Aldesleukin

Targets (3) Enzymes (5) Biointeractions (10)

IDENTIFICATION

Name

Aldesleukin

Accession Number

DB00041 (BTD00082, BIOD00082)

Type

Biotech

Groups

Approved

Biologic Classification

Protein Based Therapies
Interleukin-based products

Description

Aldesleukin, a lymphokine, is produced by recombinant DNA technology using a genetically engineered E. coli strain containing an analog of the human interleukin-2 gene. Genetic engineering techniques were used to modify the human IL-2 gene, and the resulting expression clone encodes a modified human interleukin-2. This recombinant form differs from native interleukin-2 in the following ways: a) Aldesleukin is not glycosylated because it is derived from E. coli; b) the molecule has no N-terminal alanine; the codon for this amino acid was deleted during the genetic engineering procedure; c) the molecule has serine substituted for cysteine at amino acid position 125.

Protein structure

Protein chemical formula

$C_{690}H_{1115}N_{177}O_{202}S_6$

Protein average weight

15314.8 Da

Sequences

```
>Aldesleukin sequence
MAPTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCL
EEELKPLEEVLNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLN
RWITFCQSIISTLT
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Synonyms

125-L-serine-2-133-interleukin 2 (human reduced)

Interleukin-2 aldesleukin

Interleukin-2(2-133),125-ser

Recombinant interleukin-2 human

Prescription Products

Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END	
Proleukin	Injection	1.1 mg/1mL	Intravenous	Novartis	1992-05-06	2017-01-01	
Proleukin	Powder, for solution	22000000 unit	Intravenous	Novartis	1995-12-31	Not applicable	
Proleukin	Injection, powder, lyophilized, for solution	1.1 mg/1mL	Intravenous	Prometheus Laboratories	1992-05-05	Not applicable	

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Categories

Adjuvants, Immunologic

Amino Acids, Peptides, and Proteins

Anti-HIV Agents

Anti-Infective Agents

Antineoplastic Agents

Antineoplastic and Immunomodulating Agents

Biological Factors

Cytochrome P-450 CYP2E1 Inhibitors

Cytochrome P-450 CYP3A Inhibitors

Cytochrome P-450 CYP3A4 Inhibitors

Cytochrome P-450 Enzyme Inhibitors

Cytokines

Hypotensive Agents

Immunosuppressive Agents

Increased Lymphocyte Activation

Increased Lymphocyte Cell Production

Intercellular Signaling Peptides and Proteins

Interleukin-2

Interleukins

Lymphocyte Growth Factor

Lymphokines

Myelosuppressive Agents

Peptides

M89N0Q7EQR

CAS number

110942-02-4

PHARMACOLOGY

Indication

For treatment of adults with metastatic renal cell carcinoma.

Associated Conditions

High Risk Neuroblastoma

Metastatic Melanoma

Metastatic Renal Cell Carcinoma

Pharmacodynamics

Used to treat renal cell carcinoma, Aldesleukin induces the enhancement of lymphocyte mitogenesis and stimulation of long-term growth of human interleukin-2 dependent cell lines, the enhancement of lymphocyte cytotoxicity, the induction of killer cell (lymphokine-activated (LAK) and natural (NK)) activity; and the induction of interferon-gamma production. IL-2 is normally produced by the body, secreted by T cells, and stimulates growth and differentiation of T cell response. It can be used in immunotherapy to treat cancer. It enhances the ability of the immune system to kill tumor cells and may interfere with blood flow to the tumor.

Mechanism of action

Aldesleukin binds to the IL-2 receptor which leads to heterodimerization of the cytoplasmic domains of the IL-2R beta and gamma(c) chains, activation of the tyrosine kinase Jak3, and phosphorylation of tyrosine residues on the IL-2R beta chain. These events led to the creation of an activated receptor complex, to which various cytoplasmic signaling molecules are recruited and become substrates for regulatory enzymes (especially tyrosine kinases) that are associated with the receptor. These events stimulate growth and differentiation of T cells.

A Interleukin-2 receptor subunit beta

A	Interleukin-2 receptor subunit alpha	
	agonist modulator	
	Human	
A	Cytokine receptor common subunit gamma	
	agonist	
	Human	

Absorption

Not Available

Volume of distribution

0.18 l/kg

Protein binding

Not Available

Metabolism

Not Available

Route of elimination

The pharmacokinetic profile of Proleukin is characterized by high plasma concentrations following a short IV infusion, rapid distribution into the extravascular space and elimination from the body by metabolism in the kidneys with little or no bioactive protein excreted in the urine. Following the initial rapid organ distribution, the primary route of clearance of circulating proleukin is the kidney. Greater than 80% of the amount of Proleukin distributed to plasma, cleared from the circulation and presented to the kidney is metabolized to amino acids in the cells lining the proximal convoluted tubules.

Half life

13 min-85 min

Clearance

Not Available

Affected organisms

Humans and other mammals

Pathways

Not Available

Pharmacogenomic Effects/ADRs

Not Available

INTERACTIONS

Drug Interactions

ALL DRUGS | APPROVED | VET APPROVED | NUTRACEUTICAL | ILLICIT | WITHDRAWN | INVESTIGATIONAL | EXPERIMENTAL

Search

DRUG	INTERACTION
(R)-warfarin	The metabolism of (R)-warfarin can be decreased when combined with Aldesleukin.
(S)-Warfarin	The metabolism of (S)-Warfarin can be decreased when combined with Aldesleukin.
2-Methoxyethanol	The risk or severity of adverse effects can be increased when Aldesleukin is combined with 2-Methoxyethanol.
3,5-diiodothyropropionic acid	The metabolism of 3,5-diiodothyropropionic acid can be decreased when combined with Aldesleukin.
4-hydroxycoumarin	The metabolism of 4-hydroxycoumarin can be decreased when combined with Aldesleukin.
5-androstenedione	The metabolism of 5-androstenedione can be decreased when combined with Aldesleukin.
6-O-benzylguanine	The metabolism of 6-O-benzylguanine can be decreased when combined with Aldesleukin.

	a higher serum level.
Abatacept	The risk or severity of adverse effects can be increased when Aldesleukin is combined with Abatacept.

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Food Interactions

Not Available

REFERENCES

Synthesis Reference

Hans-Ake Fabricius, Roland Stahn, "Serum-free and mitogen-free T-cell growth factor and process for making same." U.S. Patent US4464355, issued May, 1971.
US4464355

General References

Not Available

External Links

UniProt

P60569

Genbank

M11144

PubChem Substance

46508054

ChEMBL

CHEMBL1201438

Therapeutic Targets Database

DAP001099

PharmGKB

Drugs.com

Drugs.com Drug Page

Wikipedia

Aldesleukin

ATC Codes

L03AC01 — Aldesleukin

- L03AC — Interleukins
- L03A — IMMUNOSTIMULANTS
- L03 — IMMUNOSTIMULANTS
- L — ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS

AHFS Codes

10:00.00 — Antineoplastic Agents

CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
0	Active Not Recruiting	Treatment	Melanoma (Skin) / Skin Cancers	1
0	Completed	Treatment	Melanoma (Skin) / Renal Cancers	1
0	Completed	Treatment	Renal Cancers	1
0	Recruiting	Treatment	Metastatic Non-Small Cell Lung Cancer	1
1	Active Not Recruiting	Treatment	Chronic Graft Versus Host Disease	1
1	Active Not Recruiting	Treatment	Lymphoma, B-Cell / Malignant Lymphomas	1
1	Active Not Recruiting	Treatment	Melanoma (Skin)	1

	Recruiting			
1	Completed	Treatment	Anaplastic Astrocytoma (AA) / Anaplastic Ependymoma / Anaplastic Meningioma / Anaplastic Oligodendroglioma (AO) / Brain Stem Gliomas / Ependymoblastoma / Giant Cell Glioblastoma / Glioblastomas / Gliosarcoma / Grade III Meningioma / Meningeal Hemangiopericytoma / Mixed Gliomas / Neoplasms, Brain / Pineal Gland Astrocytoma	1

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PHARMACOECONOMICS

Manufacturers

Not Available

Packagers

Bayer Healthcare

Chiron Corp.

Novartis AG

Physicians Total Care Inc.

Prometheus Laboratories Inc.

Dosage forms

Search

FORM	ROUTE	STRENGTH
Injection	Intravenous	1.1 mg/1mL
Injection, powder, lyophilized, for solution	Intravenous	1.1 mg/1mL
Powder, for solution	Intravenous	22000000 unit

Showing 1 to 3 of 3 entries

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UNIT DESCRIPTION	COST	UNIT
Proleukin 22 million unit vial	1092.34USD	each
Proleukin 22000000 unit Solution Vial	976.66USD	vial

Showing 1 to 2 of 2 entries

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Patents

Not Available

PROPERTIES

State

Liquid

Experimental Properties

PROPERTY	VALUE	SOURCE
hydrophobicity	-0.192	Not Available
isoelectric point	7.31	Not Available

TAXONOMY

Description

Not Available

Kingdom

Organic Compounds

Super Class

Organic Acids

Amino Acids, Peptides, and Analogues

Direct Parent

Peptides

Alternative Parents

Not Available

Substituents

Not Available

Molecular Framework

Not Available

External Descriptors

Not Available

TARGETS

1. Interleukin-2 receptor subunit beta

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Agonist Modulator

General Function

transduces the mitogenic signals of IL2.

Gene Name

IL2RB

Uniprot ID

P14784

Uniprot Name

Interleukin-2 receptor subunit beta

Molecular Weight

61116.59 Da

References

1. Stauber DJ, Debler EW, Horton PA, Smith KA, Wilson IA: Crystal structure of the IL-2 signaling complex: paradigm for a heterotrimeric cytokine receptor. Proc Natl Acad Sci U S A. 2006 Feb 21;103(8):2788-93. Epub 2006 Feb 13. [PubMed:16477002]
2. Steppan S, Eckart MR, Bajsarowicz K, Sternberg LR, Greve JM, Cassell DJ: Reduced secondary cytokine induction by BAY 50-4798, a high-affinity receptor-specific interleukin-2 analog. J Interferon Cytokine Res. 2006 Mar;26(3):171-8. [PubMed:16542139]
3. Cornish GH, Sinclair LV, Cantrell DA: Differential regulation of T-cell growth by IL-2 and IL-15. Blood. 2006 Jul 15;108(2):600-8. Epub 2006 Mar 28. [PubMed:16569767]
4. Lee KD, Chen HW, Chen CC, Shih YC, Liu HK, Cheng ML: Construction and characterization of a novel fusion protein consisting of anti-CD3 antibody fused to recombinant interleukin-2. Oncol Rep. 2006 May;15(5):1211-6. [PubMed:16596189]
5. Maclennan C, Hutchinson P, Holdsworth S, Bardin PG, Freezer NJ: Airway inflammation in asymptomatic children with episodic wheeze. Pediatr Pulmonol. 2006 Jun;41(6):577-83. [PubMed:16617454]
6. Chen X, Ji ZL, Chen YZ: TTD: Therapeutic Target Database. Nucleic Acids Res. 2002 Jan 1;30(1):412-5. [PubMed:11752352]

2. Interleukin-2 receptor subunit alpha

Kind

Protein

Organism

Human

Agonist Modulator

General Function

Interleukin-2 receptor activity

Specific Function

Receptor for interleukin-2. The receptor is involved in the regulation of immune tolerance by controlling regulatory T cells (TREGs) activity. TREGs suppress the activation and expansion of autorea...

Gene Name

IL2RA

Uniprot ID

P01589

Uniprot Name

Interleukin-2 receptor subunit alpha

Molecular Weight

30818.915 Da

References

1. Waldmann TA: Anti-Tac (daclizumab, Zenapax) in the treatment of leukemia, autoimmune diseases, and in the prevention of allograft rejection: a 25-year personal odyssey. J Clin Immunol. 2007 Jan;27(1):1-18. Epub 2007 Jan 11. [PubMed:17216565]
2. Recchia F, Cesta A, Rea S: Low dose interleukin-2 and 13-cis-retinoic acid as maintenance therapy in patients with solid tumors responsive to chemotherapy. J Exp Clin Cancer Res. 2003 Dec;22(4 Suppl):135-43. [PubMed:16767920]
3. Waldmann TA: Daclizumab (anti-Tac, Zenapax) in the treatment of leukemia/lymphoma. Oncogene. 2007 May 28;26(25):3699-703. [PubMed:17530023]
4. Vlad G, Ho EK, Vasilescu ER, Fan J, Liu Z, Cai JW, Jin Z, Burke E, Deng M, Cadeiras M, Cortesini R, Itescu S, Marboe C, Mancini D, Suciu-Foca N: Anti-CD25 treatment and FOXP3-positive regulatory T cells in heart transplantation. Transpl Immunol. 2007 Jul;18(1):13-21. Epub 2007 Apr 2. [PubMed:17584597]
5. Liu BY, Zhu P, Luo HB, Fu N: [Screening of short peptides binding to cell surface interleukin-2 receptor alpha chain]. Nan Fang Yi Ke Da Xue Xue Bao. 2006 Jul;26(7):971-4. [PubMed:16864089]
6. Chen X, Ji ZL, Chen YZ: TTD: Therapeutic Target Database. Nucleic Acids Res. 2002 Jan 1;30(1):412-5. [PubMed:11752352]
7. Ouyang Y, Kaminski NE: Phospholipase A2 inhibitors p-bromophenacyl bromide and arachidonyl trifluoromethyl ketone suppressed interleukin-2 (IL-2) expression in murine primary splenocytes. Arch Toxicol. 1999 Feb;73(1):1-6. [PubMed:10207608]

Protein

Organism

Human

Pharmacological action

Yes

Actions

Agonist

General Function

Interleukin-2 binding

Specific Function

Common subunit for the receptors for a variety of interleukins.

Gene Name

IL2RG

Uniprot ID

P31785

Uniprot Name

Cytokine receptor common subunit gamma

Molecular Weight

42286.68 Da

References

1. Stauber DJ, Debler EW, Horton PA, Smith KA, Wilson IA: Crystal structure of the IL-2 signaling complex: paradigm for a heterotrimeric cytokine receptor. Proc Natl Acad Sci U S A. 2006 Feb 21;103(8):2788-93. Epub 2006 Feb 13. [PubMed:16477002]
2. Shibata F, Toma T, Wada T, Inoue M, Tone Y, Ohta K, Kasahara Y, Sano F, Kimura M, Ikeno M, Koizumi S, Yachie A: Skin infiltration of CD56(bright) CD16(-) natural killer cells in a case of X-SCID with Omenn syndrome-like manifestations. Eur J Haematol. 2007 Jul;79(1):81-5. [PubMed:17598841]
3. Fonseca SG, Reis MM, Coelho V, Nogueira LG, Monteiro SM, Mairena EC, Bacal F, Bocchi E, Guilherme L, Zheng XX, Liew FY, Higuchi ML, Kalil J, Cunha-Neto E: Locally produced survival cytokines IL-15 and IL-7 may be associated to the predominance of CD8+ T cells at heart lesions of human chronic Chagas disease cardiomyopathy. Scand J Immunol. 2007 Aug-Sep;66(2-3):362-71. [PubMed:17635814]
4. Blank RB, Lamb EW, Tocheva AS, Crow ET, Lim KC, McKerrow JH, Davies SJ: The common gamma chain cytokines interleukin (IL)-2 and IL-7 indirectly modulate blood fluke development via effects on CD4+ T cells. J Infect Dis. 2006 Dec 1;194(11):1609-16. Epub 2006 Oct 23. [PubMed:17083048]

ENZYMES

1. Prostaglandin G/H synthase 2

Kind

Protein

Organism

Human

Pharmacological action

Unknown

Actions

Inducer

General Function

Prostaglandin-endoperoxide synthase activity

Specific Function

Converts arachidonate to prostaglandin H2 (PGH2), a committed step in prostanoid synthesis. Constitutively expressed in some tissues in physiological conditions, such as the endothelium, kidney and...

Gene Name

PTGS2

Uniprot ID

P35354

Uniprot Name

Prostaglandin G/H synthase 2

Molecular Weight

68995.625 Da

2. Hamada T, Tsuchihashi S, Avanesyan A, Duarte S, Moore C, Busuttil RW, Coito AJ: Cyclooxygenase-2 deficiency enhances Th2 immune responses and impairs neutrophil recruitment in hepatic ischemia/reperfusion injury. J Immunol. 2008 Feb 1;180(3):1843-53. [PubMed:18209082]

2. Cytosolic phospholipase A2

Kind

Protein

Organism

Human

Pharmacological action

Unknown

Actions

Inducer

General Function

Phospholipase a2 activity

Specific Function

Selectively hydrolyzes arachidonyl phospholipids in the sn-2 position releasing arachidonic acid. Together with its lysophospholipid activity, it is implicated in the initiation of the inflammatory...

Gene Name

PLA2G4A

Uniprot ID

P47712

Uniprot Name

Cytosolic phospholipase A2

Molecular Weight

85238.2 Da

References

3. Cytochrome P450 3A4

Kind

Protein

Organism

Human

Pharmacological action

Unknown

Actions

Inhibitor

General Function

Vitamin d3 25-hydroxylase activity

Specific Function

Cytochromes P450 are a group of heme-thiolate monooxygenases. In liver microsomes, this enzyme is involved in an NADPH-dependent electron transport pathway. It performs a variety of oxidation react...

Gene Name

CYP3A4

Uniprot ID

P08684

Uniprot Name

Cytochrome P450 3A4

Molecular Weight

57342.67 Da

References

1. Elkahwaji J, Robin MA, Berson A, Tinel M, Letteron P, Labbe G, Beaune P, Elias D, Rougier P, Escudier B, Duvillard P, Pessayre D: Decrease in hepatic cytochrome P450 after interleukin-2 immunotherapy. Biochem Pharmacol. 1999 Apr 15;57(8):951-4. [PubMed:10086330]

4. Xanthine dehydrogenase/oxidase

Kind

Protein

Organism

Human

Pharmacological action

Unknown

Actions

Inducer

General Function

Xanthine oxidase activity

Specific Function

Key enzyme in purine degradation. Catalyzes the oxidation of hypoxanthine to xanthine. Catalyzes the oxidation of xanthine to uric acid. Contributes to the generation of reactive oxygen species. Ha...

Gene Name

XDH

Uniprot ID

P47989

Uniprot Name

Xanthine dehydrogenase/oxidase

Molecular Weight

146422.99 Da

References

1. Faggioni R, Allavena P, Cantoni L, Carelli M, Demitri MT, Delgado R, Gatti S, Gnocchi P, Isetta AM, Paganin C, et al.: Mechanisms of interleukin-2-induced hydrothoraxy in mice: protective effect of endotoxin tolerance and dexamethasone and possible role of reactive oxygen intermediates. J Immunother Emphasis Tumor Immunol. 1994 Apr;15(3):194-201. [PubMed:8032542]

Kind

Protein

Organism

Human

Pharmacological action

Unknown

Actions

Inhibitor

General Function

Steroid hydroxylase activity

Specific Function

Metabolizes several precarcinogens, drugs, and solvents to reactive metabolites. Inactivates a number of drugs and xenobiotics and also bioactivates many xenobiotic substrates to their hepatotoxic ...

Gene Name

CYP2E1

Uniprot ID

P05181

Uniprot Name

Cytochrome P450 2E1

Molecular Weight

56848.42 Da

References

1. Elkahwaji J, Robin MA, Berson A, Tinel M, Letteron P, Labbe G, Beaune P, Elias D, Rougier P, Escudier B, Duvillard P, Pessayre D: Decrease in hepatic cytochrome P450 after interleukin-2 immunotherapy. Biochem Pharmacol. 1999 Apr 15;57(8):951-4. [PubMed:10086330]

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