RECOMMENDATION ON VALOCTOCOGENE ROXAPARVOVEC (BMN 270) IN THE TREATMENT OF SEVERE HAEMOPHILIA A

At its meeting of 27 August 2024, the Council for Choices in Health Care in Finland (COHERE Finland) adopted a recommendation on valoctocogene roxaparvovec (BMN 270) in the treatment of severe haemophilia A.

Valoctocogene roxaparvovec (BMN 270), which is a gene therapy medicinal product, is not included in the national range of services for treating severe haemophilia A in adults without a history of Factor VIII inhibitors and without detectable antibodies to adeno-associated virus serotype 5 (AAV5). In COHERE Finland's opinion, BMN 270 is a new type of treatment, the long-term effects of which are not yet sufficiently known. As a single-dose treatment, BMN 270 is very expensive, and the presented cost-effectiveness analysis involves considerable uncertainty, especially with regard to the duration of the effect of the treatment.

Valoctocogene roxaparvovec is intended for treating severe haemophilia A in adult patients without a history of Factor VIII (FVIII) inhibitors and without detectable antibodies to adeno-associated virus serotype 5 (AAV5). Haemophilia A is a congenital bleeding disorder caused by a partial or complete deficiency of Factor VIII. Haemophilia A is an inherited disease, and its most severe forms occur almost exclusively in males, with females being carriers. It is estimated that the number of people with haemophilia A in Finland is 380, of whom 60 per cent have the severe form of the disease.

Valoctocogene roxaparvovec (BMN 270) is a single-infusion gene therapy that is meant for patients with severe haemophilia A. Its operating mechanism is based on the human Factor VIII (F8) gene that is contained in the AAV5 viral vector. When the gene therapy product is administered, the viral vector attaches to liver cells. The viral vector then releases the gene producing Factor VIII in the target cell nucleus, which triggers the

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production of the Factor VIII protein. The Factor VIII protein replaces the missing coagulation Factor VIII needed for effective haemostasis.

In the marketing authorisation study, treatment with BMN 270 reduced the annual number of treated bleeds from an average of 4.83 bleeding episodes at baseline to 0.78 bleeding episodes after the first follow-up year and to 0.75 bleeding episodes after the second follow-up year. The study found a 98.6 per cent decrease in the use of Factor VIII replacement therapy within the study population after the first year and a 98.2 per cent decrease after the second year when compared to the baseline situation. One year after a single dose of BMN 270, the median Factor VIII activity level in the study population was 23.92 IU/dl, while the corresponding value was 11.65 IU/dl in the second follow-up year. In the third year, the median Factor VIII activity level was 8.4 IU/dl.

Indirect comparisons made it possible to compare bleeding episodes after the BMN 270 treatment to the corresponding values of Factor VIII replacement therapy and emicizumab. As regards Factor VIII replacement therapy, the differences in the annualised bleeding rates were comparable to the results of the marketing authorisation study on BMN 270 gene therapy. Treatment with BMN 270 also reduced the number of bleeding episodes compared to emicizumab treatment. All patients participating in the marketing authorisation study experienced at least one adverse event during the first follow-up year. The most significant observed risk was liver damage following BMN 270 treatment, which required corticosteroid treatment.

It is estimated that 46 of the 380 patients with haemophilia A in Finland are suitable for treatment with BMN 270, and a total of 25 of them would be treated within the first five years. The medicine costs of this gene therapy are substantially higher than the patient-specific annual costs of replacement therapy and emicizumab treatment. The costs of BMN 270 treatment are incurred immediately at the start of treatment on a one-off basis, whereas the costs of regular haemophilia A treatments are accrued over time. Because it is uncertain how long the treatment effect lasts, it is also unclear what the long-term budget impact is.

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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 d 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

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