Human C1-esterase inhibitor

Targets (7) Biointeractions (7)

IDENTIFICATION

Name

Human C1-esterase inhibitor

Accession Number

DB06404 (DB05341)

Type

Biotech

Groups

Approved

Biologic Classification

Protein Based Therapies
Other protein based therapies

Description

C1 Esterase Inhibitor (Human) is composed of purified endogenous complement component-1 esterase inhibitor (hC1INH) isolated from human plasma. The primary function of endogenous C1INH is to regulate the activation of the complement and contact system pathways. It does this through inhibition of several target proteases within these pathways including activated C1s, kallikrein, factor XIIa and factor XIa. C1 esterase inhibitor has also been shown to inhibit the action of thrombin within the coagulation pathway, and tPA and plasmin within the fibrinolytic pathway. Deficiency of C1-inhibitor permits plasma kallikrein activation, which leads to the production of the vasoactive peptide bradykinin. Additionally, C4 and C2 cleavage goes unchecked, resulting in auto-activation of the complement system. Down-stream effects of the lack of enzyme inhibition by C1 esterase inhibitor results in swelling due to leakage of fluid from blood vessels into connective tissue and consequently the presentation of hereditary angioedema (HAE).

fatal swelling of several soft tissues (edema), which may last up to five days when untreated.

In June 2017 the FDA approved a formulation of human C1-esterase inhibitor for subcutaneous administration under the tradename Haegarda.

Protein structure

Protein chemical formula

Not Available

Protein average weight

Not Available

Sequences

Not Available

Synonyms

C1 Esterase Inhibitor (Human)

C1 inhibitor

C1 inhibitor (human)

C1 inhibitor human

C1-esterase inhibitor, human

C1-INH

C1-inhibiting factor

C1-inhibitor, plasma derived

Human C1 inhibitor

Human C1-esterase inhibitor

Plasma protease C1 inhibitor

External IDs

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END	
Berinert	Kit	500 [iU]/10mL		CSL Behring GmbH	2011-12-22	Not applicable	
Berinert 1500	Kit; Powder, for solution	1500 unit	Intravenous	Csl Behring	2015-05-06	Not applicable	
Berinert 500	Kit; Powder, for solution	500 unit	Intravenous	Csl Behring	2010-10-06	Not applicable	
Cinryze	Injection, powder, for solution	500 U	Intravenous	Shire Services Bvba	2011-06-15	Not applicable	
Cinryze	Powder, for solution	500 unit	Intravenous	Viropharma Biologics Inc	2016-03-08	Not applicable	
Cinryze	Injection, powder, lyophilized, for solution	500 [iU]/5mL	Intravenous	Viropharma Biologics Inc	2008-12-01	Not applicable	
Haegarda	Kit; Powder, for solution	3000 unit	Subcutaneous	Csl Behring	Not applicable	Not applicable	
Haegarda	Kit; Powder, for solution	2000 unit	Subcutaneous	Csl Behring	Not applicable	Not applicable	
HAEGARDA C1 Esterase Inhibitor Subcutaneous (Human)	Kit	3000 [iU]/6mL		CSL Behring GmbH	2017-06-22	Not applicable	
HAEGARDA C1 Esterase Inhibitor Subcutaneous (Human)	Kit	2000 [iU]/4mL		CSL Behring GmbH	2017-06-22	Not applicable	

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Categories

Amino Acids, Peptides, and Proteins

Blood and Blood Forming Organs

Blood Proteins

Complement Inactivating Agents

Complement Inactivator Proteins

Complement System Proteins

Decreased Vascular Permeability

Drugs Used in Hereditary Angioedema

Glycoconjugates

Glycoproteins

Immunologic Factors

Immunoproteins

Kallikrein Inhibitors

Peptides

Protease Inhibitors

Proteins

Serpins

UNII

6KIC4BB60G

CAS number

Not Available

PHARMACOLOGY

Indication

For routine prophylaxis against angioedema attacks in adolescent and adult patients with Hereditary Angioedema (HAE).

Associated Conditions

Acute attack of hereditary angioedema

Pharmacodynamics

Mechanism of action

C1 inhibitor is a normal constituent of human blood and is one of the serine proteinase inhibitors (serpins). The primary function of C1 inhibitor is to regulate the activation of the complement and intrinsic coagulation (contact system) pathway. C1 inhibitor also regulates the fibrinolytic system. Regulation of these systems is performed through the formation of complexes between the proteinases and the inhibitor, resulting in inactivation of both and consumption of the C1 inhibitor. HAE patients have low levels of endogenous or functional C1 inhibitor. Although the events that induce attacks of angioedema in HAE patients are not well defined, it is thought by some that increased vascular permeability and the clinical manifestation of HAE attacks are primarily mediated through contact system activation. Suppression of contact system activation by C1 inhibitor through the inactivation of plasma kallikrein and factor XIIa is thought to modulate this vascular permeability by preventing the generation of bradykinin1. Administration of C1 Esterase Inhibitor increases plasma levels of C1 inhibitor activity.

A	Complement C1r subcomponent	
	inhibitor	
	Human	
A	Complement C1s subcomponent	
	inhibitor	
	Human	
A	Plasma kallikrein	
	inhibitor	
	Human	
A	Coagulation factor XII	
	inhibitor	
	Human	
U	Prothrombin	
	inhibitor	
	Human	
A	Coagulation factor XI	
	inhibitor	
	Human	

Absorption

Cmax was found to be 0.68 units/mL and Tmax was found to be 3.9 hr after administration of a single dose. Tmax for subcutaneous administration is 48 hrs and subcutaneous bioavalability is 39.7% [A19661].

Volume of distribution

Not Available

Protein binding

Not Available

Metabolism

Not Available

Route of elimination

Not Available

Half life

56 hours (range 11 to 108 hours) for a single dose and 62 hours (range 16 to 152 hours) for the double dose. Subcutaneous administration produces a half life of 199.6 hours [A19661].

Clearance

0.85 mL/min (single dose)

Toxicity

The most common adverse reactions observed were headache, nausea, rash and vomiting.

Serious arterial and venous thromboembolic (TE) events have been reported at the recommended dose of C1 Esterase Inhibitor (Human) products following administration in patients with HAE. Risk factors may include presence of an indwelling venous catheter/access device, prior history of thrombosis, underlying atherosclerosis, use of oral contraceptives, certain androgens, morbid obesity, and immobility. Monitor patients with known risk factors for TE events during and after administration.

Because this product is made from human blood, it may carry a risk of transmitting infectious agents, e.g. viruses, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

Not Available

Pharmacogenomic Effects/ADRs

Not Available

INTERACTIONS

Drug Interactions

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

Search

DRUG	INTERACTION
Alclometasone	The risk or severity of thromboembolism can be increased when Alclometasone is combined with Human C1-esterase inhibitor.
Allylestrenol	Allylestrenol may increase the thrombogenic activities of Human C1-esterase inhibitor.
Altrenogest	Altrenogest may increase the thrombogenic activities of Human C1-esterase inhibitor.
Amcinonide	The risk or severity of thromboembolism can be increased when Amcinonide is combined with Human C1-esterase inhibitor.
Anthrax immune globulin human	The risk or severity of adverse effects can be increased when Human C1-esterase inhibitor is combined with Anthrax immune globulin human.
Bacillus calmette-guerin substrain connaught live antigen	The risk or severity of adverse effects can be increased when Human C1-esterase inhibitor is combined with Bacillus calmette-guerin substrain connaught live antigen.
Bacillus calmette-guerin substrain tice live antigen	The risk or severity of adverse effects can be increased when Human C1-esterase inhibitor is combined with Bacillus calmette-guerin substrain tice live antigen.
Bazedoxifene	Bazedoxifene may increase the thrombogenic activities of Human C1-esterase inhibitor.
BCG vaccine	The therapeutic efficacy of BCG vaccine can be decreased when used in combination with Human C1-esterase inhibitor.
Betamethasone	The risk or severity of thromboembolism can be increased when Betamethasone is combined with Human C1-esterase inhibitor.

Not Available

REFERENCES

General References

1. Cicardi M, Zingale L, Zanichelli A, Pappalardo E, Cicardi B: C1 inhibitor: molecular and clinical aspects. Springer Semin Immunopathol. 2005 Nov;27(3):286-98. Epub 2005 Nov 11. [PubMed:16267649]
2. Harpel PC, Cooper NR: Studies on human plasma C1 inactivator-enzyme interactions. I. Mechanisms of interaction with C1s, plasmin, and trypsin. J Clin Invest. 1975 Mar;55(3):593-604. [PubMed:123251]
3. PENSKY J, LEVY LR, LEPOW IH: Partial purification of a serum inhibitor of C'1-esterase. J Biol Chem. 1961 Jun;236:1674-9. [PubMed:13734157]
4. van der Graaf F, Koedam JA, Bouma BN: Inactivation of kallikrein in human plasma. J Clin Invest. 1983 Jan;71(1):149-58. [PubMed:6184384]
5. de Agostini A, Lijnen HR, Pixley RA, Colman RW, Schapira M: Inactivation of factor XII active fragment in normal plasma. Predominant role of C-1-inhibitor. J Clin Invest. 1984 Jun;73(6):1542-9. [PubMed:6725552]
6. Cugno M, Bos I, Lubbers Y, Hack CE, Agostoni A: In vitro interaction of C1-inhibitor with thrombin. Blood Coagul Fibrinolysis. 2001 Jun;12(4):253-60. [PubMed:11460008]
7. Bock SC, Skriver K, Nielsen E, Thogersen HC, Wiman B, Donaldson VH, Eddy RL, Marrinan J, Radziejewska E, Huber R, et al.: Human C1 inhibitor: primary structure, cDNA cloning, and chromosomal localization. Biochemistry. 1986 Jul 29;25(15):4292-301. [PubMed:3756141]

External Links

UniProt

P05155

PubChem Substance

347910350

RxList

RxList Drug Page

Drugs.com

Drugs.com Drug Page

Wikipedia

C1-inhibitor

ATC Codes

B06AC01 — C1-inhibitor, plasma derived

- B06AC — Drugs used in hereditary angioedema
- B06A — OTHER HEMATOLOGICAL AGENTS

92:32.00 — Complement Inhibitors

FDA label

Download (379 KB)

CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
1	Completed	Treatment	Hereditary Angioedema Types I and II	1
1	Completed	Treatment	Neuromyelitis Optica	1
1	Not Yet Recruiting	Treatment	Renal Failure	1
1, 2	Completed	Prevention	Delayed Graft Function / End Stage Renal Disease (ESRD) / Ischemic Reperfusion Injury / Renal Failure	1
1, 2	Completed	Treatment	Transplantation, Kidney	1
2	Completed	Not Available	Hereditary Angioedema	2
2	Completed	Prevention	Hereditary Angioedema	1
2	Completed	Treatment	Hereditary Angioedema	1
2	Completed	Treatment	Rejection, Transplant	1
2	Enrolling by Invitation	Treatment	Antibody Mediated Rejection of Kidney Transplant	1

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PHARMACOECONOMICS

Manufacturers

Not Available

Packagers

Not Available

FORM	ROUTE	STRENGTH
Kit		500 [iU]/10mL
Kit; powder, for solution	Intravenous	1500 unit
Kit; powder, for solution	Intravenous	500 unit
Injection, powder, for solution	Intravenous	500 U
Injection, powder, lyophilized, for solution	Intravenous	500 [iU]/5mL
Powder, for solution	Intravenous	500 unit
Kit; powder, for solution	Subcutaneous	2000 unit
Kit; powder, for solution	Subcutaneous	3000 unit
Kit		2000 [iU]/4mL
Kit		3000 [iU]/6mL

Showing 1 to 10 of 10 entries

‹ ›

Prices

Not Available

Patents

Not Available

PROPERTIES

State

Solid

Experimental Properties

Not Available

TAXONOMY

Description

Not Available

Kingdom

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. Complement C1r subcomponent

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Specific Function

C1r B chain is a serine protease that combines with C1q and C1s to form C1, the first component of the classical pathway of the complement system.

Gene Name

C1R

Uniprot ID

P00736

Uniprot Name

Complement C1r subcomponent

Molecular Weight

80118.04 Da

References

1. Harpel PC, Cooper NR: Studies on human plasma C1 inactivator-enzyme interactions. I. Mechanisms of interaction with C1s, plasmin, and trypsin. J Clin Invest. 1975 Mar;55(3):593-604. [PubMed:123251]

2. Complement C1s subcomponent

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Inhibitor

General Function

Serine-type endopeptidase activity

Specific Function

C1s B chain is a serine protease that combines with C1q and C1r to form C1, the first component of the classical pathway of the complement system. C1r activates C1s so that it can, in turn, activat...

P09871

Uniprot Name

Complement C1s subcomponent

Molecular Weight

76683.905 Da

References

1. Harpel PC, Cooper NR: Studies on human plasma C1 inactivator-enzyme interactions. I. Mechanisms of interaction with C1s, plasmin, and trypsin. J Clin Invest. 1975 Mar;55(3):593-604. [PubMed:123251]

3. Plasma kallikrein

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Inhibitor

General Function

Serine-type endopeptidase activity

Specific Function

The enzyme cleaves Lys-Arg and Arg-Ser bonds. It activates, in a reciprocal reaction, factor XII after its binding to a negatively charged surface. It also releases bradykinin from HMW kininogen an...

Gene Name

KLKB1

Uniprot ID

P03952

Uniprot Name

Plasma kallikrein

1. van der Graaf F, Koedam JA, Bouma BN: Inactivation of kallikrein in human plasma. J Clin Invest. 1983 Jan;71(1):149-58. [PubMed:6184384]

4. Coagulation factor XII

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Inhibitor

General Function

Serine-type endopeptidase activity

Specific Function

Factor XII is a serum glycoprotein that participates in the initiation of blood coagulation, fibrinolysis, and the generation of bradykinin and angiotensin. Prekallikrein is cleaved by factor XII t...

Gene Name

F12

Uniprot ID

P00748

Uniprot Name

Coagulation factor XII

Molecular Weight

67791.53 Da

References

5. Prothrombin

Kind

Protein

Organism

Human

Pharmacological action

Unknown

Actions

Inhibitor

General Function

Thrombospondin receptor activity

Specific Function

Thrombin, which cleaves bonds after Arg and Lys, converts fibrinogen to fibrin and activates factors V, VII, VIII, XIII, and, in complex with thrombomodulin, protein C. Functions in blood homeostas...

Gene Name

F2

Uniprot ID

P00734

Uniprot Name

Prothrombin

Molecular Weight

70036.295 Da

References

1. Cugno M, Bos I, Lubbers Y, Hack CE, Agostoni A: In vitro interaction of C1-inhibitor with thrombin. Blood Coagul Fibrinolysis. 2001 Jun;12(4):253-60. [PubMed:11460008]

6. Coagulation factor XI

Human

Pharmacological action

Yes

Actions

Inhibitor

General Function

Serine-type endopeptidase activity

Specific Function

Factor XI triggers the middle phase of the intrinsic pathway of blood coagulation by activating factor IX.

Gene Name

F11

Uniprot ID

P03951

Uniprot Name

Coagulation factor XI

Molecular Weight

70108.56 Da

References

1. Cicardi M, Zingale L, Zanichelli A, Pappalardo E, Cicardi B: C1 inhibitor: molecular and clinical aspects. Springer Semin Immunopathol. 2005 Nov;27(3):286-98. Epub 2005 Nov 11. [PubMed:16267649]

7. Tissue-type plasminogen activator

Kind

Protein

Organism

Human

Pharmacological action

Serine-type endopeptidase activity

Specific Function

Converts the abundant, but inactive, zymogen plasminogen to plasmin by hydrolyzing a single Arg-Val bond in plasminogen. By controlling plasmin-mediated proteolysis, it plays an important role in t...

Gene Name

PLAT

Uniprot ID

P00750

Uniprot Name

Tissue-type plasminogen activator

Molecular Weight

62916.495 Da

References

1. Cicardi M, Zingale L, Zanichelli A, Pappalardo E, Cicardi B: C1 inhibitor: molecular and clinical aspects. Springer Semin Immunopathol. 2005 Nov;27(3):286-98. Epub 2005 Nov 11. [PubMed:16267649]

Drug created on March 19, 2008 10:29 / Updated on October 04, 2018 11:48

API Docs

Data Licenses

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