Package leaflet: Information for the patient

Nexviadyme 100 mg

powder for concentrate for solution for infusion

avalglucosidase 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 start using 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, pharmacist, or nurse.
- If you get any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Nexviadyme is and what it is used for

What Nexviadyme is
Nexviadyme 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.

What Nexviadyme is used for
Nexviadyme is used to treat people of all ages who have 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 that the body can reduce the build-up of glycogen.

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

Do not use Nexviadyme
If you have had life-threatening allergic (hypersensitive) reactions to avalglucosidase alfa or any of the other ingredients of this medicine (listed in section 6) and these reactions occurred again after stopping and restarting the medicine.

Warnings and precautions
Talk to your doctor or pharmacist or nurse before using Nexviadyme

Speak to your doctor immediately if treatment with Nexviadyme causes:
- allergic reactions, including anaphylaxis (a severe allergic reaction) – see under 'Possible side effects', below for symptoms
- infusion-associated reaction while you are receiving the medicine or in the few hours afterwards – see under 'Possible side effects', below for symptoms

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

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

Pregnancy and breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant, or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.
There is no information about the use of Nexviadyme in pregnant women. You must not receive Nexviadyme during pregnancy unless your doctor specifically recommends it. You and your doctor should decide if you can use Nexviadyme if you are breast-feeding.

Driving and using machines
Nexviadyme 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 use machines on the day of the infusion.

3. How Nexviadyme is given

Nexviadyme will be given to you under the supervision of a health care professional who is experienced in the treatment of Pompe disease.

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

The dose of Nexviadyme is based on your weight and will be given to you once every 2 weeks.

- The recommended dose of Nexviadyme is 20 mg/kg of body weight.

Home infusion
Your doctor may consider that you can have home infusion of Nexviadyme if it is safe and convenient to do so. If you get any side effects during an infusion of Nexviadyme, your home infusion staff member may stop the infusion and start appropriate medical treatment.

Instructions for proper use
Nexviadyme is given through a drip into a vein (intravenous infusion). It is supplied to the healthcare professional as a powder to mix with sterile water and further dilute with glucose before infusing it.

If you are given more Nexviadyme than you should
Excessive infusion rate of Nexviadyme may result in hot flush.

If you miss your dose of Nexviadyme
If you have missed an infusion, please contact your doctor. If you have any further questions on the use of this medicine, ask your doctor, pharmacist, or nurse.

If you stop using Nexviadyme
Speak to your doctor if you wish to stop Nexviadyme treatment. The symptoms of your disease may worsen if you stop treatment.

4. Possible side effects

Side effects mainly occur while patients are being given Nexviadyme infusion or shortly afterwards. You must tell your doctor immediately if you get an infusion-associated reaction or an allergic reaction. Your doctor may give you medicines before your infusion to prevent these reactions.

Infusion-associated reactions
Mostly infusion-associated reactions are mild or moderate.
Symptoms of infusion-associated reaction include:
- chest discomfort
- increased blood pressure
- increased heart rate
- chills
- cough
- diarrhoea
- fatigue
- headache
- flu-like illness
- nausea
- vomiting
- red eye
- pain in arms and legs
- skin redness
- itchy skin
- rash
- 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
- swollen lower lip and tongue
- low levels of oxygen in the blood
- rash.

Very common (may affect more than 1 in 10 people)
- Hypersensitivity
- Headache
- Nausea
- Itchy skin
- Rash

Common (may affect up to 1 in 10 people)
- Severe allergic reaction (anaphylaxis)
- Dizziness
- Sleepiness
- Shaking
- Burning sensation
- Red eyes
- Itchy eyes
- Swelling of eyelid
- Rapid heartbeat
- Flushing
- Raised blood pressure
- Low blood pressure
- Skin and lips turning blue
- Hot flush
- Pale skin
- Cough
- Difficulty breathing
- Throat irritation
- Mouth and throat pain
- Diarrhoea
- Vomiting
- Lip swelling
- Swollen tongue
- Abdominal (belly) pain

The following information is intended for healthcare professionals only:

Reconstitution
Use aseptic technique during reconstitution.
1. Determine the number of vials to be reconstituted based on the individual patient's weight and the recommended dose of 20 mg/kg or 40 mg/kg.
   Patient weight (kg) x dose (mg/kg) = patient dose (in mg).
   Patient dose (in mg) divided by 100 mg/vial = number of vials to reconstitute. If the number of vials includes a fraction, round up to the next whole number.
   Example: Patient weight (16 kg) x dose (20 mg/kg) = patient dose (320 mg).
   320 mg divided by 100 mg/vial = 3.2 vials; therefore, 4 vials should be reconstituted.
   Example: Patient weight (16 kg) x dose (40 mg/kg) = patient dose (640 mg).
   640 mg divided by 100 mg/vial = 6.4 vials; therefore, 7 vials should be reconstituted.
2. Remove the required number of vials needed for the infusion from the refrigerator and set aside for approximately 30 minutes to allow them to reach room temperature.
3. Reconstitute each vial by slowly injecting 10.0 ml of water for injections (WFI) to each vial. Each vial will yield 100 mg/10 ml (10 mg/ml). Avoid forceful impact of the WFI on the powder and avoid foaming. This is done by slow drop-wise addition of the water for injection down the inside of the vial and not directly onto the lyophilised powder. Tilt and roll each vial gently. Do not invert, swirl, or shake.
4. Perform an immediate visual inspection on the reconstituted vials for particulate matter and discoloration. If upon immediate inspection, particles are observed or if the solution is discoloured, do not use. Allow the solution to become dissolved.

Dilution
1. The reconstituted solution should be diluted in 5% glucose in water to a final concentration of 0.5 mg/ml to 4 mg/ml. See Table 1 for the recommended total infusion volume based on the patient weight.
2. Slowly withdraw the volume of reconstituted solution from each vial (calculated according to the patient's weight).
3. Add the reconstituted solution slowly and directly into the 5% glucose solution. Avoid foaming or agitation of the infusion bag. Avoid air introduction into the infusion bag.
4. Gently invert or massage the infusion bag to mix. Do not shake.
5. To avoid administration of inadvertently introduced particles during dose IV preparation, it is recommended to use an in-line low protein binding 0.2 µm filter to administer Nexviadyme. After the infusion is complete, flush the intravenous line with glucose 5% in water.
6. Do not infuse Nexviadyme in the same intravenous line with other medicines.

- Abdominal (belly) pain upper
- Indigestion
- Itchy, lumpy rash (hives)
- Redness of hands
- Redness of skin
- Red rash
- Excessive sweating
- Itchy rash
- Skin plaque
- Muscle spasms
- Muscle aches
- Pain in arm or leg
- Flank pain
- Fatigue
- Chills
- Fever
- Chest discomfort
- Pain
- Flu-like illness
- Infusion site pain
- Low blood oxygen
- Weakness
- Swelling of face
- Feeling cold or hot

Uncommon (may affect up to 1 in 100 people)
- Inflammation of eyes
- Numbness or tingling
- Watery eyes
- Extra heart beats
- Rapid breathing
- Swelling of throat
- Numbness in the mouth, tongue, or lip
- Tingling in the mouth, tongue, or lip
- Difficulty swallowing
- Swelling of skin
- Skin discolouration
- Facial pain
- Increased body temperature
- Infusion site tissue leakage
- Infusion site joint pain
- Infusion site rash
- Infusion site reaction
- Infusion site itching
- Localised swelling
- Swelling in the arms and legs
- Wheezing
- Blood test for inflammation
- Reduced sensation to touch, pain, and temperature
- Oral discomfort (including lip burning sensation)

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

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist, 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 Nexviadyme

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

Do not use this medicine after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

Unopened vials:
Store in a refrigerator (2°C - 8°C).

Reconstituted solution:
After reconstitution, immediate use for dilution is recommended. The reconstituted solution can be stored up to 24 hours when refrigerated at 2°C to 8°C.

Diluted solution:
After dilution, immediate use is recommended. The diluted solution can be stored for 24 hours at 2°C to 8°C followed by 9 hours at room temperature (up to 25°C).

Do not throw away any medicines via wastewater or household waste. Ask your doctor, pharmacist, 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 Nexviadyme contains
The active substance is avalglucosidase alfa. One vial contains 100 mg of avalglucosidase alfa. After reconstitution, the solution contains 10 mg of avalglucosidase alfa per ml and after dilution the concentration varies from 0.5 mg/ml to 4 mg/ml.
The other ingredients are
- Histidine
- Histidine hydrochloride monohydrate
- Glycine
- Mannitol
- Polysorbate 80

What Nexviadyme looks like and contents of the pack
Avalglucosidase alfa is a powder for concentrate for solution for infusion in a vial (100 mg/vial). Each pack contains 1, 5, 10, or 25 vials. Not all pack sizes may be marketed.

The powder is white to pale yellow. After reconstitution it is a clear, colourless to pale yellow solution. The reconstituted solution must be further diluted.

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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: Projected Intravenous Infusion Volumes for Nexviadyme Administration by Patient Weight at 20 mg/kg and 40 mg/kg Dose

Patient Weight Range (kg)	Total infusion volume (ml) for 20 mg/kg	Total infusion volume (ml) for 40 mg/kg
1.25 to 5	50	50
5.1 to 10	50	100
10.1 to 20	100	200
20.1 to 30	150	300
30.1 to 35	200	400
35.1 to 50	250	500
50.1 to 60	300	600
60.1 to 100	500	1000
100.1 to 120	600	1200
120.1 to 140	700	1400
140.1 to 160	800	1600
160.1 to 180	900	1800
180.1 to 200	1000	2000

Any unused medicine or waste material should be disposed of in accordance with local requirements.

Home infusion
Infusion of Nexviadyme at home may be considered for patients who are tolerating their infusions well and have no history of moderate or severe IARs for a few months. The decision to have a patient move to home infusion should be made after evaluation and upon recommendation by the treating physician. A patient's underlying co-morbidities and ability to adhere to the home infusion requirements need to be taken into account when evaluating the patient for eligibility to receive home infusion. The following criteria should be considered:
- The patient must have no ongoing concurrent condition that, in the opinion of the physician, may affect patient's ability to tolerate the infusion.
- The patient is considered medically stable. A comprehensive evaluation must be completed before the initiation of home infusion.
- The patient must have received Nexviadyme infusions supervised by a physician with expertise in management of Pompe patients for a few months that could be in a hospital or in another appropriate setting of outpatient care. Documentation of a pattern of well-tolerated infusions with no IARs, or mild IARs that have been controlled with premedication, is a prerequisite for the initiation of home infusion.
- The patient must be willing and able to comply with home infusion procedures.
- Home infusion infrastructure, resources, and procedures, including training, must be established and available to the healthcare professional. The healthcare professional should be available at all times during the home infusion and a specified time after infusion, depending on patient's tolerance prior to starting home infusion.

If the patient experiences adverse reactions during the home infusion, the infusion process should be stopped immediately, and appropriate medical treatment should be initiated. Subsequent infusions may need to occur in a hospital or in an appropriate setting of outpatient care until no such adverse reaction is present. Dose and infusion rate must not be changed without consulting the responsible physician.