Idursulfase

Targets (3)

IDENTIFICATION

Name

Idursulfase

Accession Number

DB01271

Type

Biotech

Groups

Approved

Biologic Classification

Protein Based Therapies
Recombinant Enzymes

Description

Idursulfase is a purified form of human iduronate-2-sulfatase, a lysosomal enzyme. Idursulfase is produced by recombinant DNA technology in a human cell line. Idursulfase is an enzyme that hydrolyzes the 2-sulfate esters of terminal iduronate sulfate residues from the glycosaminoglycans dermatan sulfate and heparan sulfate in the lysosomes of various cell types. Idursulfase is a 525-amino acid glycoprotein with a molecular weight of approximately 76 kilodaltons. The enzyme contains eight asparagine-linked glycosylation sites occupied by complex oligosaccharide structures. The enzyme activity of idursulfase is dependent on the post-translational modification of a specific cysteine to formylglycine.

Protein chemical formula

$C_{2654}H_{4000}N_{688}O_{774}S_{14}$

Sequences

```
>Idursulfase heavy chain
SETQANSTTDALNVLLIIVDDLRPSLGCYGDKLVRSPNIDQLASHSLLFQNAFAQQAVCA
PSRVSFLTGRRPDTTRLYDFNSYWRVHAGNFSTIPQYFKENGYVTMSVGKVFHPGISSNH
TDDSPYSWSFPPYHPSSEKYENTKTCRGPDGELHANLLCPVDVLDVPEGTLPDKQSTEQA
IQLLEKMKTSASPFFLAVGYHKPHIPFRYPKEFQKLYPLENITLAPDPEVPDGLPPVAYN
PWMDIRQREDVQALNISVPYGPIPVDFQRKIRQSYFASVSYLDTQVGRLLSALDDLQLAN
STIIAFTSDHGWALGEHGEWAKYSNFDVATHVPLIFYVPGRTASLPEAGEKLFPYLDPFD
SASQLMEPGRQSMDLVELVSLFPTLAGLAGLQVPPRCPVPSFHVELCREGKNLLKHFRFR
DLEEDPYLPG
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>Idursulfase light chain
NPRELIAYSQYPRPSDIPQWNSDKPSLKDIKIMGYSIRTIDYRYTVWVGFNPDEFLANFS
DIHAGELYFVDSDPLQDHNMYNDSQGGDLFQLLMP
```

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Synonyms

Alpha-L-iduronate sulfate sulfatase

Iduronate 2-sulfatase

Prescription Products

Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END		
Elaprase	Solution	2 mg	Intravenous	Shire Human Genetic Therapies, Inc.	2007-08-01	Not applicable		
Elaprase	Solution, concentrate	6 mg/3mL	Intravenous	Shire	2006-07-24	Not applicable		

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Categories

Alimentary Tract and Metabolism

Esterases

Hydrolases

Hydrolytic Lysosomal Glycosaminoglycan-specific Enzyme

Sulfatases

UNII

5W8JGG2651

CAS number

50936-59-9

PHARMACOLOGY

Indication

For the treatment of Hunter syndrome in adults and children ages 5 and older.

Associated Conditions

Mucopolysaccharidosis II

Pharmacodynamics

Idursulfase is a purified form of the lysosomal enzyme human iduronate-2-sulfatase of recombinant DNA origin. It is designed to replace the natural enzyme, increasing catabolism of certain accumulated glycosaminoglycans (GAG), which abnormally accumulate in multiple tissue types in patients with mucopolysaccharidosis II (MPS-II, or Hunter syndrome).

Mechanism of action

Hunter's Syndrome is an X-linked recessive disease caused by insufficient levels of the lysosomal enzyme iduronate-2-sulfatase. This enzyme cleaves the terminal 2-O-sulfate moieties from the glycosaminoglycans (GAG) dermatan sulfate and heparan sulfate. Due to the missing or defective iduronate-2-sulfatase enzyme in patients with Hunter's Syndrome, GAG progressively accumulate in the lysosomes of a variety of cells, leading to cellular engorgement, organomegaly, tissue destruction and organ system dysfunction. Treatment of Hunter's Syndrome patients with

idursulfase provides exogenous enzyme for uptake into cellular lysosomes. Targeting of

(A) Dermatan sulfate	
Not Available	
Human	
(A) Heparan sulfate	
Not Available	
Human	
(N) Perilipin-3	
Not Available	
Human	

Absorption

Not Available

Volume of distribution

Not Available

Protein binding

Not Available

Metabolism

Not Available

Route of elimination

Not Available

Half life

44 ± 19 minutes

Clearance

- 3 mL/min/kg [Patients (7.7 – 27 years) with Hunter syndrome with treatment week 1(0.5 mg/kg ELAPRASE administered weekly as a 3-hour infusion)]
- 3.4 mL/min/kg [patients (7.7 – 27 years) with Hunter syndrome with treatment week 27 (0.5

There is no experience with overdosage of idursulfase in humans. Single intravenous doses of idursulfase up to 20 mg/kg were not lethal in male rats and cynomolgus monkeys (approximately 6.5 and 13 times, respectively, of the recommended human dose based on body surface area) and there were no clinical signs of toxicity.

Affected organisms

Humans and other mammals

Pathways

Not Available

Pharmacogenomic Effects/ADRs

Not Available

INTERACTIONS

Drug Interactions

No interactions found.

Food Interactions

Not Available

REFERENCES

General References

1. Garcia AR, DaCosta JM, Pan J, Muenzer J, Lamsa JC: Preclinical dose ranging studies for enzyme replacement therapy with idursulfase in a knock-out mouse model of MPS II. Mol Genet Metab. 2007 Jun;91(2):183-90. Epub 2007 Apr 24. [PubMed:17459751]
2. Zareba G: Idursulfase in Hunter syndrome treatment. Drugs Today (Barc). 2007 Nov;43(11):759-67. doi: 10.1358/dot.2007.43.11.1157619. [PubMed:18174963]
3. Clarke LA: Idursulfase for the treatment of mucopolysaccharidosis II. Expert Opin Pharmacother. 2008 Feb;9(2):311-7. doi: 10.1517/14656566.9.2.311 . [PubMed:18201153]
4. Burrow TA, Leslie ND: Review of the use of idursulfase in the treatment of mucopolysaccharidosis II. Biologics. 2008 Jun;2(2):311-20. [PubMed:19707363]
5. Scarpa M: Mucopolysaccharidosis Type II . [PubMed:20301451]

External Links

PubChem Substance

46507347

ChEMBL

CHEMBL1201826

PharmGKB

PA164749134

Drugs.com

Drugs.com Drug Page

Wikipedia

Idursulfase

ATC Codes

A16AB09 — Idursulfase

- A16AB — Enzymes
- A16A — OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS
- A16 — OTHER ALIMENTARY TRACT AND METABOLISM PRODUCTS
- A — ALIMENTARY TRACT AND METABOLISM

AHFS Codes

44:00.00 — Enzymes

CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
2	Not Yet Recruiting	Treatment	Mucopolysaccharidosis II	1

4	Active Not Recruiting	Treatment	Hunter Syndrome	1
4	Completed	Treatment	Hunter Syndrome / MPS II / Mucopolysaccharidosis II	1
Not Available	Completed	Not Available	Hunter Syndrome	1
Not Available	Completed	Not Available	Mucopolysaccharidosis II	1

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PHARMACOECONOMICS

Manufacturers

Not Available

Packagers

Baxter International Inc.

Shire Inc.

Dosage forms

Search

FORM	ROUTE	STRENGTH
Solution	Intravenous	2 mg
Solution, concentrate	Intravenous	6 mg/3mL

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Prices

Search

UNIT DESCRIPTION	COST	UNIT

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Patents

Not Available

PROPERTIES

State

Solid

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

Substituents

Not Available

Molecular Framework

Not Available

External Descriptors

Not Available

TARGETS

1. Dermatan sulfate

Kind
Small molecule

Organism
Human

Pharmacological action
Yes

References

1. Burrow TA, Leslie ND: Review of the use of idursulfase in the treatment of mucopolysaccharidosis II. Biologics. 2008 Jun;2(2):311-20. [PubMed:19707363]
2. Wraith JE, Scarpa M, Beck M, Bodamer OA, De Meirleir L, Guffon N, Meldgaard Lund A, Malm G, Van der Ploeg AT, Zeman J: Mucopolysaccharidosis type II (Hunter syndrome): a clinical review and recommendations for treatment in the era of enzyme replacement therapy. Eur J Pediatr. 2008 Mar;167(3):267-77. Epub 2007 Nov 23. [PubMed:18038146]
3. Garcia AR, Pan J, Lamsa JC, Muenzer J: The characterization of a murine model of mucopolysaccharidosis II (Hunter syndrome). J Inherit Metab Dis. 2007 Nov;30(6):924-34. Epub 2007 Sep 16. [PubMed:17876721]

2. Heparan sulfate

Human

Pharmacological action

Yes

References

1. Burrow TA, Leslie ND: Review of the use of idursulfase in the treatment of mucopolysaccharidosis II. Biologics. 2008 Jun;2(2):311-20. [PubMed:19707363]
2. Wraith JE, Scarpa M, Beck M, Bodamer OA, De Meirleir L, Guffon N, Meldgaard Lund A, Malm G, Van der Ploeg AT, Zeman J: Mucopolysaccharidosis type II (Hunter syndrome): a clinical review and recommendations for treatment in the era of enzyme replacement therapy. Eur J Pediatr. 2008 Mar;167(3):267-77. Epub 2007 Nov 23. [PubMed:18038146]
3. Garcia AR, Pan J, Lamsa JC, Muenzer J: The characterization of a murine model of mucopolysaccharidosis II (Hunter syndrome). J Inherit Metab Dis. 2007 Nov;30(6):924-34. Epub 2007 Sep 16. [PubMed:17876721]

3. Perilipin-3

Kind

Protein

Organism

Human

Pharmacological action

No

General Function

Not Available

Specific Function

Required for the transport of mannose 6-phosphate receptors (MPR) from endosomes to the trans-Golgi network.

Gene Name

PLIN3

Uniprot ID

O60664

47074.665 Da

References

1. Overington JP, Al-Lazikani B, Hopkins AL: How many drug targets are there? Nat Rev Drug Discov. 2006 Dec;5(12):993-6. [PubMed:17139284]
2. Imming P, Sinning C, Meyer A: Drugs, their targets and the nature and number of drug targets. Nat Rev Drug Discov. 2006 Oct;5(10):821-34. [PubMed:17016423]
3. Clarke LA: Idursulfase for the treatment of mucopolysaccharidosis II. Expert Opin Pharmacother. 2008 Feb;9(2):311-7. doi: 10.1517/14656566.9.2.311 . [PubMed:18201153]
4. Burrow TA, Leslie ND: Review of the use of idursulfase in the treatment of mucopolysaccharidosis II. Biologics. 2008 Jun;2(2):311-20. [PubMed:19707363]
5. Wraith JE, Scarpa M, Beck M, Bodamer OA, De Meirleir L, Guffon N, Meldgaard Lund A, Malm G, Van der Ploeg AT, Zeman J: Mucopolysaccharidosis type II (Hunter syndrome): a clinical review and recommendations for treatment in the era of enzyme replacement therapy. Eur J Pediatr. 2008 Mar;167(3):267-77. Epub 2007 Nov 23. [PubMed:18038146]

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