Vestronidase alfa

IDENTIFICATION

Name

Vestronidase alfa

Accession Number

DB12366

Type

Biotech

Groups

Approved, Investigational

Biologic Classification

Protein Based Therapies
Recombinant Enzymes

Description

Vestronidase alfa, or vestronidase alfa-vjbk, is a recombinant human lysosomal beta glucuronidase that is a purified enzyme produced by recombinant DNA technology in a Chinese hamster ovary cell line. The enzyme is a homotetramer consisted of 4 monomers with 629 amino acids, and holds the same amino acid sequence as human beta-glucuronidase (GUS) [Label]. Vestronidase alfa is an enzyme replacement therapy for the treatment of mucopolysaccharidosis type VII (MPS VII), also known as Sly syndrome, which is an inherited, rare genetic metabolic condition that targets a small subset of population. MPS VII is a progressive condition that affects most tissues and organs due to the lack of a lysosomal enzyme called beta-glucuronidase, leading to buildup of toxic metabolites. The disorder is initiated with skeletal abnormalities, including short stature, along with other pathological conditions including enlarged liver and spleen, heart valve abnormalities, and narrowed airways which can lead to lung infections and trouble breathing. Last two conditions are leading causes of fatalities in patients with MPS VII.

disability [Label]. In clinical trials, vestronidase alfa treatment demonstrated improvement and stabilization in motor symptoms by increasing the patients' ability to walk longer distances in comparison to treatment with placebo . Few patients also experienced improved pulmonary function.

Vestronidase alfa was FDA-approved on November 17th, 2017 under the trade name Mepsevii as an intravenous infusion for the treatment of pediatric and adult patients.

Protein chemical formula

Not Available

Protein average weight

72562.0 Da (Non-glycosylated)

Sequences

Not Available

Synonyms

Recombinant human beta-glucuronidase

Vestronidase alfa-vjbk

External IDs

UX-003 / UX003

Prescription Products

Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END		
Mepsevii	Injection	2 mg/mL	Intravenous	Ultragenyx Pharmaceutical Inc.	2017-11-15	Not applicable		

Showing 1 to 1 of 1 entries

‹ ›

Categories

Not Available

7XZ4062R17

CAS number

1638194-78-1

PHARMACOLOGY

Indication

Indicated in pediatric and adult patients for the treatment of Mucopolysaccharidosis VII (MPS VII, Sly syndrome).

Associated Conditions

Mucopolysaccharidosis VII

Pharmacodynamics

In all patients evaluated, MEPSEVII treatment resulted in reduction of urinary excretion of GAGs including chondroitin sulfate and dermatan sulfate, which was sustained with continued treatment [Label].

Mechanism of action

Beta-glucuronidase (GUS) is a lysosomal enzyme responsible for degradation of glucuronate-containing glycosaminoglycan (GAG) [2]. Resulting lysosomal storage and GAG accumulation in cells from incomplete metabolic degradation of macromolecules leads to damage to multiple tissues and organs. Vestronidase alfa serves as an exogenous source of GUS enzyme for uptake into cellular lysosomes, which is facilitated by the presence of mannose-6-phosphate (M6P) residues on the oligosaccharide chains of the recombinant enzyme. The chains allow binding of the enzyme to cell surface receptors to promote cellular uptake, and targets the lysosomes to achieve catabolism of accumulated GAGs in affected tissues [Label].

Absorption

Serum exposures of vestronidase alfa increases in a dose-proportional manner, from 1 mg/kg (0.25 times the approved recommended dosage) to 2 mg/kg (0.5 times the approved recommended dosage), and 4 mg/kg (the recommended dosage). After repeated dosing of 4 mg/kg every other week in patients with MPS VII, the mean ± standard deviation of maximal concentration (Cmax) was 20.0 ± 8.1 mcg/mL (range: 6.6 to 34.9 mcg/mL). The mean ± standard deviation of area under the concentration-time curve from time zero to the last measurable concentration (AUC0-t) was 3440 ± 1430 mcg x min/mL (range: 1130 to 5820 mcg x min/mL) [Label].

deviation of the total volume of distribution (Vss) was 260 ± 130 mL/kg (range: 97 to 598 mL/kg) [Label].

Protein binding

Not Available

Metabolism

Vestronidase alfa is eliminated by nonspecific proteolytic degradation into small peptides and amino acids [Label].

Route of elimination

Vestronidase alfa-vjbk is not expected to be eliminated through renal or fecal excretion. No excretion studies have been conducted [Label].

Half life

After repeated dosing of 4 mg/kg every other week in MPS VII patients, the mean ± standard deviation of the elimination half-life (t1/2) was 155 ± 37 minutes (range: 51 to 213 minutes) [Label].

Clearance

After repeated dosing of 4 mg/kg every other week in MPS VII patients, the mean ± standard deviation of the total clearance (CL) was 1.3 ± 0.7 mL/min/kg (range: 0.6 to 3.3 mL/min/kg) [Label].

Toxicity

Treatment of vestronidase alfa with doses up to 20 mg/kg administered weekly in rats did not result in adverse effect on fertility and reproductive performance of male and female rats. Studies assessing the mutagenic or carcinogenic potential of vestronidase alfa have not been performed [Label].

Affected organisms

Not Available

Pathways

Not Available

Pharmacogenomic Effects/ADRs

INTERACTIONS

Drug Interactions

Not Available

Food Interactions

Not Available

REFERENCES

General References

1. Basinska A, Florianczyk B: Beta-glucuronidase in physiology and disease. Ann Univ Mariae Curie Sklodowska Med. 2003;58(2):386-9. [PubMed:15323223]
2. Naz H, Islam A, Waheed A, Sly WS, Ahmad F, Hassan I: Human beta-glucuronidase: structure, function, and application in enzyme replacement therapy. Rejuvenation Res. 2013 Oct;16(5):352-63. doi: 10.1089/rej.2013.1407. [PubMed:23777470]

External Links

PubChem Substance

347911326

Wikipedia

Vestronidase_alfa

FDA label

Download (369 KB)

CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
1, 2	Completed	Treatment	Mucopolysaccharidosis Type 7	1

	Recruiting		Mucopolysaccharidosis VII / Sly Syndrome	
3	Active Not Recruiting	Treatment	MPS VII / Mucopolysaccharidosis / Mucopolysaccharidosis VII / Sly Syndrome	1
3	Completed	Treatment	MPS 7 / MPS VII / Mucopolysaccharidosis / Sly Syndrome	1
Not Available	No Longer Available	Not Available	Mucopolysaccharidosis Type 7	1

Showing 1 to 5 of 5 entries

‹ ›

PHARMACOECONOMICS

Manufacturers

Not Available

Packagers

Not Available

Dosage forms

Search

FORM	ROUTE	STRENGTH
Injection	Intravenous	2 mg/mL

Showing 1 to 1 of 1 entries

‹ ›

Prices

Not Available

Patents

Not Available

PROPERTIES

State

Experimental Properties

Not Available

TAXONOMY

Description

Not Available

Kingdom

Organic Compounds

Super Class

Organic Acids

Class

Carboxylic Acids and Derivatives

Sub Class

Amino Acids, Peptides, and Analogues

Direct Parent

Peptides

Alternative Parents

Not Available

Substituents

Not Available

Molecular Framework

Not Available

External Descriptors

Not Available

Drug created on October 20, 2016 16:05 / Updated on August 02, 2018 06:37

About DrugBank

DrugBank Blog

Wishart Research Group

Terms of Use

Privacy Policy

Support

FAQ

Help

Email Support

Commercial Products

API Pricing

API Docs

Data Licenses

Support

This project is supported by the **Canadian Institutes of Health Research** (award #111062), **Alberta Innovates - Health Solutions**, and by **The Metabolomics Innovation Centre (TMIC)**, a nationally-funded research and core facility that supports a wide range of cutting-edge metabolomic studies. TMIC is funded by **Genome Alberta**, **Genome British Columbia**, and **Genome Canada**, a not-for-profit organization that is leading Canada's national genomics strategy with funding from the federal government. Maintenance, support, and commercial licensing is provided by **OMx Personal Health Analytics, Inc.** Designed by **Educe Design & Innovation Inc.**