



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

```

SETQANSTTDALNVLLIIVDDLRLPSLGCYGDKLVRSFNIDQLASHSLLFQNAFAQQAVCA
PSRVSFLTGRRPDTRLTYDFNSYWRVHAGNFSTIPQYFKENGYVTMSVGKVFHPGISSNH
TDDSPYSWSFPPYHPSSEKYENTKTCRGPDGELHANLLCPVDVLDVPEGTLDPKQSTEQA
IQLLEKMKTSASPFFLAVGYHKPHIPFRYPKEFQKLYPLENITLAPDPEVPDGLPPVAYN
PWMDIRQREDVQALNISVPYGPVDFQIRQSYFASVSYLDTQVGRLLSALDDLQLAN
STIIAFTSDHGVALGEGEWAKYSNFDVATHVPLIFYVPGRTASLPEAGEKLPYLDPFD
SASQLMEPGRQSMDELVELVSLFPTLAGLAGLQVPPRCVPSFHVELCREGKNLLKHFRFR
DLEEDPYLPG

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>Idursulfase light chain

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NPRELIAYSQYPRPSDIPQWNSDKPSLKDIIKIMGYSIRTIDYRYTVWVGFNPDEFANFS
DIHAGELYFVSDPLQDHNMYNDSQGGDLFQLLMP

```

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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](#)



Enzymes and Cofactors

[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](#)

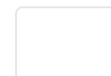
Pharmacodynamics

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

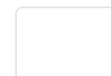
Half life

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 [i](#)

Not Available

INTERACTIONS

Drug Interactions [i](#)

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 ⓘ

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

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

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Prices

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

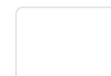
Carboxylic Acids and Derivatives

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 Inher 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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