Economical comparison of APCC vs. rFVIIa for mild-to-moderate bleeding episodes in haemophilia patients with inhibitors

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
The study assessed the cost-effectiveness of activated prothrombin complex concentrates versus recombinant factor VIIa for treatment of mild-to-moderate bleeding in haemophilia patients with inhibitory antibodies to clotting. The authors concluded that first-line activated prothrombin complex concentrates was as effective as recombinant factor VIIa but led to third-party payer cost-savings. The study used a conventional cost-effectiveness framework that relied on the assumption of equal efficacy/safety for both treatments. The authors’ conclusions appear robust.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The study assessed the cost-effectiveness of activated prothrombin complex concentrates versus recombinant factor VIIa in the treatment of mild to moderate bleeding in haemophilia patients with inhibitory antibodies to clotting.

Interventions
The two first-line interventions compared were activated prothrombin complex concentrates (75 IU/kg \(^{-1}\) two infusions) and recombinant factor VIIa (90μg/kg \(^{-1}\) three infusions). After first-line treatment failure patients might continue on the same treatment, doubling the initial dose or switching to another drug.

Location/setting
USA/community (home).

Methods
Analytical approach:
The analysis was based on a decision-tree model with a short-term horizon. The authors stated that the perspective of the third-party payer was adopted.

Effectiveness data:
Clinical data for the model were from a literature review and expert opinion. The efficacy of treatments was the key input of the model, which was assumed to have been similar for each drug (existing clinical trials failed to demonstrate differences in the relative efficacy and safety of the two treatments). Information on the quality of the included data sources was not given. Experts’ opinions were used to estimate the switch rate between the two drugs.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
No summary benefit measure was used because a clinical trial found that there was no conclusive evidence that one product was superior to the other for efficacy or safety. A cost-minimisation analysis was performed instead.

Cost data:
The costs of drugs and hospitalisations (including physician fees) were included. Resource use was based on clinical trials for drug doses and experts’ opinions. Unit costs were based on US Medicare databases. A cost-to-charge ratio was
calculated for hospitalisation costs. Costs were in US $. The price year was 2009.

Analysis of uncertainty:
One-way and two-way sensitivity analyses were carried out to investigate uncertainty. Ranges for each parameter were based on ±20% of the base-case value or clinically reasonable estimates.

Results
Efficacy rates were assumed to be 85% for either treatment.

Expected medical costs to treat a bleed were $25,969 with activated prothrombin complex concentrates and $35,838 with recombinant factor VIIa.

The most influential inputs were doses of both drugs and efficacy of activated prothrombin complex concentrates. Recombinant factor VIIa could reach cost neutrality when the efficacy of activated prothrombin complex concentrates was as low as 60% or recombinant factor VIIa was infused only twice for each line, or activated prothrombin complex concentrates was infused three times for each line. A reduction of one-third in the unit price of recombinant factor VIIa or an increase of 50% in the unit price of activated prothrombin complex concentrates would make recombinant factor VIIa the preferred option.

Authors' conclusions
The authors concluded that first-line activated prothrombin complex concentrates treatment was as effective as recombinant factor VIIa but led to cost-savings to a third-party payer for home treatment of mild-to-moderate haemophilia. The authors noted that further head-to-head comparative studies should be carried out to investigate the cost-effectiveness of these two treatments.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the two available treatments for this specific patient population were considered. They were likely to be relevant in other settings.

Effectiveness/benefits:
The clinical analysis was based on the assumption that the two treatments had the same efficacy and safety profiles. This was based on the fact that two clinical trials had shown no statistically significant differences. However, the use of a cost-minimisation analysis might not have been appropriate as one of the agents may have work better for some patients and/or for some bleed sites. Experts' opinions were used to supplement published studies where there was lack of valid data.

Costs:
The economic analysis was consistent with the perspective of the third-party payer for data sources and types of costs included. Unit prices were presented and drug dosages were clearly reported, which enhanced the economic transparency of the study. The impact of variations in economic estimates was extensively investigated in the sensitivity analyses. Reflation exercises in other time periods would be possible as the price year was included.

Analysis and results:
A description of key pathways and assumptions of the decision tree was provided. Uncertainty was investigated using a deterministic approach that considered variations in all inputs of the model. The results were clearly reported. An incremental cost-effectiveness ratio was not calculated because of the cost-minimisation framework of the analysis. The authors stated that several previous economic evaluations had shown contrasting results due to the use of different efficacy data or dosage assumptions. The model results were strongly influenced by the number of dosages assumed to treat a bleeding episode with the two products. Applicability of data to other settings was not explicitly addressed; the results appear to be specific to the US context.

Concluding remarks:
The study used a conventional cost-effectiveness framework that relied on the assumption of equal efficacy/safety of the two anti-inhibitor coagulant complex treatments. The authors' conclusions appear robust.
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