Tertiary/Quaternary Level Essential Drug List
Medication Review Summary

MEDICATION: Recombinant Factor VIIa

INDICATION:

1. Adjunct in the management of coagulopathy following trauma with massive bleeding or the need to enter the massive transfusion protocol.
2. Management of intracranial haemorrhage (ICH) within 4 hours of onset.
3. Intractable bleeding after cardiac surgery.

Clinical background

Recombinant factor VIIA is registered for use in haemophiliac patients, however over the last few years it has been used in the clinical setting in public hospitals for management of intractable bleeding in trauma and cardiac surgery as well as intracranial haemorrhage. The cost associate with the use of the drug has gone up significantly.

RESULTS:

The rFVIIa did not have any effect on mortality in all the 3 indications. It did however reduce respiratory distress syndrome.

EFFICACY:

1. **Trauma:**
   a. **South African Based Randomised Controlled studies: Boffard et al, Rizoli et al[1, 2]**

   rFVIIa reduced the risk of multiple organ failure, respiratory distress syndrome. There was *no difference in mortality between treatment and placebo group*. A sub-analysis of the Boffard study by Rizoli et al, analyzed outcomes

   in severe trauma patient, *similar results including no difference in ventilator and ICU free days were reported*. Patients receiving rFVIIa required 3 **units less** blood compared to controls.

   b. **Systematic reviews of RCTs: Lin et al, Yank et al[3,4]**

   There was no difference in mortality between the treatment and placebo group. The treatment reduced the risk of acute respiratory distress syndrome (ARDS) but not multiple end-organ damage (MOF).
2. **Intracranial Hemorrhage: Systematic Reviews Al-Shashi, Yuan et al, Yank et al [4, 5, 6][4,5,6,]**

   rFVIIa did not significantly reduce death or dependence on the modified Rankin Scale (grades 4 to 6) within 90 days of ICH (RR 0.91).
3. **Cardiac Surgery: Yank et al [4]**

   rFVIIa did not significantly reduce death.
4. **All cause - Prophylactic treatment: Simpson et al [7]**

   rFVIIa did not significantly reduce death; Non-significant trends of thromboembolic events, however, there was a significant increase in arterial thromboembolic events.
5. **All-cause treatment: Simpson et al [7]**

   rFVIIa did not significantly reduce death; non-significant trends of thromboembolic events, however, there was a significant increase in arterial thromboembolic events.

SAFETY CONCERNS:

The recombinant rFVIIa is associated with increased risks of thromboembolic events

RECOMMENDATION

rFVIIa is not recommended for treatment of intracerebral haemorrhage, and intractable bleeding in trauma and cardiac surgery.

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[1] Boffard KD, et al. Recombinant factor VIIa as adjunctive therapy for bleeding control in severely injured trauma patients: two parallel randomized, placebo-controlled, double-blind clinical trials. *J Trauma*. 2005; 59(1): 8-15.

[2] Risoli SB, et al. Recombinant Activated Factor VII as an djunctive therapy for bleeding control in severe trauma patients with coagulopathy: subgroup analysis from two randomized trials. *Critical Care*. 2006; 10(6): R178.

[3] Lin Y, et.al.. Use of recombinant factor VIIa for the prevention and treatment of bleeding in patients without hemophilia: a systematic review and meta-analysis. *Canadian Medical Association Journal*. 2010; 183(1).

[4] Yank V, et al. Systematic Review: Benefits and Harms of In-Hospital Use of Recombinant Factor VIIa for Off-Label Indications. *Ann Intern Med*. 2011; 154(8): 529-540.

[5] Al-Shashi Salman R. Haemostatic drug therapies for acute spontaneous intacerebral haemorrhage. *Cochrane Database Systematic Review*. 2009; 7(4): CD005951.

[6] Yuan ZH, et.al. A meta-analysis of the efficacy and safety of recombinant activated factor VII for patients with acute intracerebral haemorrhage without haemophilia. *J Clin Neurosci*. 2010; 17(6): 685-693.