EDA Assessment Report for Biological Medicinal Product

(Scientific Discussion)

Nexviazyme

Date: August 2024

Assessment report

Unit: Technical Assessment Unit

Nexviazyme

Administrative information:

Trade name of the medicinal product:	Nexviazyme
INN (or common name) of the active substance(s):	Avalglucosidase alfa 100 mg
Manufacturer of the finished product	Genzyme Ireland Limited, Old Kilmeaden Road, IDA Industrial Park, Waterford - Ireland.
Marketing Authorization holder	Sanofi BV., Paasheuvelweg 25,1105 BP Amsterdam-The Netherlands
Applied Indication(s):	- Nexviazyme is indicated for long-term enzyme replacement therapy for the treatment of patients with Pompe disease (acid alfa glucosidase deficiency)
Pharmaceutical form(s) and strength(s):	- Powder for concentrate for solution for infusion. - The strength is 100mg/vial
Route of administration	Intravenous (IV) administration
Approved pack	-Carton box contains one clear colorless 20 mL glass (type 1) vial closed with gray chlorobutyl elastomeric stopper with FluroTec® on the top of stopper (no product contact) and B2-04 cross-linked silicone coating on the product contact side of the stopper. The stoppers are crimped with an aluminum seal with a flip-OFF® button and inner leaflet.

List of abbreviations

AS	Active substance
CTD	Common Technical Document
WFI	Water For Injection
EMA	European medicines Agency
ERT	Enzyme Replacement Therapy
FP	Finished product
GAA	Acid α-glucosidase
IV	Intervenous
M6P	mannose-6-phosphate

Dossier initial submission and evaluation process.

- The product was submitted for registration via reliance level I.
- The dossier evaluation by the registration administration units was started on 11.10.2023 after providing all the required documents (EMA list of questions along with Full CTD for the product)

1. **'General introduction about the product including brief description of the AI, its mode of action and indications:**

- Avalglucosidase alfa is a recombinant human α-glucosidase conjugated with synthetic bis-mannose-6-phosphate-Man6 glycan for the treatment of Pompe disease as an enzyme replacement therapy (ERT). Pompe disease, also known as acid maltase deficiency or glycogen storage disease Type II is an autosomal recessive genetic disorder caused by the deficiency of lysosomal acid α-glucosidase, an enzyme that degrades glycogen.

- Avalglucosidase alfa is a modification of alglucosidase alfa resulting from the conjugation of a number of hexamannose structures containing 2 terminal M6P moieties to oxidized sialic acid residues on alglucosidase alfa to increase bis-M6P levels.

- Avalglucosidase alfa drug product is a sterile lyophilized powder administered by intravenous (IV) infusion following reconstitution and dilution. It is supplied in an aseptically filled single-use glass vial with a nominal strength of 100 mg/vial. Prior to lyophilization, the nominal fill volume is 10.0 mL. The powder for injection is reconstituted with 10.0 mL sterile water for injection (WFI). The formulation is 10 mg/mL avalglucosidase alfa, 10 mM L-histidine/L-histidine hydrochloride monohydrate, 2% (w/v) glycine, 2% (w/v) mannitol, and 0.01% (w/v) polysorbate 80 at pH 6.2.

-The finished product (FP) is presented as a powder for concentrate for solution for infusion containing 100 mg of avalglucosidase alfa as active substance (AS). Other ingredients are histidine, histidine hydrochloride monohydrate, glycine, mannitol and polysorbate 80.

- Nexviazyme is presented in a 20 mL USP-NF/Ph. Eur. Type I clear colorless glass vial closed with 20 mm gray elastomeric stopper with FluroTec® and B2-04 coating. The stoppered vials are crimped with an aluminum seal with a Flip-Off® button.

- Nexviazyme 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 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. Quality aspects:

- **Manufacturer(s):**

  Drug substance:

  Active substance is manufactured at Genzyme Flanders BV, Cipalstraat 8, Geel, 2440-Belgium.

  Drug product:

- Finished product is manufactured at Genzyme Ireland Limited, Old Kilmeaden Road, IDA Industrial Park. Waterford-Ireland.
- **Stability**

  Drug substance:

  Approved Storage Conditions: 5°C ± 3°C

  Approved shelf life: 3 months

  Drug product:

  Approved Storage Conditions:

1- For drug product: Store in a refrigerator (2°C - 8°C).

2- Reconstituted medicinal product:

After reconstitution, chemical, physical, and microbiological in-use stability has been demonstrated for 24 hours at 2°C - 8°C.
From a microbiological point of view, the reconstituted product should be used immediately.
If not used for dilution immediately, in-use storage times and conditions prior to dilution are the responsibility of the user and would normally not be longer than 24 hours at 2°C - 8°C.

3- Diluted medicinal product:

After dilution, chemical, physical and microbiological in-use stability has been demonstrated between 0.5 mg/ml and 4 mg/ml for 24 hours at 2°C - 8°C, followed by 9 hours at room temperature (up to 25°C) to allow for infusion. Use Aseptic Techniques.
From a microbiological point of view, the medicinal product should be used immediately.
If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 24 hours at 2°C - 8°C, followed by 9 hours at room temperature (up to 25°C) to allow for infusion.

Approved shelf life for the finished product: 48 months

3. Non-clinical and clinical aspects:

- The nonclinical efficacy and safety programme provides sufficient data to support the registration of avalglucosidase alfa in patients with Pompe disease.
-In conclusion the overall benefit/risk of Nexviazyme product is favorable for long-term enzyme replacement therapy for the treatment of patients with Pompe disease (acid α-glucosidase deficiency).

- **General Conclusion and Recommendations if any:**

Based on the review of CTD modules and other supplementary documents, the product is approved.

For more information, please visit EMA published assessment report link:

https://www.ema.europa.eu/en/documents/assessment-report/nexviadyme-epar-public-assessment-report_en.pdf

****knowing that Nexviazyme was approved by EMA under the name " Nexviadyme "**