Recombinant Activated Factor VII in Treatment of Hemorrhage Unrelated to Hemophilia: A Systematic Review and Economic Evaluation

Technologies and Conditions
Hemostatic (stops bleeding) agent recombinant activated factor VII (eptacog alfa or rFVIIa) used for the off-label management of uncontrolled bleeding in individuals without inherited bleeding disorders or hemophilia. Recombinant activated factor VII has the approved indication in Canada to control bleeding in hemophilia (A or B) patients having inhibitors to clotting factors VIII or IX. It has also been used, in clinical practice, as a hemostatic agent for other conditions.

Issue
Funding for rFVIIa is provided through the provincial and territorial budgets, with distribution to hospitals through the Canadian Blood Services. There is little cost incentive to control usage and studies suggest that the majority of use is off-label, for which its impact on health care is unclear.

Methods and Results
To assess the implications of select off-label use of rFVIIa for uncontrolled bleeding, a systematic review of clinical and economic literature was performed. Information from the literature review provided data for an economic evaluation and budget impact analysis. The economic evaluation focused on comparisons of routine use of rFVIIa compared to standard care without rFVIIa, from the perspective of the publically funded health care system. The budget impact of using rFVIIa for blunt trauma was from the Canadian Blood Services perspective.

Statistically significant differences in mortality, functional, and clinical outcomes, and dose-response relationships could not be found. The economic findings suggest that additional clinical research is of value.

Implications for Decision Making
• The impact on patient health is unclear. The potential for harm or benefit with rFVIIa could not be ruled out, compared with usual care, for off-label use in uncontrolled bleeding due to blunt or penetrating trauma, surgery unrelated to trauma, gastrointestinal bleeding, or intracerebral hemorrhage. Based on available evidence, dose-dependant safety and efficacy relationships for rFVIIa were inconsistent.

• Reimbursement decisions are highly uncertain. A reliable estimate of a tradeoff of health for resources was not possible given the existing clinical findings in patients with severe bleeding blunt trauma. Additional clinical research appears to be a better use of public funds.

• Routine use of rFVIIa in severe bleeding blunt trauma could lead to substantial expenditure. As many as 6,416 cases of severe blunt trauma may be eligible for treatment with rFVIIa in Canada each year leading to incremental costs of between C$ 48.3 and C$211.8 million dollars.

This summary is based on a comprehensive health technology assessment available from CADTH’s website (www.cadth.ca): Pohar SL, Tsakonas E, Murphy G, Anderson D, Carney D, Moltzan C, Banks R. Recombinant activated factor VII in treatment of hemorrhage unrelated to hemophilia: a systematic review and economic evaluation [Technology report number 118]