Emicizumab

Targets (2) Biointeractions (2)

IDENTIFICATION

Name

Emicizumab

Accession Number

DB13923

Type

Biotech

Groups

Approved, Investigational

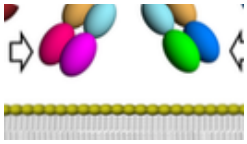
Biologic Classification

Protein Based Therapies
Monoclonal antibody (mAb)

Description

Emicizumab is a humanized recombinant monoclonal antibody that mimics the function of the coagulation Factor VIII and it has the capacity to bind simultaneously to activated Factor IX and Factor X. The ability of Emicizumab to bind to all these three different factors allows it to overcome immunogenicity and unstable hemostatic efficacy produced by previous Factor VII agents. Emicizumab was originated as an improved form of hBS23 and it was approved on November 16, 2017, for the treatment of hemophilia A with factor VIII inhibitors.[1, 6] It was created by Chugai Pharmaceuticals Co. Ltd. and co-developed with Roche and Genentech.[5]

Protein structure



Protein chemical formula

C_{6434}-H_{9940}-N_{1724}-O_{2047}-S_{45}

Protein average weight

145.6 Da

Sequences

Not Available

Synonyms

emicizumab-kxwh

External IDs

ACE 910 / ACE-910 / ACE910

Prescription Products

Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END		
Hemlibra	Injection, solution	30 mg/mL	Subcutaneous	Genentech, Inc.	2017-11-16	Not applicable		
Hemlibra	Injection, solution	150 mg/mL	Subcutaneous	Genentech, Inc.	2017-11-16	Not applicable		
Hemlibra	Injection, solution	150 mg/mL	Subcutaneous	Genentech, Inc.	2017-11-16	Not applicable		
Hemlibra	Injection, solution	150 mg/mL	Subcutaneous	Genentech, Inc.	2017-11-16	Not applicable		

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Categories

Antibodies

Antibodies, Monoclonal

Blood Proteins

Globulins

Immunoglobulins

Immunoproteins

Proteins

Serum Globulins

UNII

7NL2E3F6K3

CAS number

1610943-06-0

PHARMACOLOGY

Indication

The main function of Emicizumab is the prevention of bleeding episodes. Thus, Emicizumab is approved for the routine prophylaxis of patients with hemophilia A that present Factor VIII inhibitors. Hemophilia A is a deficiency of coagulation Factor VIII which causes a serious bleeding disorder. The standard treatment is done with the administration of recombinant or serum-deriver Factor VIII which induces the formation of anti-factor VIII alloantibodies (Factor VIII inhibitors) and renders the standard treatment ineffective.[2]

Structured Indications

Hemophilia A

Pharmacodynamics

Emicizumab mimics the function of coagulation factor VIII, therefore it binds to the activated form of Factor IX (Factor IXa). This binding forms a complex that will later bind to the X factor of the coagulation factor. [4] The ability of Emicizumab to interact with both factors (Factor IXa and Factor X) activates the coagulation cascade that will subsequently lead to the segmentation of fibrinogen into fibrin and the formation of blood clots. [3] The effect of Emicizumab is translated into the restoration of the blood coagulation process and, therefore, in the reduction of

[10] In addition, the unique bispecific structure of Emicizumab prevents the formation of Factor VIII inhibitors or their effect. [2]

Mechanism of action

Emicizumab exerts its action by performing the function of the coagulation Factor VIII without presenting a structural homology.[7] It presents a dual specificity which allows it to bind to both the Factor IXa and the Factor X, performing the required bridgning activity for the launch of the coagulation cascade.[2]

A Coagulation factor IX	
cofactor	
Human	
A Coagulation factor X	
activator	
Human	

Absorption

Subcutaneous administration of Emicizumab presents a very high bioavailability ranging from 80.4% to 93.1% when administered subcutaneously in a dose of 1 mg/kg.[FDA Label] In clinical trials, at the same dose, Emicizumab presented a linear exposure which concentration peaked 1-2 weeks after administration and presented a profile framed by a Cmax of 5.92 mcg/ml and a AUC of 304 mcg day/ml.[1]

Volume of distribution

The apparent volume of distribution is 11.4L and there are reports indicating that this value can increased with increasing body weight.[FDA Label]

Protein binding

No information available

Metabolism

No information available

Route of elimination

The elimination of Emicizumab was monophasic in clinical trials.[1]

Clearance

The apparent clearance is 0.24 L/day and there are reports indicating that this value can increased with increasing body weight.[FDA Label]

Toxicity

The administration of Emicizumab has reported cases of microangiopathy and thrombotic events with concomitant use of activated prothrombin complex concentrate at doses higher of 100 U/kg/24 hours. There are also reports of injection site reaction, headaches and arthralgia.[8]

Affected organisms

Humans and other mammals

Pathways

Not Available

Pharmacogenomic Effects/ADRs

Not Available

INTERACTIONS

Drug Interactions

Search

DRUG	INTERACTION	DRUG GROUP
Anthrax immune globulin human	The therapeutic efficacy of Anthrax immune globulin human can be decreased when used in combination with Emicizumab.	Approved
Anti-inhibitor coagulant complex	The risk or severity of thrombotic microangiopathy can be increased when Emicizumab is combined with Anti-inhibitor coagulant complex.	Approved, Investigational
Antihemophilic factor, human recombinant	The risk or severity of hypercoagulability can be increased when Emicizumab is combined with Antihemophilic factor, human recombinant.	Approved, Investigational

Bacillus calmette-guerin substrain connaught live antigen	The therapeutic efficacy of Bacillus calmette-guerin substrain connaught live antigen can be decreased when used in combination with Emicizumab.	Approved, Investigational
Bacillus calmette-guerin substrain tice live antigen	The therapeutic efficacy of Bacillus calmette-guerin substrain tice live antigen can be decreased when used in combination with Emicizumab.	Approved
BCG vaccine	The therapeutic efficacy of BCG vaccine can be decreased when used in combination with Emicizumab.	Investigational
Belimumab	The risk or severity of adverse effects can be increased when Emicizumab is combined with Belimumab.	Approved
Clostridium tetani toxoid antigen (formaldehyde inactivated)	The therapeutic efficacy of Clostridium tetani toxoid antigen (formaldehyde inactivated) can be decreased when used in combination with Emicizumab.	Approved
Corynebacterium diphtheriae toxoid antigen (formaldehyde inactivated)	The therapeutic efficacy of Corynebacterium diphtheriae toxoid antigen (formaldehyde inactivated) can be decreased when used in combination with Emicizumab.	Approved
G17DT	The therapeutic efficacy of G17DT can be decreased when used in combination with Emicizumab.	Investigational

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Food Interactions

Not Available

REFERENCES

General References

1. Uchida N, Sambe T, Yoneyama K, Fukazawa N, Kawanishi T, Kobayashi S, Shima M: A first-in-human phase 1 study of ACE910, a novel factor VIII-mimetic bispecific antibody, in healthy subjects. Blood. 2016 Mar 31;127(13):1633-41. doi: 10.1182/blood-2015-06-650226. Epub 2015 Dec 1. [PubMed:26626991]
2. Shima M, Hanabusa H, Taki M, Matsushita T, Sato T, Fukutake K, Fukazawa N, Yoneyama K, Yoshida H, Nogami K: Factor VIII-Mimetic Function of Humanized Bispecific Antibody in Hemophilia A. N Engl J Med. 2016 May 26;374(21):2044-53. doi: 10.1056/NEJMoa1511769. [PubMed:27223146]
3. Chavin SI: Factor VIII: structure and function in blood clotting. Am J Hematol. 1984 Apr;16(3):297-306. [PubMed:6424437]
4. Nogami K: Bispecific antibody mimicking factor VIII. Thromb Res. 2016 May;141 Suppl 2:S34-5. doi: 10.1016/S0049-3848(16)30361-9. [PubMed:27207420]
5. Roche news [Link]
6. Bussiness wire [Link]
7. Roche study [Link]
8. Genentech professionals information [Link]

Wikipedia

Emicizumab

FDA label

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CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
1	Recruiting	Treatment	Healthy Volunteers / Hemophilia A	1
3	Active Not Recruiting	Prevention	Hemophilia A	1
3	Active Not Recruiting	Treatment	Hemophilia A	3
3	Recruiting	Prevention	Hemophilia A	1
3	Recruiting	Treatment	Hemophilia A	1
4	Recruiting	Treatment	Hemophilia A	1
Not Available	Available	Not Available	Hemophilia A	1

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PHARMACOECONOMICS

Manufacturers

Not Available

Packagers

Not Available

Dosage forms

Search

Injection, solution	Subcutaneous	30 mg/mL

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Prices

Not Available

Patents

Not Available

PROPERTIES

State

Solid

Experimental Properties

PROPERTY	VALUE	SOURCE
melting point (°C)	78ºC	Ji-Hee, et al. Front Immunol, 7:394 (2016)
isoelectric point	6.6 - 7.2	Jin, et al. Electrophoresis. Sep;23(19):3385-91. (2002).

TAXONOMY

Description

Not Available

Kingdom

Organic Compounds

Super Class

Organic Acids

Class

Carboxylic Acids and Derivatives

Sub Class

Direct Parent

Peptides

Alternative Parents

Not Available

Substituents

Not Available

Molecular Framework

Not Available

External Descriptors

Not Available

TARGETS

1. Coagulation factor IX

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Cofactor

General Function

Serine-type endopeptidase activity

Specific Function

Factor IX is a vitamin K-dependent plasma protein that participates in the intrinsic pathway of blood coagulation by converting factor X to its active form in the presence of Ca(2+) ions, phospholi...

Uniprot ID

P00740

Uniprot Name

Coagulation factor IX

Molecular Weight

51778.11 Da

References

1. Uchida N, Sambe T, Yoneyama K, Fukazawa N, Kawanishi T, Kobayashi S, Shima M: A first-in-human phase 1 study of ACE910, a novel factor VIII-mimetic bispecific antibody, in healthy subjects. Blood. 2016 Mar 31;127(13):1633-41. doi: 10.1182/blood-2015-06-650226. Epub 2015 Dec 1. [PubMed:26626991]
2. Shima M, Hanabusa H, Taki M, Matsushita T, Sato T, Fukutake K, Fukazawa N, Yoneyama K, Yoshida H, Nogami K: Factor VIII-Mimetic Function of Humanized Bispecific Antibody in Hemophilia A. N Engl J Med. 2016 May 26;374(21):2044-53. doi: 10.1056/NEJMoa1511769. [PubMed:27223146]
3. Chavin SI: Factor VIII: structure and function in blood clotting. Am J Hematol. 1984 Apr;16(3):297-306. [PubMed:6424437]
4. Nogami K: Bispecific antibody mimicking factor VIII. Thromb Res. 2016 May;141 Suppl 2:S34-5. doi: 10.1016/S0049-3848(16)30361-9. [PubMed:27207420]

2. Coagulation factor X

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Activator

General Function

Serine-type endopeptidase activity

Specific Function

Factor Xa is a vitamin K-dependent glycoprotein that converts prothrombin to thrombin in the presence of factor Va, calcium and phospholipid during blood clotting.

Uniprot ID

P00742

Uniprot Name

Coagulation factor X

Molecular Weight

54731.255 Da

References

1. Uchida N, Sambe T, Yoneyama K, Fukazawa N, Kawanishi T, Kobayashi S, Shima M: A first-in-human phase 1 study of ACE910, a novel factor VIII-mimetic bispecific antibody, in healthy subjects. Blood. 2016 Mar 31;127(13):1633-41. doi: 10.1182/blood-2015-06-650226. Epub 2015 Dec 1. [PubMed:26626991]
2. Shima M, Hanabusa H, Taki M, Matsushita T, Sato T, Fukutake K, Fukazawa N, Yoneyama K, Yoshida H, Nogami K: Factor VIII-Mimetic Function of Humanized Bispecific Antibody in Hemophilia A. N Engl J Med. 2016 May 26;374(21):2044-53. doi: 10.1056/NEJMoa1511769. [PubMed:27223146]
3. Chavin SI: Factor VIII: structure and function in blood clotting. Am J Hematol. 1984 Apr;16(3):297-306. [PubMed:6424437]
4. Nogami K: Bispecific antibody mimicking factor VIII. Thromb Res. 2016 May;141 Suppl 2:S34-5. doi: 10.1016/S0049-3848(16)30361-9. [PubMed:27207420]

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API Docs

Data Licenses

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