Blinatumomab

Targets (2) Biointeractions (2)

IDENTIFICATION

Name

Blinatumomab

Accession Number

DB09052

Type

Biotech

Groups

Approved, Investigational

Biologic Classification

Protein Based Therapies
Monoclonal antibody (mAb)

Description

Blinatumomab is a BiTE-class (bi-specific T-cell engagers) constructed monoclonal antibody indicated for the treatment of Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). Blinatumomab is manufactured by Amgen Inc. and marketed under the brand Blincyto™. A full treatment regimen consisting of two cycles of four weeks each, is priced at $178 000 USD. Blinatumomab was approved in December 2014 under the FDA's accelerated approval program, which allows approval of a drug to treat a serious or life-threatening disease based on clinical data showing the drug has an effect on a surrogate endpoint reasonably likely to predict clinical benefit to patients.

Protein structure

Protein chemical formula

$C_{2367}H_{3577}N_{649}O_{772}S_{19}$

Protein average weight

54100.0 Da

Sequences

```
>single chain variable fragment fusion protein
DIQLTQSPASLAVSLGQRATISCKASQSVDYDGDSYLNWYQQIPGQPPKLLIYDASNLVS
GIPPRFSGSGSGTDFTLNIHPVEKVDAATYHCQQSTEDPWTFGGGTKLEIKGGGGSGGGG
SGGGGSQVQLQQSGAELVRPGSSVKISCKASGYAFSSYWMNWVKQRPGQGLEWIGQIWPG
DGDTNYNGKFKGKATLTADESSSTAYMQLSSLASEDSAVYFCARRETTTVGRYYYAMDYW
GQGTTVTVSSGGGGSDIKLQQSGAELARPGASVKMSCKTSGYTFTRYTMHWVKQRPGQGL
EWIGYINPSRGYTNYNQKFKDKATLTTDKSSSTAYMQLSSLTSEDSAVYYCARYYDDHYC
LDYWGQGTTLTVSSVEGGSGGSGGSGGSGGVDDIQLTQSPAIMSASPGEKVTMTCRASSS
VSYMNWYQQKSGTSPKRWIYDTSKVASGVPYRFSGSGSGTSYSLTISSMEAEDAATYYCQ
QWSSNPLTFGAGTKLELKHHHHHH
```

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Synonyms

Not Available

External IDs

AMG103 / MEDI 538 / MEDI-538 / MEDI538 / MT 103 / MT-103 / MT103

Prescription Products

Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END		
Blincyto	Powder, for solution	38.5 mcg	Intravenous	Amgen	2016-03-17	Not applicable		
Blincyto	Kit	12.5 ug/1mL	Intravenous	Amgen	2014-12-18	Not applicable		

Categories

Amides

Amino Acids, Peptides, and Proteins

Antibodies

Antibodies, Monoclonal

Antineoplastic Agents

Antineoplastic and Immunomodulating Agents

Bispecific CD19-directed CD3-directed T Cell Engager

Blood Proteins

CD19-directed Antibody Interactions

CD3 Receptor Agonists

CD3-directed Antibody Interactions

Globulins

Immunoglobulins

Immunoproteins

Immunosuppressive Agents

Monoterpenes

Myelosuppressive Agents

Norbornanes

Proteins

Recombinant Fusion Proteins

Serum Globulins

Sulfones

Sulfur Compounds

Terpenes

UNII

4FR53SIF3A

853426-35-4

PHARMACOLOGY

Indication

Indicated for the treatment of Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

Associated Conditions

Refractory B cell precursor Acute lymphoblastic leukemia

Relapsed B cell precursor Acute lymphoblastic leukemia

Pharmacodynamics

Not Available

Mechanism of action

Blinatumomab is a bispecific CD19-directed CD3 T-cell engager that binds to CD19 expressed on the surface of cells of B-lineage origin and CD3 expressed on the surface of T cells. It activates endogenous T cells by connecting CD3 in the T-cell receptor (TCR) complex with CD19 on benign and malignant B cells. Blinatumomab mediates the formation of a synapse between the T cell and the tumor cell, upregulation of cell adhesion molecules, production of cytolytic proteins, release of inflammatory cytokines, and proliferation of T cells, which result in redirected lysis of CD19+ cells.

(A) B-lymphocyte antigen CD19	
activator	
Human	
(A) T-cell surface glycoprotein CD3 delta chain	
activator	
Human	

Absorption

Not Available

Volume of distribution

Protein binding

Not Available

Metabolism

The metabolic pathway of blinatumomab has not been characterized. Like other protein therapeutics, blinatumomab is expected to be degraded into small peptides and amino acids via catabolic pathways.

Route of elimination

Not Available

Half life

2.11 hours, standard deviation 1.42.

Clearance

2.92 L/hour, standard deviation 2.83.

Toxicity

- Cytokine Release Syndrome (CRS), which may be life-threatening or fatal, occurred in patients receiving blinatumomab. Interrupt or discontinue blinatumomab as recommended.
- Neurological toxicities, which may be severe, life-threatening, or fatal, occurred in patients receiving blinatumomab. Interrupt or discontinue blinatumomab as recommended.
- In patients receiving blinatumomab in clinical trials, serious infections such as sepsis, pneumonia, bacteremia, opportunistic infections, and catheter-site infections were observed in approximately 25% of patients, some of which were life-threatening or fatal.
- Tumor lysis syndrome (TLS), which may be life-threatening or fatal, has been observed in patients.
- Neutropenia and febrile neutropenia, including life-threatening cases, have been observed in patients.
- Treatment with blinatumomab was associated with transient elevations in liver enzymes.
- Cranial magnetic resonance imaging (MRI) changes showing leukoencephalopathy have been observed in patients receiving blinatumomab, especially in patients with prior treatment with cranial irradiation and antileukemic chemotherapy (including systemic high-dose methotrexate or intrathecal cytarabine).

Affected organisms

Humans and other mammals

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 risk or severity of bleeding can be increased when (R)-warfarin is combined with Blinatumomab.
(S)-Warfarin	The risk or severity of bleeding can be increased when (S)-Warfarin is combined with Blinatumomab.
2-Methoxyethanol	The risk or severity of adverse effects can be increased when 2-Methoxyethanol is combined with Blinatumomab.
4-hydroxycoumarin	The risk or severity of bleeding can be increased when 4-hydroxycoumarin is combined with Blinatumomab.
9-(N-methyl-L-isoleucine)-cyclosporin A	The risk or severity of adverse effects can be increased when Blinatumomab is combined with 9-(N-methyl-L-isoleucine)-cyclosporin A.
Abatacept	The risk or severity of adverse effects can be increased when Abatacept is combined with Blinatumomab.
Abciximab	The risk or severity of adverse effects can be increased when Abciximab is combined with Blinatumomab.
Abetimus	The risk or severity of adverse effects can be increased when Abetimus is combined with Blinatumomab.
Abituzumab	The risk or severity of adverse effects can be increased when Blinatumomab is combined with Abituzumab.
Acenocoumarol	The risk or severity of bleeding can be increased when Acenocoumarol is combined with Blinatumomab.

Food Interactions

Not Available

REFERENCES

General References

1. Zugmaier G, Klinger M, Schmidt M, Subklewe M: Clinical overview of anti-CD19 BiTE((R)) and ex vivo data from anti-CD33 BiTE((R)) as examples for retargeting T cells in hematologic malignancies. Mol Immunol. 2015 Oct;67(2 Pt A):58-66. doi: 10.1016/j.molimm.2015.02.033. Epub 2015 Apr 13. [PubMed:25883042]
2. Garber K: Bispecific antibodies rise again. Nat Rev Drug Discov. 2014 Nov;13(11):799-801. doi: 10.1038/nrd4478. [PubMed:25359367]

External Links

KEGG Drug

D09325

PubChem Substance

347910400

ChEMBL

CHEMBL1742992

Drugs.com

Drugs.com Drug Page

Wikipedia

Blinatumomab

ATC Codes

L01XC19 — Blinatumomab

- L01XC — Monoclonal antibodies
- L01X — OTHER ANTINEOPLASTIC AGENTS
- L01 — ANTINEOPLASTIC AGENTS
- L — ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS

AHFS Codes

10:00.00 — Antineoplastic Agents

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CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
0	Recruiting	Treatment	Acute Lymphoblastic Leukaemias (ALL) / B-cell Non Hodgkin's Lymphoma / Pre B-Cell Acute Lymphoblastic Leukaemia	1
0	Recruiting	Treatment	Multiple Myeloma (MM)	1
1	Completed	Treatment	Non-Hodgkin's Lymphoma, Relapsed	1
1	Recruiting	Treatment	B Acute Lymphoblastic Leukemia / B Acute Lymphoblastic Leukemia With t(9;22)(q34.1;q11.2); BCR-ABL1 / CD19-Positive Neoplastic Cells Present / Mixed Phenotype Acute Leukemia (MPAL) / Mixed Phenotype Acute Leukemia With t(9;22)(q34.1;q11.2); BCR-ABL1 / Recurrent B Acute Lymphoblastic Leukemia / Refractory B Acute Lymphoblastic Leukemia	1

			Intermediate Between Diffuse Large B-Cell Lymphoma and Classical Hodgkin Lymphoma / CD19 Positive / Mediastinal Lymphoma / Recurrent Adult Burkitt Lymphoma / Recurrent B-Cell Lymphoma, Unclassifiable, With Features Intermediate Between Diffuse Large B-Cell Lymphoma and Classic Hodgkin Lymphoma / Recurrent B-Cell Lymphoma, Unclassifiable, With Features Intermediate Between Diffuse Large B-Cell Lymphoma and Classical Hodgkin Lymphoma / Recurrent Burkitt Lymphoma / Recurrent Diffuse Large B-Cell Lymphoma / Recurrent Grade 1 Follicular Lymphoma / Recurrent Grade 2 Follicular Lymphoma / Recurrent Grade 3 Follicular Lymphoma / Recurrent Mantle Cell Lymphoma / Recurrent Marginal Zone Lymphoma / Recurrent Mediastinal Lymphoma / Recurrent Non-Hodgkin Lymphoma / Recurrent Small Lymphocytic Lymphoma / Refractory B-Cell Lymphoma, Unclassifiable, With Features Intermediate Between Diffuse Large B-Cell Lymphoma and Classic Hodgkin Lymphoma / Refractory B-Cell Lymphoma, Unclassifiable, With Features Intermediate Between Diffuse Large B-Cell Lymphoma and Classical Hodgkin Lymphoma / Refractory Burkitt Lymphoma / Refractory Diffuse Large B Cell Lymphoma / Refractory Follicular Lymphoma / Refractory Mantle Cell Lymphoma / Refractory Marginal Zone Lymphoma / Refractory Mediastinal Lymphoma / Refractory Non-Hodgkin's lymphoma / Refractory Small Lymphocytic Lymphoma	
1	Recruiting	Treatment	Leukemia, B-Cell / Lymphoma, B-Cell	1
1	Recruiting	Treatment	Lymphoma, Large B-Cell, Diffuse (DLBCL)	1
1	Recruiting	Treatment	Non-Hodgkin's Lymphoma (NHL)	1
1	Recruiting	Treatment	Relapsed or Refractory Diffuse Large B Cell Lymphoma (DLBCL)	1
1	Withdrawn	Treatment	Lymphoma, B-Cell / Non-Hodgkin's Lymphoma (NHL)	1

Showing 1 to 10 of 48 entries

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PHARMACOECONOMICS

Manufacturers

Not Available

Dosage forms

Search

FORM	ROUTE	STRENGTH
Kit	Intravenous	12.5 ug/1mL
Powder, for solution	Intravenous	38.5 mcg

Showing 1 to 2 of 2 entries

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Prices

Not Available

Patents

Search

PATENT NUMBER	PEDIATRIC EXTENSION	APPROVED	EXPIRES (ESTIMATED)	
US7235641	No	2007-06-26	2023-12-22	
US7575923	No	2009-08-18	2018-04-21	
US7635472	No	2009-12-22	2023-05-31	
US8247194	No	2012-08-21	2024-05-05	
US20120328618	No	2009-10-27	2029-10-27	
US20130323247	No	2008-11-07	2028-11-07	

Showing 1 to 6 of 6 entries

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PROPERTIES

State

Solid

Experimental Properties

Not Available

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

TARGETS

1. B-lymphocyte antigen CD19

Protein

Organism

Human

Pharmacological action

Yes

Actions

Activator

General Function

Receptor signaling protein activity

Specific Function

Assembles with the antigen receptor of B-lymphocytes in order to decrease the threshold for antigen receptor-dependent stimulation.

Gene Name

CD19

Uniprot ID

P15391

Uniprot Name

B-lymphocyte antigen CD19

Molecular Weight

61127.985 Da

References

1. Zugmaier G, Klinger M, Schmidt M, Subklewe M: Clinical overview of anti-CD19 BiTE((R)) and ex vivo data from anti-CD33 BiTE((R)) as examples for retargeting T cells in hematologic malignancies. Mol Immunol. 2015 Oct;67(2 Pt A):58-66. doi: 10.1016/j.molimm.2015.02.033. Epub 2015 Apr 13. [PubMed:25883042]

2. T-cell surface glycoprotein CD3 delta chain

Kind

Protein

Pharmacological action

Yes

Actions

Activator

General Function

Transmembrane signaling receptor activity

Specific Function

The CD3 complex mediates signal transduction.

Gene Name

CD3D

Uniprot ID

P04234

Uniprot Name

T-cell surface glycoprotein CD3 delta chain

Molecular Weight

18929.38 Da

References

1. Zugmaier G, Klinger M, Schmidt M, Subklewe M: Clinical overview of anti-CD19 BiTE((R)) and ex vivo data from anti-CD33 BiTE((R)) as examples for retargeting T cells in hematologic malignancies. Mol Immunol. 2015 Oct;67(2 Pt A):58-66. doi: 10.1016/j.molimm.2015.02.033. Epub 2015 Apr 13. [PubMed:25883042]

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Support

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