Coagulation Factor IX (Recombinant)

Targets (7) Biointeractions (4)

IDENTIFICATION

Name

Coagulation Factor IX (Recombinant)

Accession Number

DB00100 (BTD00038, BIOD00038)

Type

Biotech

Groups

Approved

Biologic Classification

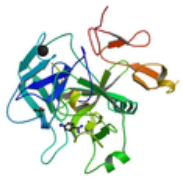
Protein Based Therapies
Blood factors

Description

Recombinant Coagulation Factor IX is a purified Factor IX glycoprotein produced by recombinant DNA technology. It has a primary amino acid sequence that is identical to the Ala148 allelic form of human factor IX, and has structural and functional characteristics similar to those of endogenous factor IX. It is not derived from human blood (unlike human Factor IX complex), and is instead produced by a genetically engineered Chinese hamster ovary (CHO) cell line that secretes recombinant Factor IX into cell medium that is then processed and purified for use as a pharmaceutical agent.

Recombinant Factor IX is indicated for the control and prevention of bleeding episodes in adult and pediatric patients with congenital factor IX deficiency (Hemophilia B).

Protein structure



Protein chemical formula

$C_{2041}H_{3136}N_{558}O_{641}S_{25}$

Protein average weight

46548.2 Da

```
>DB00100 sequence
YNSGKLEEFVQGNLERECMEEKCSFEEAREVFENTERTTEFWKQYVDGDQCESNPCLNGG
SCKDDINSYECWCPFGFEGKNCELDVTCNIKNGRCEQFCKNSADNKVVCSCTEGYRLAEN
QKSCEPAVPFPCGRVSVSQTSKLTRAEAVFPDVDYVNSTEAETILDNITQSTQSFNDFTR
VVGGEDAKPGQFPWQVVLNGKVDAFCGGSIVNEKWIVTAAHCVETGVKITVVAGEHNIEE
TEHTEQKRNVIRIIPHHNYNAAINKYNHDIALLELDEPLVLNSYVTPICIADKEYTNIFL
KFGSGYVSGWGRVFHKGRSALVLQYLRVPLVDRATCLRSTKFTIYNNMFCAGFHEGGRDS
CQGDSGGPHVTEVEGTSFLTGIISWGEECAMKGKYGIYTKVSRYVNWIKEKTKLT
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Synonyms

Coagulation factor IX (recombinant)

Coagulation factor IX recombinant human

Factor IX (Recombinant)

nonacog alfa

Recombinant factor IX

Prescription Products

Search

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END	
BeneFIX	Kit			Wyeth Bio Pharma Division Of Wyeth Pharmaceuticals Inc., A Subsidiary Of Pfizer Inc.	1997-02-01	Not Applicable	
BeneFIX	Powder, for solution	3000 unit	Intravenous	Pfizer	2013-02-12	Not Applicable	
BeneFIX	Powder, for solution	250 unit	Intravenous	Pfizer	2007-04-14	Not Applicable	
BeneFIX	Kit			Wyeth Bio Pharma Division Of Wyeth Pharmaceuticals Inc., A Subsidiary Of Pfizer Inc.	2012-02-01	Not Applicable	
BeneFIX	Kit			Wyeth Bio Pharma Division Of Wyeth Pharmaceuticals Inc., A Subsidiary Of Pfizer Inc.	1997-02-01	Not Applicable	
BeneFIX	Powder, for solution	2000 unit	Intravenous	Pfizer	2008-07-12	Not Applicable	
BeneFIX	Kit			Wyeth Bio Pharma Division Of Wyeth Pharmaceuticals Inc., A Subsidiary Of Pfizer Inc.	1997-02-01	Not Applicable	
BeneFIX	Powder, for solution	1000 unit	Intravenous	Pfizer	2007-04-14	Not Applicable	
BeneFIX	Kit			Wyeth Bio Pharma Division Of Wyeth Pharmaceuticals Inc., A Subsidiary Of Pfizer Inc.	1997-02-01	Not Applicable	
BeneFIX	Powder, for solution	1500 unit	Intravenous	Pfizer	Not Applicable	Not Applicable	
BeneFIX	Powder, for solution	500 unit	Intravenous	Pfizer	2007-04-14	Not Applicable	

				Facility Ag			
Idelvion	Kit			Csl Behring Recombinant Facility Ag	2016-03-04	Not Applicable	
Idelvion	Kit			Csl Behring Recombinant Facility Ag	2016-03-04	Not Applicable	
Ixinity	Kit			Aptevo Bio Therapeutics Llc	2017-05-12	Not Applicable	
Ixinity	Kit			Cangene Bio Pharma	2015-05-01	Not Applicable	
Ixinity	Kit			Aptevo Bio Therapeutics Llc	2017-05-12	Not Applicable	
Ixinity	Kit			Aptevo Bio Therapeutics Llc	2017-05-12	Not Applicable	
Ixinity	Kit			Aptevo Bio Therapeutics Llc	2017-05-12	Not Applicable	
Ixinity	Kit			Cangene Bio Pharma	2015-05-01	Not Applicable	
Ixinity	Kit			Aptevo Bio Therapeutics Llc	2017-05-12	Not Applicable	
Ixinity	Kit			Aptevo Bio Therapeutics Llc	2017-05-12	Not Applicable	
Ixinity	Kit			Aptevo Bio Therapeutics Llc	2017-05-12	Not Applicable	
Ixinity	Kit			Cangene Bio Pharma	2015-05-01	Not Applicable	
Ixinity	Kit			Aptevo Bio Therapeutics Llc	2017-05-12	Not Applicable	
Rixubis	Kit			Baxalta Canada Corporation	2013-06-26	Not Applicable	
Rixubis	Kit			Baxalta Canada Corporation	2013-06-26	Not Applicable	
Rixubis	Kit			Baxalta Canada Corporation	2013-06-26	Not Applicable	
Rixubis	Kit			Baxalta Canada Corporation	2013-06-26	Not Applicable	
Rixubis	Kit			Baxalta Canada Corporation	2013-06-26	Not Applicable	

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Mixture Products

Search

NAME	INGREDIENTS	DOSAGE	ROUTE	LABELLER	MARKETING START	MARKETING END	
Benefix - (250iu)	Coagulation Factor IX (Recombinant) (250 unit) + Water (5 ml)	Kit; Liquid; Powder, for solution	Intravenous	Wyeth Ltd.	1998-08-12	2008-06-19	
Benefix - (500iu)	Coagulation Factor IX (Recombinant) (500 unit) + Water (5 ml)	Kit; Liquid; Powder, for solution	Intravenous	Wyeth Ltd.	1998-08-12	2008-06-19	
Benefix - (1000iu)	Coagulation Factor IX (Recombinant) (1000 unit) + Water (10 ml)	Kit; Liquid; Powder, for solution	Intravenous	Wyeth Ltd.	1998-08-12	2008-06-19	

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Categories

Hemostatics

UNII

382L14738L

CAS number

181054-95-5

PHARMACOLOGY

Indication

For treatment of hemophilia (Christmas disease).

Structured Indications

Hereditary factor IX deficiency

Pharmacodynamics

Binds vitamin K and factor VIIIa. Cleaves the Arg-Ile bond in factor X to form active factor Xa. Plays a key role in blood coagulation and clotting. Injections of factor IX are used to treat hemophilia B, which is sometimes called Christmas disease. AlphaNine is injected to increase plasma levels of Factor IX and can temporarily correct this coagulation defect. The activated partial thromboplastin time (aPTT) is prolonged in people with hemophilia B. Treatment with factor IX concentrate may normalize the aPTT by temporarily replacing the factor IX. The administration of BeneFIX increases plasma levels of factor IX, and can temporarily correct the coagulation defect in these patients.

Mechanism of action

Coagulation Factor IX is an important protein in the process of hemostasis and normal blood clotting as it plays a key role within the coagulation cascade. It is located within the blood plasma as a zymogen, an antecedent to enzymatic function, in its inactivated state. Factor IX is dependent on the presence of Vitamin K, and is activated to a serine protease by the function of Coagulation Factor XIa. Factor XIa cleaves the peptide bond associated with protein activation in Factor IX, leaving Factor IX with two exposed chains, a light chain and a heavy chain. These two chains are held together by several disulfide bonds that reinforce the structure of Factor IX's activated form. After being activated, Factor IX forms a complex with calcium ions, membrane phospholipids and Coagulation Factor VIII to activate Coagulation Factor X. The activation of Factor X then performs a similarly integral step in the blood coagulation cascade. The ultimate result of phenotypically normal coagulation factors is the creation of platelets for normal blood clotting.

A	Coagulation factor X
activator	
Human	
A	Coagulation factor XI
ligand	
Human	
A	Coagulation factor VII
ligand	

(A) Coagulation factor VIII	
cofactor	
Human	
(U) Prothrombin	
Not Available	
Human	
(U) Prolow-density lipoprotein receptor-related protein 1	
Not Available	
Human	
(U) Vitamin K-dependent gamma-carboxylase	
Not Available	
Human	

Absorption

Not Available

Volume of distribution

Not Available

Protein binding

Not Available

Metabolism

Not Available

Route of elimination

Not Available

Half life

18.8 ± 5.4 hours

Clearance

8.62 ± 1.7

Toxicity

Not Available

Affected organisms

Humans and other mammals

Pathways

Not Available

Not Available

INTERACTIONS

Drug Interactions

Search

DRUG	INTERACTION	DRUG GROUP
Aminocaproic Acid	The risk or severity of adverse effects can be increased when Aminocaproic Acid is combined with Coagulation Factor IX (Recombinant).	Approved, Investigational

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Food Interactions

Not Available

REFERENCES

Synthesis Reference

Volker Schellenberger, Joshua Silverman, Willem Stemmer, Chia-wei Wang, Benjamin Spink, Nathan Geething, Wayne To, "Coagulation factor IX compositions and methods of making and using same." U.S. Patent US20110046060, issued February 24, 2011.
US20110046060

General References

1. BIGGS R, DOUGLAS AS, MACFARLANE RG, DACIE JV, PITNEY WR, MERSKEY: Christmas disease: a condition previously mistaken for haemophilia. Br Med J. 1952 Dec 27;2(4799):1378-82. [PubMed:12997790]
2. Kurachi K, Davie EW: Isolation and characterization of a cDNA coding for human factor IX. Proc Natl Acad Sci U S A. 1982 Nov;79(21):6461-4. [PubMed:6959130]

External Links

UniProt

P00740

Genbank

K02402

KEGG Compound

C03101

PubChem Substance

46508858

Therapeutic Targets Database

DAP000964

PharmGKB

PA164744952

RxList

Drugs.com

Drugs.com Drug Page

Wikipedia

Factor_IX

ATC Codes

B02BD09 — Nonacog alfa

- B02BD — Blood coagulation factors
- B02B — VITAMIN K AND OTHER HEMOSTATICS
- B02 — ANTIHEMORRHAGICS
- B — BLOOD AND BLOOD FORMING ORGANS

AHFS Codes

20:28.16 — Hemostatics

FDA label

Download (18.9 MB)

MSDS

Download (125 KB)

CLINICAL TRIALS

Clinical Trials

Search

PHASE	STATUS	PURPOSE	CONDITIONS	COUNT
1	Completed	Treatment	Hereditary factor IX deficiency	1
1	Recruiting	Treatment	Hereditary factor IX deficiency	1
2	Completed	Treatment	Hereditary factor IX deficiency	1
2, 3	Completed	Treatment	Hereditary factor IX deficiency	1
3	Completed	Prevention	Hereditary factor IX deficiency	1
3	Completed	Treatment	Hereditary factor IX deficiency	6
3	Completed	Treatment	Severe Hemophilia B	1
4	Completed	Treatment	Hereditary factor IX deficiency	1
Not Available	Completed	Not Available	Hemophilia A / Hereditary factor IX deficiency	1
Not Available	Completed	Not Available	Hereditary factor IX deficiency	2
Not Available	Recruiting	Not Available	Hemophilia	1
Not Available	Recruiting	Not Available	Hereditary factor IX deficiency	2

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PHARMACOECONOMICS

Not Available

Packagers

CSL Behring LLC

Grifols SA

Hospira Inc.

Wyeth Pharmaceuticals

Dosage forms

Search

FORM	ROUTE	STRENGTH
Powder, for solution	Intravenous	1000 unit
Powder, for solution	Intravenous	1500 unit
Powder, for solution	Intravenous	2000 unit
Powder, for solution	Intravenous	250 unit
Powder, for solution	Intravenous	3000 unit
Powder, for solution	Intravenous	500 unit
Kit; liquid; powder, for solution	Intravenous	
Kit		

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Prices

Search

UNIT DESCRIPTION	COST	UNIT
Alphanine sd 250-1500 unit vial	1.42USD	vial
Mononine 1000 unit vial	1.2USD	vial
Mononine 500 unit vial	1.2USD	vial
Benefix 2000 unit vial	1.12USD	vial
Benefix 1000 unit vial	1.0USD	vial
Benefix 250 unit vial	1.0USD	vial
Benefix 500 unit vial	1.0USD	vial

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Patents

Not Available

PROPERTIES

Liquid

Experimental Properties

PROPERTY	VALUE	SOURCE
melting point (°C)	54 °C	Link, R.P., Castellino, F.J. Arch. Biochem. Biophsy. 227:259-265 (1983)
hydrophobicity	-0.431	Not Available
isoelectric point	5.20	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

Substituents

Not Available

Molecular Framework

Not Available

External Descriptors

Not Available

TARGETS

1. Coagulation factor X

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.

Gene Name

F10

Uniprot ID

P00742

Uniprot Name

Coagulation factor X

Molecular Weight

54731.255 Da

References

1. Worfolk LA, Robinson RA, Tracy PB: Factor Xa interacts with two sites on monocytes with different functional activities. Blood. 1992 Oct 15;80(8):1989-97. [PubMed:1391956]
2. Jones KC, Mann KG: A model for the tissue factor pathway to thrombin. II. A mathematical simulation. J Biol Chem. 1994 Sep 16;269(37):23367-73. [PubMed:8083242]
3. Ambrosini G, Plescia J, Chu KC, High KA, Altieri DC: Activation-dependent exposure of the inter-EGF sequence Leu83-Leu88 in factor Xa mediates ligand binding to effector cell protease receptor-1. J Biol Chem. 1997 Mar 28;272(13):8340-5. [PubMed:9079657]
4. London FS, Walsh PN: Zymogen factor IX potentiates factor IXa-catalyzed factor X activation. Biochemistry. 2000 Aug 15;39(32):9850-8. [PubMed:10933803]
5. Scandella DH: Properties of anti-factor VIII inhibitor antibodies in hemophilia A patients. Semin Thromb Hemost. 2000;26(2):137-42. [PubMed:10919405]
6. Chen X, Ji ZL, Chen YZ: TTD: Therapeutic Target Database. Nucleic Acids Res. 2002 Jan 1;30(1):412-5. [PubMed:11752352]
7. Di Scipio RG, Kurachi K, Davie EW: Activation of human factor IX (Christmas factor). J Clin Invest. 1978 Jun;61(6):1528-38. [PubMed:659613]

2. Coagulation factor XI

Kind

Protein

Organism

Human

Pharmacological action

Yes

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. Sun MF, Zhao M, Gailani D: Identification of amino acids in the factor XI apple 3 domain required for activation of factor IX. J Biol Chem. 1999 Dec 17;274(51):36373-8. [PubMed:10593931]
2. Gailani D, Ho D, Sun MF, Cheng Q, Walsh PN: Model for a factor IX activation complex on blood platelets: dimeric conformation of factor XIa is essential. Blood. 2001 May 15;97(10):3117-22. [PubMed:11342438]
3. Di Scipio RG, Kurachi K, Davie EW: Activation of human factor IX (Christmas factor). J Clin Invest. 1978 Jun;61(6):1528-38. [PubMed:659613]

3. Coagulation factor VII

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Ligand

General Function

Serine-type peptidase activity

Specific Function

Initiates the extrinsic pathway of blood coagulation. Serine protease that circulates in the blood in a zymogen form. Factor VII is converted to factor VIIa by factor Xa, factor XIIa, factor IXa, o...

Gene Name

F7

Uniprot ID

P08709

Molecular Weight

51593.465 Da

References

1. Baker DC, Robbe SL, Jacobson L, Manco-Johnson MJ, Holler L, Lefkowitz J: Hereditary deficiency of vitamin-K-dependent coagulation factors in Rambouillet sheep. Blood Coagul Fibrinolysis. 1999 Mar;10(2):75-80. [PubMed:10192655]
2. Hertzberg MS, Facey SL, Hogg PJ: An Arg/Ser substitution in the second epidermal growth factor-like module of factor IX introduces an O-linked carbohydrate and markedly impairs activation by factor XIa and factor VIIa/Tissue factor and catalytic efficiency of factor IXa. Blood. 1999 Jul 1;94(1):156-63. [PubMed:10381508]
3. Butenas S, van't Veer C, Mann KG: "Normal" thrombin generation. Blood. 1999 Oct 1;94(7):2169-78. [PubMed:10498586]
4. Celie PH, Lenting PJ, Mertens K: Hydrophobic contact between the two epidermal growth factor-like domains of blood coagulation factor IX contributes to enzymatic activity. J Biol Chem. 2000 Jan 7;275(1):229-34. [PubMed:10617609]
5. Shord SS, Lindley CM: Coagulation products and their uses. Am J Health Syst Pharm. 2000 Aug 1;57(15):1403-17; quiz 1418-20. [PubMed:10938981]
6. Di Scipio RG, Kurachi K, Davie EW: Activation of human factor IX (Christmas factor). J Clin Invest. 1978 Jun;61(6):1528-38. [PubMed:659613]

4. Coagulation factor VIII

Kind

Protein

Organism

Human

Pharmacological action

Yes

Actions

Cofactor

General Function

Oxidoreductase activity

Specific Function

Factor VIII, along with calcium and phospholipid, acts as a cofactor for factor IXa when it converts factor X to the activated form, factor Xa.

Gene Name

F8

Uniprot ID

P00451

Uniprot Name

Coagulation factor VIII

Molecular Weight

267007.42 Da

References

1. Neels JG, Bovenschen N, van Zonneveld AJ, Lenting PJ: Interaction between factor VIII and LDL receptor-related protein. Modulation of coagulation? Trends Cardiovasc Med. 2000 Jan;10(1):8-14. [PubMed:11150722]

Jun;88(6):EREP02. [PubMed:12826528]
4. Kalashnikova LA, Berkovskii AL, Dobrynina LA, Sergeeva EV, Kozlov AA, Aleksandrova EN, Nasonov EL: [Clotting factor VIII in Sneddon syndrome]. Klin Med (Mosk). 2003;81(9):42-5. [PubMed:14598591]
5. Johansen RF, Sorensen B, Ingerslev J: Acquired haemophilia: dynamic whole blood coagulation utilized to guide haemostatic therapy. Haemophilia. 2006 Mar;12(2):190-7. [PubMed:16476097]
6. Di Scipio RG, Kurachi K, Davie EW: Activation of human factor IX (Christmas factor). J Clin Invest. 1978 Jun;61(6):1528-38. [PubMed:659613]

5. Prothrombin

Kind

Protein

Organism

Human

Pharmacological action

Unknown

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. Butenas S, van't Veer C, Mann KG: "Normal" thrombin generation. Blood. 1999 Oct 1;94(7):2169-78. [PubMed:10498586]
2. Kohler M: Thrombogenicity of prothrombin complex concentrates. Thromb Res. 1999 Aug 15;95(4 Suppl 1):S13-7. [PubMed:10499904]
3. Seitz R, Dodt J: Virus safety of prothrombin complex concentrates and factor IX concentrates. Thromb Res. 1999 Aug 15;95(4 Suppl 1):S19-23. [PubMed:10499905]
4. Samis JA, Ramsey GD, Walker JB, Nesheim ME, Giles AR: Proteolytic processing of human coagulation factor IX by plasmin. Blood. 2000 Feb 1;95(3):943-51. [PubMed:10648407]
5. Bauer KA, Humphries S, Smillie B, Li L, Cooper JA, Barzegar S, Rosenberg RD, Miller GJ: Prothrombin activation is increased among asymptomatic carriers of the prothrombin G20210A and factor V Arg506Gln mutations. Thromb Haemost. 2000 Sep;84(3):396-400. [PubMed:11019961]

6. Prolow-density lipoprotein receptor-related protein 1