

Factor VIIa: Off-label Usage for Adults at UKHealthcare



Coagulopathy, either drug related or multifactorial, is a major contributing factor to bleeding related mortality in a variety of clinical settings. Standard therapy for control of coagulopathy related bleeding has traditionally been limited to the utilization of available blood products and reversal of drug-induced anticoagulation. Recombinant activated factor VII (rFVIIa) is a prothrombotic agent that is approved for the treatment of bleeding in hemophilia patients that has been utilized in refractory bleeding in patients that demonstrate a severe coagulopathy. rFVIIa is an effective prothrombotic agent, but at present the most appropriate indications and dosing scheme for off-label indications is not known. The extent and frequency of serious adverse events has also not been fully elucidated, but it has become more and more clear that there is a significant risk of thromboembolic events, both arterial and venous, following the administration of rFVIIa.

Given the catastrophic nature of bleeding secondary to severe coagulopathy and the uncertain nature of implementing rFVIIa therapy in this setting, UKHealthcare has developed the following guidelines to standardize the utilization, dosing, monitoring, and dispensing of rFVIIa for off-label usage in adult patients. This document describes the two primary facets of these guidelines, which include a list of reasonable indications and associated doses and the process by which pharmacy services will facilitate the ordering, delivery, preparation, and dosing of the agent.

Approved Indications and associated suggested dosing

The P&T committee in consultation with representatives from a variety of medical and surgical services has compiled a list of the indications for which rFVIIa could be a reasonable option during the management of severe, refractory coagulopathy associated with bleeding. The patient should have ongoing excessive intractable coagulopathic bleeding (not simply a history of massive transfusion) and all surgical and endovascular techniques should be used as appropriate. Ideally the site of bleeding should be observable or the amount of bleeding measurable and the patient must be deemed otherwise salvageable. In addition, the literature will be reviewed on a regular basis to update this guideline as new information emerges.

Dosing will be adjusted by pharmacy services such that it results in the usage of a complete vial. Based upon the half life and the physiologic effect of the agent, rFVIIa can be redosed within 15-60 minutes of the original dose if there is no response or a less than adequate response to the initial dose. There are several other factors that should be considered prior to the administration of rFVIIa, included in the list below. The clinical pharmacist responding to the request for rFVIIa is responsible for addressing these things with the patient care team.

In addition, one should be cautious of use in patients who are thought to be at increased risk for thromboembolic complications : DIC, advanced atherosclerotic disease, crush injury, septicemia, history of TE, vascular grafts, patients on ECMO or VADs, patients with prosthetic heart valves, sepsis, endotoxemia, sickle cell disease, unstable CAD, Cerebrovascular disease, and those > 64 years of age.

Consider prior to administration of rFVIIa:

1. Whenever possible the decision, rational, and unknown benefits and risks discussed with next- of- kin.
2. Correct pH (FVII activity decreased as much as 90% at pH of 7.0)
3. Correct temperature (FVII activity decreased by 20% at temperature of 33°C)
4. Maintain adequate circulating platelets and fibrinogen
5. Discontinue all antiplatelet/anticoagulants. (Utilize appropriate reversal agents if available)
6. Utilize traditional treatment modalities (blood products, reversal agents, surgical control, etc)
7. Consider Hematology consult.

Dosing Recommendations for Off-label Factor VII Indications	
UK Healthcare General Dosing Scheme for Off-label Indications	
Diffuse alveolar hemorrhage (BMT patients)	30 mcg/kg repeated q15min to a max dose of 90 mcg/kg or *90 mcg/kg as a single dose (based on attending MD discretion)
End stage liver disease (bridge to transplantation only)	
Trauma related coagulopathy	
Refractory perioperative bleeding (non-cardiac)	
Life threatening refractory hemorrhage of any cause in a severely coagulopathic patient	
Patient population/Indication Specific Recommended Dosing Regimens	
Reversal of <u>Therapeutic Anticoagulation</u> during a Life-threatening Bleeding Event Warfarin Direct Thrombin inhibitors (argatroban, bivalirudin) Fondaparinux	1 mg (should be given with FFP and phytonadione) 1 mg 1 mg
Intracranial Hemorrhage secondary to oral anticoagulants	1 mg (~10-20 mcg/kg)
Refractory perioperative bleeding for Cardiothoracic surgery	1 mg (~10-20 mcg/kg) repeated as necessary

The available vial sizes will be changing from 1.2, 2.4, and 4.8mg to 1, 2, and 5 mg in the next few months. In the interim, please use the 1.2mg vial for the 1 mg doses.

*If the attending involved in the case determines that the patient would benefit from a large bolus dose and would not tolerate the observation period between doses, a one-time dose of 90 mcg/kg is an acceptable option.

Procedure for ordering and dispensing:

1. If ordered via SCM, order “pharmacy to dose Factor VIIa”, select an indication and provide weight. Always order STAT.
2. If verbally ordering. Contact Pharmacy and relay the following: patient name, location, indication, and weight.

Pharmacy Contact Information	
OR Pharmacy	323-7899
Central Pharmacy	323-5641 / 323-5642
Pharm.D. On Call	330-3883
Critical Care Pharmacist	330-4237

3. Pharm.D. will bring the drug to the bedside, discuss with appropriate physician, and prepare the dose for administration. (This includes the Operating room).
4. Pharm.D. will also be responsible for discussing alternative/adjunct therapies as well as factors that might impact the efficacy of the agent.
5. The physician will be asked to assist (the Pharm D with filling out a report form which will briefly summarize the circumstances and indications for the use of rFVIIa, and the short term outcome

Followup Procedure

1. All cases will be audited by the Adhoc rFVII committee, who will report back to the P&T committee at least every 3 months or sooner if indicated, until further notice.