Pegaspargase

Targets (1)

IDENTIFICATION

Name

Pegaspargase

Accession Number

DB00059 (BTD00079, BIOD00079)

Type

Biotech

Groups

Approved, Investigational

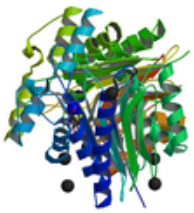
Biologic Classification

Protein Based Therapies
Other protein based therapies

Description

Pegylated L-asparagine amidohydrolase from E. coli. Pegylation substantially (by a factor of 4) extends the protein half life.

Protein structure



Protein chemical formula

$C_{1377}H_{2208}N_{382}O_{442}S_{17}$

Protein average weight

31731.9 Da

DVTKTNTTDVATFKSVNYGPLGYIHNGKIDYQRTPARKHTSDTPFDVSKLNELPKVGIVY
NYANASDLPAKALVDAGYDGIVSAGVGNGNLYKSVFDTLATAAKTGTAVVRSSRVPTGAT
TQDAEVDDAKYGFVASGTLNPQKARVLLQLALTQTKDPQQIQQIFNQY

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Synonyms

Peg-asparaginase

Peg/L-asparaginase

Prescription Products

Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END		
Oncaspar	Injection, solution	750 [iU]/mL	Intramuscular; Intravenous	Baxalta Canada Corporation	1994-02-01	Not applicable		
Oncaspar	Liquid	750 unit	Intramuscular; Intravenous	Aventis Pharma Ltd.	1998-10-13	Not applicable		
Oncaspar	Injection, solution	750 [iU]/mL	Intramuscular; Intravenous	Sigma Tau Pharmaceuticals, Inc.	1994-02-01	2016-11-30		
Oncaspar	Solution	750 unit	Intramuscular; Intravenous	Shire Pharma Canada Ulc	2017-06-01	Not applicable		
Oncaspar Use	Injection, solution	750 U/ml		Baxalta Innovations Gmb H	2016-01-14	Not applicable		

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Categories

Alcohols

Amidohydrolases

Antineoplastic Agents

Antineoplastic and Immunomodulating Agents

Asparagine-specific Enzyme

Biomedical and Dental Materials

Delayed-Action Preparations

Ethylene Glycols

Glycols

Hydrolases

Immunosuppressive Agents

Macromolecular Substances

Polymers

UNII

7D96IR0PPM

CAS number

130167-69-0

PHARMACOLOGY

Indication

For treatment of acute lymphoblastic leukemia

Structured Indications

Acute Lymphoblastic Leukaemias (ALL)

Pharmacodynamics

In a significant number of patients with acute leukemia, the malignant cells are dependent on an exogenous source of asparagine for survival. Normal cells, however, are able to synthesize asparagine and thus are affected less by the rapid depletion produced by treatment with the enzyme asparaginase. Oncaspar exploits a metabolic defect in asparagine synthesis of some malignant cells.

Mechanism of action

Pegaspargase, more effective than asparaginase, converts asparagine to aspartic acid and ammonia. It facilitates production of oxaloacetate which is needed for general cellular metabolism. Some malignant cells lose the ability to produce asparagine and so the loss of exogenous sources of asparagine leads to cell death.

A L-asparagine

other/unknown

Human

IV: Adults (asparaginase naive): 2.4 L/m2 Distributes into CSF (reportedly reducing CSF asparagine concentrations to a similar extent as asparaginase

Protein binding

Not Available

Metabolism

Not Available

Route of elimination

Not Available

Half life

IM: ~6 days; half-life decreased to ~3 days (range: 1.4 to 5 days) in patients with previous hypersensitivity to native L-asparaginase; IV: Adults (asparaginase naive): 7 days

Clearance

Not Available

Toxicity

Adverse effects that occur more than 10% of the time include hepatotoxicity as it is known to increase serum transaminases (ALT, AST). Also known to induce hypersensitivity reactions including anaphylaxis, erythema and bronchospasm.

Affected organisms

Humans and other mammals

Pathways

Not Available

Pharmacogenomic Effects/ADRs

Not Available

INTERACTIONS

Drug Interactions

Search

	Pegaspargase.	
Ancestim	The risk or severity of cytotoxicity can be increased when Ancestim is combined with Pegaspargase.	Approved, Investigational, Withdrawn
Anthrax immune globulin human	The risk or severity of adverse effects can be increased when Pegaspargase is combined with Anthrax immune globulin human.	Approved
Bacillus calmette-guerin substrain connaught live antigen	The risk or severity of adverse effects can be increased when Pegaspargase is combined with Bacillus calmette-guerin substrain connaught live antigen.	Approved, Investigational
Bacillus calmette-guerin substrain tice live antigen	The risk or severity of adverse effects can be increased when Pegaspargase is combined with Bacillus calmette-guerin substrain tice live antigen.	Approved
BCG vaccine	The therapeutic efficacy of BCG vaccine can be decreased when used in combination with Pegaspargase.	Investigational
Bevacizumab	Bevacizumab may increase the cardiotoxic activities of Pegaspargase.	Approved, Investigational
Cabazitaxel	The risk or severity of adverse effects can be increased when Cabazitaxel is combined with Pegaspargase.	Approved
Clostridium tetani toxoid antigen (formaldehyde inactivated)	The risk or severity of adverse effects can be increased when Pegaspargase is combined with Clostridium tetani toxoid antigen (formaldehyde inactivated).	Approved

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Food Interactions

Not Available

REFERENCES

General References

1. Graham ML: Pegaspargase: a review of clinical studies. Adv Drug Deliv Rev. 2003 Sep 26;55(10):1293-302. [PubMed:14499708]
2. Link [Link]

External Links

UniProt

P37595

Genbank

U00096

CHEMBL2108546

PharmGKB

PA164760860

RxList

RxList Drug Page

Drugs.com

Drugs.com Drug Page

Wikipedia

Pegaspargase

ATC Codes

L01XX24 — Pegaspargase

- L01XX — Other antineoplastic agents
- L01X — OTHER ANTINEOPLASTIC AGENTS
- L01 — ANTINEOPLASTIC AGENTS
- L — ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS

AHFS Codes

10:00.00 — Antineoplastic Agents

FDA label

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CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
0	Terminated	Treatment	Recurrent Cutaneous T-cell lymphoma / Refractory T-Cell Lymphoma / T-Cell Lymphomas	1
1	Active Not Recruiting	Treatment	Acute Lymphoblastic Leukaemias (ALL)	2
1	Completed	Treatment	Childhood B Acute Lymphoblastic Leukemia / Childhood T Acute Lymphoblastic Leukemia / Mature T-Cell and NK-Cell Non-Hodgkin Lymphoma / Recurrent Childhood Acute Lymphoblastic Leukemia / Recurrent Childhood Lymphoblastic Lymphoma	1

1	Terminated	Treatment	Acute Lymphoblastic Leukaemias (ALL) / Recurrent Pediatric ALL / Refractory Pediatric ALL / Relapsed Pediatric ALL	1
1	Terminated	Treatment	Leukemia, Lymphoblastic, Acute / Leukemia, Lymphoblastic, Acute, T Cell / Lymphoblastic Leukemia, Acute / Lymphoblastic Leukemia, Acute, Childhood	1
1	Withdrawn	Treatment	Acute Lymphoblastic Leukaemias (ALL)	1
1, 2	Completed	Treatment	Acute Lymphoblastic Leukaemias (ALL)	1
1, 2	Completed	Treatment	Recurrent Childhood Acute Lymphoblastic Leukemia	1

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PHARMACOECONOMICS

Manufacturers

Not Available

Packagers

Ben Venue Laboratories Inc.

Enzon Inc.

Dosage forms

Search

FORM	ROUTE	STRENGTH
Injection, solution	Intramuscular; Intravenous	750 [iU]/mL
Liquid	Intramuscular; Intravenous	750 unit
Solution	Intramuscular; Intravenous	750 unit
Injection, solution		750 U/ml

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Prices

Search

UNIT DESCRIPTION	COST	UNIT

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Patents

Not Available

PROPERTIES

State

Liquid

Experimental Properties

PROPERTY	VALUE	SOURCE
hydrophobicity	0.059	Not Available
isoelectric point	4.67	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

Not Available

External Descriptors

Not Available

TARGETS

1. L-asparagine

Kind
Small molecule

Organism
Human

Pharmacological action
Yes

Actions
Other/unknown

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. Douer D, Yampolsky H, Cohen LJ, Watkins K, Levine AM, Periclou AP, Avramis VI: Pharmacodynamics and safety of intravenous pegaspargase during remission induction in adults aged 55 years or younger with newly diagnosed acute lymphoblastic leukemia. Blood. 2007 Apr 1;109(7):2744-50. [PubMed:17132721]
4. Wetzler M, Sanford BL, Kurtzberg J, DeOliveira D, Frankel SR, Powell BL, Kolitz JE, Bloomfield CD, Larson RA: Effective asparagine depletion with pegylated asparaginase results in improved outcomes in adult acute lymphoblastic leukemia: Cancer and Leukemia Group B Study 9511. Blood. 2007 May 15;109(10):4164-7. Epub 2007 Jan 30. [PubMed:17264295]
5. Dinndorf PA, Gootenberg J, Cohen MH, Keegan P, Pazdur R: FDA drug approval summary: pegaspargase (oncaspar) for the first-line treatment of children with acute lymphoblastic leukemia (ALL). Oncologist. 2007 Aug;12(8):991-8. [PubMed:17766659]

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About

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