# FACTOR VIIa (Novoseven)

**Factor VIIa also known as Recombinant factor VIIa (rFVIIa) may only be used under the supervision of the haematologist on call.**

All administrations must be reported to the Therapeutic & Drug Utilisation Committee.

**Recombinant Factor VIIa (rFVIIa)**: (NovoSeven) is the recombinant form of activated plasma coagulation Factor VII and is also known as eptacog alfa. rFVIIa is an activated coagulation factor that binds Tissue Factor at sites of tissue injury. The rFVIIA-Tissue factor complex activates Factor X and generates a burst of thrombin, bypassing the initiation steps in coagulation. In the therapeutic doses rFVIIa can attenuate macrovascular and control microvascular bleeding.

Recombinant Factor VIIa (rFVIIa) is Therapeutics Goods Administration (TGA) approved for the control of bleeding and surgery prophylaxis in patients with inhibitors to coagulation factors VIII or IX.

Additionally the TGA designates rFVIIa as an orphan drug for control of bleeding in FVII deficiency, inherited platelet disorders (Glanzmann's Thrombasthenia), and post-partum haemorrhage refractory to conventional therapies.

**Current Formulary Approved indications for rFVIIa at POWH– policy**
**Recombinant Factor VIIa (Novoseven RT) for Life-threatening Bleeding - September 2017**

- Post-partum haemorrhage with coagulopathy not correcting with standard blood products.
- Patients with haemophilia.
- Severe trauma with coagulopathy not correcting with standard blood products.
- Liver failure and coagulopathy not correcting with standard blood products.
- Current usage has decreased with the adoption of ROTEM guided transfusion via the Critical Bleeding Protocol. rFVIIa is still indicated on the protocol after the ROTEM algorithm has been fully utilized but bleeding is still an issue. Consultation with a Haematologist will be required to confirm the indication for its use.

**Non-Formulary Approved indications for rFVIIa**
rFVIIa may be considered in a situation of life-threatening haemorrhage despite adequate platelet and clotting factor replacement.

This may occur in
1. Massively transfused patients (e.g. more than 10 units of packed cells in 24 hours or replacement of blood volume within 3 hours) with ongoing bleeding and coagulopathy.
2. Trauma patients
3. Intractable "surgical" haemorrhage (e.g. post-cardiac bypass, post-aneurysm or vascular surgery, post-liver surgery, post-peritonectomy, post-caesarean, post-partum)
4. Intractable "medical" haemorrhage (e.g. pulmonary haemorrhage).
5. Postpartum haemorrhage
6. Select intra-cerebral haemorrhage if identified within three hours of onset.

**For non-formulary indications a Haematologist MUST be consulted before use of this product and an individual patient use (IPU) approval obtained.**

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## FACTOR VIIa (Novoseven) cont'd

**This policy should be read in conjunction with the:**

- **POST PARTUM HAEMORRHAGE – PREVENTION AND MANAGEMENT LOP**
- **CRITICAL BLEEDING PROTOCOL (CBP)**
- **CLINICAL BUSINESS RULE: Recombinant Factor VIIa for life threatening bleeding for administration guidelines**. **POWH**

**Prior to use of rFVIIa:**

1. Correct coagulopathy
   a. FFP with aim of INR < 1.5 - 2
   b. 10 units of cryoprecipitate if fibrinogen < 1.0g/L
2. Correct thrombocytopenia. Aim for platelets > 50 x $10^9$/L due to coexisting platelet dysfunction
3. Ensure adequate RBC replacement and fluid replacement
4. Consider uterotonic agents, uterine massage, examination under anaesthetic, tranexamic acid.
5. Re-consider surgical bleeding site. Consider B-lynch suture, internal iliac or uterine artery ligation, internal uterine tamponade (e.g. with Bakri Balloon), uterine artery radiological embolisation and tranexamic acid IV.
6. Ensure calcium, acidosis and hypothermia correction. (rFVIIa works best above a pH of 7.2)
7. Delay in recombinant Factor VIIa therapy may reduce efficacy
8. A full blood count and coagulation profile (platelet count, APTT, PT, INR and fibrinogen) should be available immediately prior to the proposed use of rFVIIa.

**Availability and Administration of rFVIIa**

1. Location:
   It is available from POWH blood bank (Ext 29145/29146). Before calling blood bank approval must have been sought from the oncall haematologist AND an 'Authority to issue blood products form' completed. .

NovoSeven is kept in Randwick Blood Bank and use must be authorised by a Haematologist. Recombinant Products are manufactured in laboratories. They do not come from blood. They are made with recombinant DNA technology. These product are supplied by Blood Bank, however aren't theoretically a blood product therefore consent for blood & blood product administration is not required.

NB RHW pharmacy does not hold additional supplies of rFVIIa (NovoSeven) and it is not available in POW pharmacy or the POW and RHW after hours drug cupboard.

2. Dose:
   Give 90 micrograms per kilogram, given as an intravenous bolus injection over 2-5 minutes (1mg for every 11kg body weight). The dose should be rounded to the nearest whole vial to inimize wastage. A second dose may occasionally be required 2-4 hours after the first dose.

**Reconstitution**

rFVIIa is presented as 1mg or 5mg vials which should be stored below $25^0$ C (Do NOT freeze). Novoseven RT® is presented as a powder which must be reconstituted with the specified volume of the provided sterile solvent (solution of L-histidine in water for injection) as follows:-

- 1mg vial of Novoseven RT should be reconstituted with 1.1mL of Histidine solvent.
- 5mg vial of Novoseven RT should be reconstituted with 5.2mL of Histidine solvent.

The vial should be swirled gently until all material is dissolved. The reconstituted volume contains 1mg/mL rFVIIa and appears as a clear colourless solution.
Refer to Product information for further details.

## FACTOR VIIa (Novoseven) cont'd

**Pharmacokinetic Properties of rFVIIa**
After intravenous bolus injection, the time to peak concentration is 15 minutes. The elimination half-life is 2 – 3 hours.

**Precautions**
The administration of rFVIIa may be associated with thrombotic complications, including myocardial infarction, stroke, or venous thromboembolism. The risk of thrombotic complications is likely to be greatest in patients with a recent history of arterial or venous thrombosis, advanced atherosclerotic disease or disseminated intravascular coagulation. Any adverse reaction should be reported to Pharmacy, ADRAC and IIMS.

**Cost**
The drug cost at September 2015 was $1359 per 1mg vial and $6796 per 5mg vial. The cost of administration of rFVIIa is charged to the cost centre of the ward the patient is on. A single bolus for an 80kg adult (7mg dose) costs $9514

**References**

1. Eptacog alfa (Novoseven RT) – Consumer Medicine Information. Novo Nordisk Pharmaceuticals. September 2014
2. Eptacog alfa (Novoseven RT) – Product Information. Novo Nordisk Pharmaceuticals. Last updated 26th May 2017.
3. Phillips LE, McLintock C, Pollock W, Gatt S, Popham P, Jankelowitz G, et al. Recombinant activated factor VII in obstetric hemorrhage: experiences from the Australian and New Zealand Haemostasis Registry. *Anesthesia & Analgesia* 2009;109(6):1908-15.
4. Welsh A, McLintock C, Gatt S, Somerset D, Popham P, Ogle R. Guidelines for the use of recombinant activated factor VII in massive obstetric haemorrhage. *Australian & New Zealand Journal of Obstetrics & Gynaecology* 2008;48(1):12-6.

**RISK RATING**: High. Review in 2 years
**NATIONAL STANDARD:** Standard 4 - Medication Safety

**REVISION & APPROVAL HISTORY**
Reviewed and endorsed Therapeutic & Drug Utilisation Committee 1/7/19
Approved Quality & Patient Care Committee 16/2/17
Reviewed and endorsed Therapeutic & Drug Utilisation Committee 13/12/16
Approved Quality & Patient Safety Committee 19/11/15
Reviewed and endorsed Therapeutic & Drug Utilisation Committee 13/10/15
Approved Quality & Patient Safety Committee 20/11/14
Reviewed and endorsed Therapeutic & Drug Utilisation Committee 14/10/14
Approved Quality & Patient Safety Committee 157/10
Reviewed and endorsed Obstetric Clinical Guidelines Group June 2010
Approved Quality Council 15/12/03

**FOR REVIEW : SEPTEMBR 2021**