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Our reference
2023004477

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Date 9 January 2025
Subject Package advice for the package lock drug efanesoctocog alfa (Altuvoct®) for haemophilia A.

Dear Ms Agema,

The National Health Care Institute is hereby advising you about the assessment of efanesoctocog alfa (Altuvoct®) for treating haemophilia A. The reason for this advice was efanesoctocog alfa being placed in the lock procedure for expensive medicinal products.

Haemophilia A is a rare, hereditary clotting disorder. Due to a deficiency of coagulation factor VIII, the blood does not clot properly. As a result, haemophilia patients have a greater risk of haemorrhages and bruising. There are about 1400 haemophilia A patients in the Netherlands. Patients can be treated prophylactically with products containing factor VIII or with emicizumab. In addition, factor VIII products are also used for on-demand treatment of haemorrhage or breakthrough bleeding.

Registered indication
Efanesoctocog alfa (Altuvoct®) is indicated for treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency). The medicinal product can be used for all age groups.

Claim by the marketing authorisation holder
Efanesoctocog alfa (Altuvoct®) when used for treatment and prophylaxis of bleeding in patients of all ages with haemophilia A, has a therapeutic effect comparable to the standard treatment with emicizumab (Hemlibra®).

Because the factor VIII products are also deemed to be the standard prophylactic treatment and these products can – like efanesoctocog alfa – be used as on-demand treatment, the National Health Care Institute has also assessed the value of efanesoctocog alfa as compared to the factor VIII products. One aspect of this is that the National Health Care Institute previously determined that emicizumab has a therapeutic effect that is at least comparable to the factor VIII products when used as a prophylactic treatment in haemophilia A.

Package advice
The National Health Care Institute advises you to include efanesoctocog alfa (Altuvoct®) in the basic health insurance package for the the licensed indication

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in its entirety, i.e. treatment and prophylaxis of bleeding in patients with haemophilia A, provided that the price negotiations successfully deliver a net price that does not exceed that of the existing standard treatment with factor VIII products. This advice is in line with previous advisory reports for emicizumab. The National Health Care Institute has determined that efanesoctocog alfa meets the legal criterion of 'established medical science and medical practice' for the indication stated. For prophylaxis and treatment of bleeding, efanesoctocog alfa has a therapeutic effect that is at least comparable to the factor VIII products. For prophylaxis of bleeding, efanesoctocog alfa has a therapeutic effect comparable to emicizumab.

We have explained the preparation of this package advice below.

General

At your request, the National Health Care Institute assessed whether care should be part of the basic healthcare package from the perspective of being paid from joint premiums.

The National Health Care Institute assesses against the four package criteria[1] of effectiveness[2], cost-effectiveness[3], necessity[4] and feasibility[5]. The Scientific Advisory Board (WAR) advises the National Health Care Institute on the (scientific) basis and the conclusion of the assessment. Stakeholders are consulted during the process.

Comprehensive weighting of package criteria

Effectiveness

Established medical science and medical practice

The results of the non-randomised, open-label, phase 3 study XTEND–1 in adults with severe haemophilia A show that efanesoctocog is at least equally effective in preventing bleeding, as compared to the factor VIII products. Based on the mechanism of action, the National Health Care Institute expects that efanesoctocog alfa will also be effective in patients with moderately severe haemophilia A, despite these patients not having been included in the XTEND–1 study. The results of the XTEND–1 study show moreover that efanesoctocog alfa can also be used as an on-demand treatment for haemorrhage and breakthrough bleeding, as well as in the perioperative setting. The side-effect profile of efanesoctocog alfa is comparable to that of the factor VIII products. The results of the XTEND-kids study confirm that this medicinal product can also be used in children.

Given that previous assessments by the National Health Care Institute concluded that prophylaxis by emicizumab and by factor VIII were therapeutically

[1] *Pakketbeheer in de praktijk 4* (Real-world package management 4, 2023). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl.

[2] Assessment of the established medical science and medical practice (2023). National Health Care Institute. Via www.zorginstituutnederland.nl.

[3] Cost-effectiveness report (2015). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl.

[4] Necessity is related to both the medical need due to the severity of a disease for the patient (burden of disease) and the need to insure something. See the report on real-world package management 4 (2023).

[5] The package criterion of feasibility deals with whether it is feasible or sustainable to include a specific form of care in the basic healthcare package. It is therefore mainly a test of various implementation aspects, such as the healthcare organisation, the support base, ethical and legal aspects, budget impact, etc. See the report on real-world package management 4 (2023).

comparable, the National Health Care Institute also deems efanesoctocog alfa to be an alternative that is therapeutically comparable to prophylaxis with emicizumab.

The National Health Care Institute concludes that efanesoctocog alfa meets established medical science and medical practice for the indication mentioned above. For prophylaxis and treatment of bleeding, the therapeutic value of efanesoctocog alfa is at least comparable with factor VIII. For prophylaxis of bleeding, the therapeutic value of efanesoctocog alfa is at least comparable to emicizumab.

Cost-effectiveness
Because of the comparable therapeutic value, an evaluation of the cost-effectiveness is not necessary.

Budget impact analysis
The National Health Care Institute estimates that 139 patients will be treated prophylactically and 251 on demand with efanesoctocog alfa for haemophilia A in year 3 after inclusion in the basic healthcare package. The total costs per patient per year are €67,170 to €214,865 for prophylactic treatment and €1,288 to €4,120 for on-demand treatment. These costs vary depending on the patient's age and weight. This results in macro costs of €27.2 million for prophylactic treatment and €940,648 for on-demand treatment in the third year.

When substitution of the factor VIII projects and emicizumab is also taken into account, the resulting budget impact (based on list prices) in year 3 is a saving of €28.3 million. The National Health Care Institute emphasises, however, that the negotiated prices for the factor VIII products and emicizumab will be considerably lower than the list prices. This means that the budgetary impact of efanesoctocog alfa will be higher in reality. In addition, there is uncertainty about the market penetration.

Should you need any further information, please do not hesitate to contact us. The assessment reports have been added as annexes (pharmacotherapeutic report and budget impact analysis).

Yours sincerely,

Mark Jansen
Chair of the Executive Board

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