INAHTA Brief

Issue 2019/031

Title Extended half-life clotting factor concentrates for treatment of haemophilia A and B

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Reference Milverton, J, Vogan, A, Newton, S, Parsons J, Schubert, C, Merlin, T. (2018). Extended half-life clotting factor concentrates for the treatment of haemophilia A and B. MSAC Application 1511, Assessment Report. Commonwealth of Australia, Canberra, ACT.

Aim

To assess the clinical evidence, and perform an economic analysis, to inform public funding for extended half-life (EHL) clotting factors VIII (for the treatment of haemophilia A) and IX (for the treatment of haemophilia B) products through the National Blood Authority (NBA) in Australia.

Conclusions and results

Safety: Haemophilia A

No studies directly compared the safety of standard half-life (SHL) products and EHL products, however the overall rate of adverse events due to EHL products was low. There were no data to suggest that EHL products are associated with a higher rate of adverse events than SHL products.

Safety: Haemophilia B

There were no data to suggest that EHL products are associated with a higher rate of adverse events than SHL products.

Effectiveness: Haemophilia A

The primary clinical outcome of interest was annualised bleeding rate (ABR). Four EHL products (BAX 855, BAY 81-8973, N8-GP and rFVIIIFc) provided historical data on bleeding rates of patients when they were receiving SHL factors. In these studies, the ABRs in the patients receiving prophylactic treatment with EHL products were between 11-83% of the rates of patients receiving SHL prophylaxis.

Effectiveness: Haemophilia B

The primary clinical outcome of interest was ABR. All studies comparing prophylaxis with SHL factor IX products (historical data) with prophylaxis with EHL factor IX products (trial data) in adolescents and adults reported that bleeding rates were reduced when using EHL products. Likewise, bleeding rates in those treated on-demand were reduced with EHL products compared to historical bleeding rates in those treated on-demand with SHL products.

Economic analysis

Cost-utility analyses were conducted for patients switching from SHL to EHL prophylaxis. Cost-effectiveness analyses estimated cost per infusion avoided (ICER A$177 for haemophilia A, and A$26 for haemophilia B) and cost per bleed avoided (ICER A$5,235 for haemophilia A and $753 for haemophilia B). For haemophilia A the analyses were most sensitive to the source of data used to inform comparative factor VIII consumption and ABR, and the frequency of SHL factor VIII infusion. For haemophilia B the analyses were most sensitive to the source of data used to inform comparative factor IX consumption and ABR and to utility weights used.

Financial implications were found to be dependent on rate of uptake, change in factor use and price per IU using a market-based approach to estimation.

Recommendations

A decision was made to support the inclusion of EHL products (factors VIII and IX) in the National Products Price List maintained by the NBA. Detailed advice was given on establishing prices for the requested products, relative to the existing SHL products. It was advised that appropriate risk-sharing arrangements be implemented to manage the budget uncertainties associated with the listings.

Methods

A systematic review was performed to update the AHCDO review (Newton et al. 2017). The initial assessment incorporated articles published between 2010 and November 2016, and in-house data or studies provided by companies. For the current update, further searches were conducted up to to February 2018.

Study eligibility was initially determined independently by two people on the basis of the title and abstract. Disagreements were treated conservatively. Agreed criteria were used for selecting studies that reported on the safety, effectiveness and pharmacokinetic profile of EHL factor versus SHL factor concentrates. Company submissions were received by four companies (CSL Behring, Novo Nordisk, Baxalta/Shire and Biogen), and were assessed using the same study eligibility criteria.

Methodological quality of the studies was assessed using appropriate critical appraisal checklists. The majority of studies were found to be of low or moderate risk of bias. The quality of the body of evidence was summarised for each pre-specified outcome according to GRADE methodology (Guyatt et al, 2011). Meta-analyses could not be conducted due to the low quality and heterogenic nature of the data, therefore a narrative meta-synthesis of the data was undertaken.

Further research/reviews required

N/A

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