COMPOUND DETAILS NNC0078-0007

FVIIa analogue

NOVO NORDISK COMPOUND SHARING

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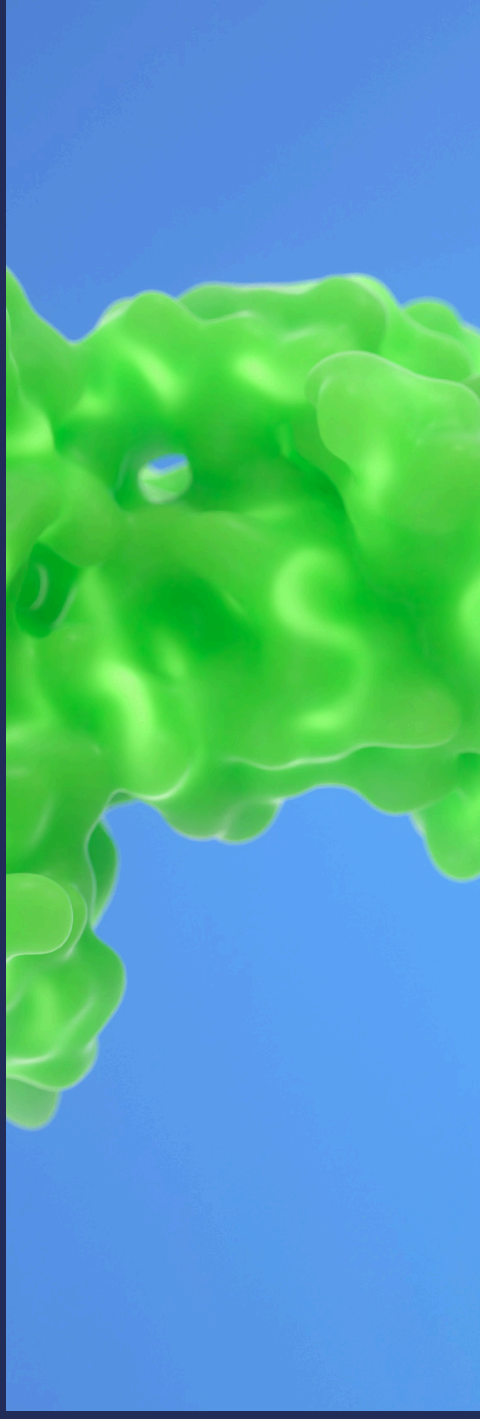
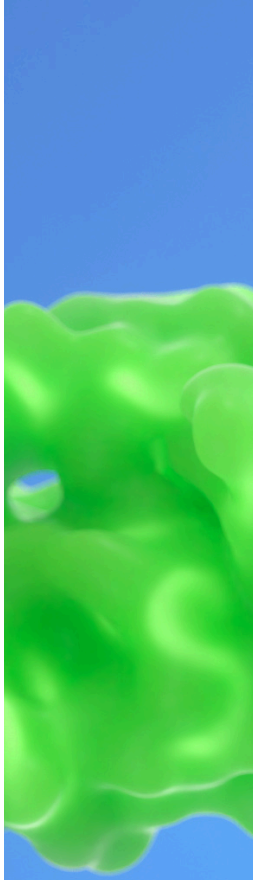
Content



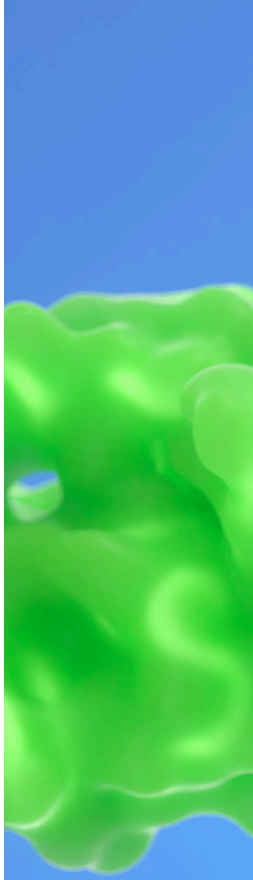
FVIIa analogue



Vatreptacog alfa (see the Persson E et al. reference listed in the reference section below) is a variant of human coagulation factor VIIa (hFVIIa), also known as “rFVIIa analog NN1731” or “$FVIIa_{DVQ}$”. It is a two-chain recombinant protein produced in mammalian cells. The heavy and light chains are connected via a disulfide bond. The LC features an N-terminal Gla-domain containing multiple gamma-carboxy glutaminyl residues as well as two EGF-like domains. The catalytic domain is part of the HC. Compared to hFVIIa, vatreptacog alfa contains three amino acid changes, V158D, E296V, and M298Q. These substitutions result in considerable enhancement of the intrinsic (tissue factor-independent) activity. The enhanced activity of vatreptacog alfa has been demonstrated in numerous in vitro systems and in vivo model mimicking hemophilia. Vatreptacog alfa has been investigated in phase 1, 2, and 3 clinical trials. Vatreptacog alfa was discontinued after phase 3 clinical trial due to anti-drug antibodies (Mahlangu J N et al. et al. - reference section) in a few patients. A post hoc assessment of the immunogenicity of vatreptacog alfa was subsequently performed in collaboration with FDA (see the Lamberth K et al. reference listed in the reference section below).

Category	FVIIa
ID	NNC0078-0007
Amount pr. vial	2.2 mg

Calculated properties



Parameter	NNC0078-0007
pI	5.6
MW average	50 kDa
MW LC	20 kDa
MW HC	30 kDa
A280 (1 mg/ml)	1.37
Glycosylations	Asn145 and Asn322 (complex biatennary)
Max thrombin generation rate	3-10 times higher than rhFVIIa (see fourth reference below)

Structural information

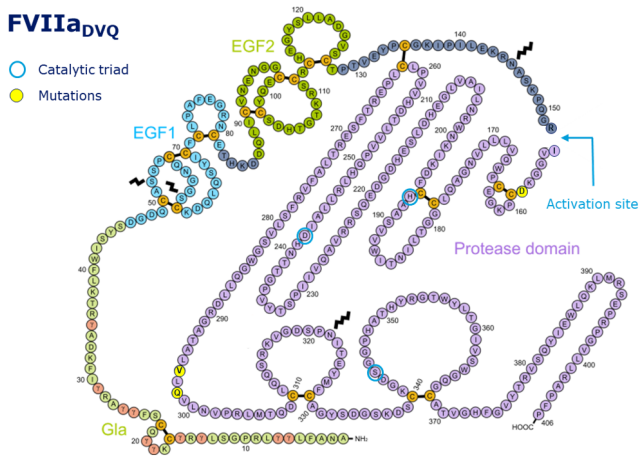
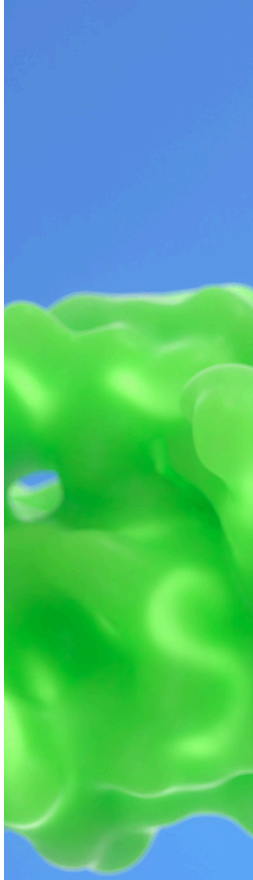


Figure 1

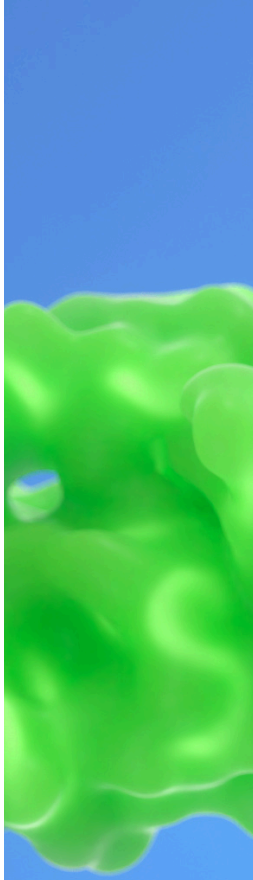
Figure 1

2D structure of vatreptacoq alfa with domains, post-translational modifications, and special residues indicated.

In vitro data



Properties	NNC0078-0007
Content;	2.2 mg/vial
HMWP	2.4%
Total impurities	9.7%
Oxidized forms	2.7%
Heavy chain degradation	4.3%
Gamma-carboxylation	Complies
N-terminal sequence	Complies
Specific activity	1085 U/ug
Bacterial Endotoxin	<0.10 U/mg



Reference Compound

No reference compound available

Compound handling instructions

The freeze dried material can be stored at +5C or below. Reconstitute one vial of Vatreptacoq alfa in 2.1 ml 10 mM histidine, pH 6.0. The reconstituted protein contains various salts and additives.

References

1. Persson E et al.
Vatreptacog alfa from conception to clinical proof of concept.

Seminars in Thrombosis and Hemostasis 2012,38(3):274-281

2. Mahlangu J N et al.
Changes in the amino acid sequence of the recombinant human factor VIIa analog, vatreptacog alfa, are associated with clinical immunogenicity

Journal of Thrombosis and Haemostasis 2015,13(11): 1989-1998

3. Lamberth K et al.
Post hoc assessment of the immunogenicity of bioengineered factor VIIa demonstrates the use of preclinical tools

Science Translational Medicine 2017, 9 (372): eaag1286

4. Allen G A et al.
A Variant of Recombinant Factor VIIa With Enhanced Procoagulant and Antifibrinolytic Activities in an In Vitro Model of Hemophilia

Arteriosclerosis, Thrombosis, and Vascular Biology 2007, 27(3): 683-689