RECOMMENDATION ON ETRANACOGENE DEZAPARVOVEC (AMT-061) IN THE TREATMENT OF HAEMOPHILIA B

At its meeting of 23 Septembet 2024, the Council for Choices in Health Care in Finland (COHERE Finland) adopted a recommendation on etranacogene dezaparvovec (AMT-061) in the treatment of Haemophilia B.

Etranacogene dezaparvovec (AMT-061), which is a gene therapy medicinal product, is not included in the national range of services for treating severe and moderately severe haemophilia B in adults without a history of antibodies against Factor IX (Factor IX inhibitors). In COHERE Finland's opinion, AMT-061 is a new type of treatment, the long-term effects of which are not yet known. As a single-dose treatment, AMT-061 is extremely expensive, and the presented cost-effectiveness analysis involves considerable uncertainty, especially with regard to the duration of the effect of the treatment.

Etranacogene dezaparvovec (AMT-061) is intended for treating severe and moderately severe haemophilia B in adults who have demonstrated absence of Factor IX inhibitors. Haemophilia B is a congenital bleeding disorder caused by a partial or complete deficiency of coagulation Factor IX (FIX). Haemophilia B is an inherited disorder, and its most severe forms occur almost exclusively in males, with females being carriers. Haemophilia B is a rare disease, and it is estimated that 1 in every 20,000 males born has haemophilia B. Etranacogene dezaparvovec (AMT-061) is a gene therapy medicinal product which has a viral vector containing copies of the gene responsible for producing Factor IX. When the product is administered, the viral vector attaches to liver cells. The viral vector then releases the gene producing Factor IX in the target cell nucleus, which triggers the production of the Factor IX protein.

The marketing authorisation study shows that, once the response to AMT-061 gene therapy treatment had stabilised at 6–18 months post-treatment, 37 per cent of patients

The Council for Choices in Health Care in Finland
PO BOX 33 (Meritullinkatu 8, Helsinki)
00023 GOVERNMENT, Finland
Tel 358 295 16001
www.palveluvalikoima.fi
palveluvalikoima.stm@gov.fi

experienced bleeding episodes within a year, while 74 per cent of patients had bleeding episodes prior to the treatment. At 18 months post-treatment, 50 per cent of patients experienced bleeding episodes. When patients were on Factor IX replacement therapy, they had an average of four bleeds per year, while they had an average of 1.5 episodes per year following AMT-061 gene therapy. The differences in the annualised bleeding rates prior to and 3 years after gene therapy were statistically significant. The total number of bleeds prior to gene therapy was 136 per six months, and after therapy, the number of bleeds was 55 during the first year, 48 during the second year and 37 during the third year. In addition, the annual number of spontaneous bleeds and joint bleeds decreased statistically significantly. The results obtained with secondary endpoints supported the evidence of the efficacy of this gene therapy; it was observed that Factor IX activity levels increased as a result of gene therapy, and the use of Factor IX replacement therapy decreased significantly. The endpoints have remained similar during the three-year follow-up period. Despite the improvements observed with clinical endpoint indicators, no changes were observed in the quality of life experienced by patients.

All patients who participated in the marketing authorisation study experienced at least one adverse event. Most of the adverse reactions were mild or moderate. Severe adverse reactions were reported in 4 per cent of the patients. The most frequently reported adverse effects were joint pain, headache, nasopharyngeal inflammation, fatigue and an increased level of alanine aminotransferase. A sustained increase in the levels of antibodies to the viral vector was observed in all patients treated with gene therapy. The risks of gene therapy treatment may include that viral vector integration into human cells may cause malignant changes in tissues.

The greatest benefit of the AMT-061 gene therapy treatment is the costs of Factor IX replacement therapy that are saved over the years. Thus, the main uncertainty factor is the duration of the effect of the gene therapy. In the model by the marketing authorisation holder, the duration of the therapeutic effect is estimated over a timespan of 59 years. However, the currently available observation data on the duration of the therapeutic effect covers only 3–4 years. The patient-specific cost of the AMT-061 treatment (EUR 2.8 million) is more than ten times higher than the annual cost of the Factor IX replacement therapy (about EUR 216,00 per patient a year) at public list prices.

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FI-00023 GOVERNMENT, Finland
Tel. +358 295 16001
www.palveluvalikoima.fi
email: palveluvalikoima.stm@gov.fi

This is a summary of a recommendation adopted by the Council for Choices in Health Care in Finland (COHERE Finland). The actual recommendation and the related background material are available in Finnish on the website of COHERE Finland under Valmiit suositukset. The summary of the recommendation is also available in Swedish and English on the website.

The Council for Choices in Health Care in Finland (COHERE Finland) works in conjunction with the Ministry of Social Affairs and Health, and its task is to issue recommendations on services that should be included in the range of public health services. Further information about service choices in healthcare is available on the COHERE Finland website.

Ministry of Social Affairs and Health

The Council for Choices in Health Care in Finland
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