up of glycogen.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

You have had life-threatening allergic (hypersensitivity) reactions to avalglucosidase alfa or to any of the additional ingredients contained in the medicine (listed in section 6) and these reactions occurred again after stopping and restarting treatment with the medicine.

Special warnings regarding use of the medicine

Speak to the doctor immediately if treatment with Nexviazyme causes:

- Allergic reactions, including anaphylaxis (severe allergic reaction) – see in the section "Side Effects".
- Infusion-associated reaction while receiving the medicine or in the few hours afterwards – see symptoms in the section "Side Effects."

Also, inform the doctor if you have swelling in the legs or widespread swelling in the body. Your doctor will decide if your Nexviazyme infusion should stop and will give you the appropriate medical treatment. The doctor will also decide if you can continue receiving avalglucosidase alfa.

Drug interactions

If you are taking, have recently taken, or might take other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you might be pregnant or are planning to have a baby, consult with the doctor or pharmacist before using this medicine. There is no information about the use of Nexviazyme in pregnant women. You must not receive Nexviazyme during pregnancy unless the doctor specifically recommends it. You and the doctor should decide if you can use Nexviazyme if you are breastfeeding.

Driving and operating machinery

Nexviazyme may have a minor effect on the ability to drive and use machines. Because dizziness, low blood pressure and sleepiness can occur as infusion-associated reactions, this may affect the ability to drive and operate machinery on the day of the infusion.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation. The dosage and treatment regimen will be determined by the doctor only. Nexviazyme will be given to you under the supervision of a healthcare professional experienced in treating Pompe disease.

You may be given other medicines before you receive Nexviazyme, to reduce some side effects. Such medicines include an anti-histamine, a steroid and a medicine (such as paracetamol) to reduce fever.

The dose of Nexviazyme is based on your weight and the medicine will be given to you once every two weeks.

The recommended dosage of Nexviazyme is 20 mg/kg of body weight.

Do not exceed the recommended dose.

Home infusion

The doctor may determine that you can have home infusion of Nexviazyme if it is safe and convenient to do so. If you develop any side effects during the Nexviazyme infusion, a home infusion staff member may stop the infusion and begin appropriate medical treatment.

Instructions for proper use

Nexviazyme is given through an infusion drip into the vein (intravenous infusion). It is supplied to the healthcare professional as a powder to be mixed with sterile water and then diluted in a glucose solution before infusing it.

If you are given more Nexviazyme than you should

Excessive infusion rate of Nexviazyme may cause hot flush.

If you missed a dose of Nexviazyme

If you missed an infusion, please contact the doctor. If you have further questions about the use of this medicine, refer to the doctor, pharmacist or nurse.

If you stop using Nexviazyme

Speak with the doctor if you wish to stop Nexviazyme treatment. The disease symptoms may worsen if you stop treatment.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Nexviazyme may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Side effects mainly occur during or shortly after the Nexviazyme infusion. **You must tell the doctor immediately if you develop an infusion-associated reaction or an allergic reaction.** The doctor may give you medicines before the infusion to prevent these reactions.

Infusion-associated reactions

Mostly infusion-associated reactions are mild or moderate. Symptons of infusion-associated reaction include chest discomfort, increased blood pressure, increased heart rate, chills, cough, diarrhea, fatigue, headache, flu-like illness, nausea, vomiting, red eyes, pain in the arms and legs, skin redness, itchy skin, rash and hives.

Allergic reactions

Allergic reactions may include symptoms such as difficulty breathing, chest pressure, flushing, cough, dizziness, nausea, redness on palms and feet, itchy palms and feet, swelling of the lower lip and tongue, low blood oxygen level and rash.

Additional side effects

Common side effects – effects that occur in up to 1 in 10 users

- Anaphylaxis (severe allergic reaction)
- Tremor (shaking)
- Red eyes
- Increased blood pressure
- Headache
- Dizziness
- Cough
- Difficulty breathing
- Nausea
- Diarrhea
- Vomiting
- Lip swelling
- Swollen tongue
- Itchy skin
- Hives
- Rash
- Redness of hands
- Redness of skin
- Muscle spasms
- Muscle aches
- Fatigue
- Chills
- Chest discomfort
- Pain
- Flu-like illness
- Low blood oxygen

Uncommon side effects – effects that occur in up to 1 in 100 users

- Eye inflammation
- Numbness or tingling
- Itchy eyes
- Watery eyes
- Rapid heartbeat
- Extra heartbeats
- Flushing
- Low blood pressure
- Rapid breathing
- Swelling of throat
- Throat irritation
- Abdominal (belly) pain
- Swelling of skin
- Sweating
- Facial pain
- Increased body temperature
- Infusion site tissue leakage
- Infusion site joint pain
- Infusion site rash
- Infusion site itching
- Localised edema
- Swelling in the arms and legs
- Fever
- Abnormal breathing sounds (wheezing)
- Feeling tired
- Pain in arm or leg
- Pale skin
- Marks for inflammation in blood test
- Weakness
- Indigestion
- Reduced sensation to touch, pain and temperature
- Numbness in the mouth, tongue or lip
- Tingling in the mouth, tongue or lip
- Difficulty swallowing
- Pain on one side of the body or in the lower back (flank pain)
- Feeling cold
- Oral discomfort (including lip burning sensation)
- Burning sensation
- Upper abdominal pain

The reported side effects seen in children and adolescents were similar to those seen in adults.

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (exp. date) that appears on the package/vial. The expiry date refers to the last day of that month.

Storage conditions

Unopened vials:

Store in a refrigerator (2°-8°C). Do not freeze. Store in the original packaging to protect from light.

Reconstituted solution:

After reconstitution, it is recommended to dilute the solution immediately. The reconstituted solution may be stored refrigerated at 2°-8°C for up to 24 hours.

Diluted solution:

After dilution, immediate use is recommended. The diluted solution may be stored for up to 24 hours at 2°-8°C, followed by 9 hours (including infusion time) at room temperature (up to 25°C).

Do not discard medicines into the wastewater or household waste. Ask the doctor, pharmacist or nurse how to dispose of medicines no longer in use. These measures will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

glycine, mannitol, L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80, water for injection

What the medicine looks like and the contents of the package

A powder for concentrate for solution for infusion in a vial (100 mg/vial). Each package contains 1, 5, 10 or 25 vials. Not all package sizes may be marketed.

The powder is white to pale yellow. After reconstitution the solution is clear to pale yellow. The reconstituted solution must be further diluted.

Registration holder, importer and address: sanofi-aventis Israel ltd.,10 Beni Gaon St., Netanya.

This leaflet does not contain all of the information about the preparations. If you have any question or are unsure about something, please refer to a doctor.

Approved in October 2022

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
170-81-37090