SUMMARY OF PRODUCT

STRUCTURE

Human activated recombinant coagulation factor VII (rFVIIa) is a glycoprotein consisting of 406 amino acids (MW 50 kDa) which is structurally similar to human plasma-derived Factor VIIa. The gene for human Factor VII is cloned and expressed in baby hamster kidney cells (BHK cells). Recombinant FVII is secreted into the culture medium in its single-chain form. rFVII contains four domains: a gamma-carboxyglutamic acid domain in amino terminal, two epidermal growth factor-like (EGF-like) domains and a serine protease domain.

Conversion of this zymogene to activated form is done proteolytically during a chromatographic purification process. As a result, rFVIIa contains two jointed peptide chains, a light chain of 152 amino acids and a heavy chain of 254 amino acids. These chains are attached with a single disulfide bond in Cys135-Cys262.

Light chain begins from amino terminal of rFVIIa and contains 10 gamma-carboxyglutamic acid groups. In order to start proteolytic activity on FIX and FX due to interaction between FVII and tissue factor these gamma-carboxyglutamic acid groups are vital.

Factor VII is a vitamin K-dependent gamma-carboxylated glycoprotein, which in its activated form, FVIIa, activates FX to FXa and FIX to FIXa by limited proteolysis. FVIIa full enzymatic activity is appeared when make a complex with tissue factor (TF) in the presence of calcium ions. Gamma-carboxyglutamic acid groups in light chain are essential for FVII proteolytic activity.

Some other post-translational modifications are N-glycosylation on asparagine 145 and 322 and O-glycosylation of serine 52 and 60.

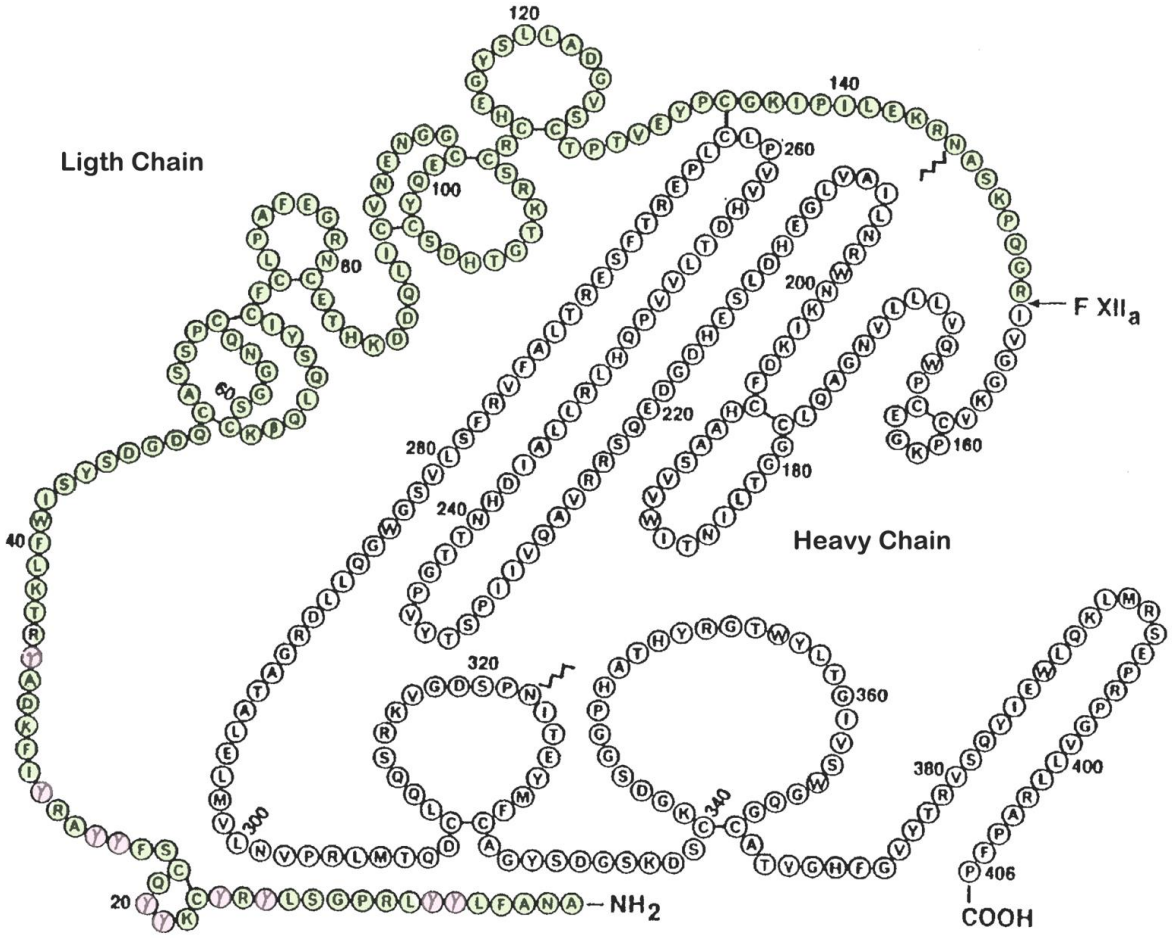
Amino Acid Sequence of Coagulation rFactor VIIa

light chain

ANAFLEELRP	GSLERECKEE	QCSFEEAREI	FKDAERTKLF	40
WISYSDGDQC	ASSPCQNGGS	CKDQLQSYIC	FCLPAFEGRN	80
CETHKDDQLI	CVNENGGCEQ	YCSDHTGTKR	SCRCHEGYSL	120
LADGVSCTPT	VEYPCGKIPI	LEKRNASKPQ	GR	152

heavy chain

			IVGGKVCP	160
KGECPWQVLL	LVNGAQLCGG	TLINTIWVVS	AAHCFDKIKN	200
WRNLIAVLGE	HDLSEHDGDE	QSRRVAQVII	PSTYVPGTTN	240
HDIALLRLHQ	PVVLTDHVVP	LCLPERTFSE	RTLAFVRFSL	280
VSGWGQLLDR	GATALELMVL	NVPRLMTQDC	LQQSRKVGDS	320
PNITEYMFCA	GYSDGSKDSC	KGDSGGPHAT	HYRGTWYLTG	360
IVSWGQGCAT	VGHFGVYTRV	SQYIEWLQKL	MRSEPRPGVL	400
LRAPFP				406



Molecular structure of Human FVII.

Nomenclature information of rFVIIa.

Recommended International Nonproprietary Name (INN)	Coagulation rFVIIa
Anatomical Therapeutic Chemical (ATC) *code*	B02BD08
Chemical Name	Activated recombinant coagulation factor VII Blood-coagulation factor VII (Human clone λHVII2463 protein moiety)
Chemical Abstracts Service (CAS) registry number	102786-61-8
Molecular Formula	$C_{1982}H_{3054}N_{560}O_{618}S_{28}$
Molecular weight	~ 50 KDa

Name of the medicinal product

AryoSeven 1.2 mg (60 KIU) – powder and solvent for solution for injection

Reference Product

NovoSeven, from Novo Nordisk

Quantitative and Qualitative composition

1.2 mg Eptacog alfa (activated) per vial (corresponds to 60 KIU/vial).

1 KIU equals 1,000 IU (International Units).

Eptacog alfa (activated) is a recombinant coagulation factor VIIa (rFVIIa), a vitamin K-dependent glycoprotein consisting of 406 amino acid residues (MW approximately 50 kDa), produced in baby hamster kidney cells (BHK Cells) by recombinant DNA technology.

AryoSeven is structurally similar to human plasma-derived Factor VIIa.

After reconstitution with the solvent, it contains approximately 0.6 mg/ml Eptacog alfa (activated).

Each vial of powder of AryoSeven powder consist of Sodium chloride, Calcium chloride dihydrate, Glycylglycine, Polysorbate 80 and D-Mannitol.

Therapeutic indications

Congenital haemophilia with inhibitors to coagulation factors VIII or IX > 5 Bethesda Units (BU)

Congenital haemophilia with a high anamnestic response to factor VIII or factor IX administration

Acquired haemophilia

Congenital FVII deficiency

Glanzmann's thrombasthenia

Pharmacological properties

Blood coagulation factors, ATC code: B02BD08

Route of Administration

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