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Our reference
2023030148

Date 28 July 2023
Re: Package advice eptinezumab (Vyepti®)

Dear Mr Kuipers,

In this communication, the National Health Care Institute advises you about eptinezumab (Vyepti®) for the treatment of adult patients with therapy-resistant chronic migraine (CM). Eptinezumab (Vyepti®) is an *inpatient* medicinal product. The reason for this advice was the placing of eptinezumab (Vyepti®) in the lock procedure for expensive medicinal products.

The National Health Care Institute has concluded that eptinezumab (Vyepti®) meets the legal criterion of 'established medical science and medical practice' for this indication. The therapeutic value of eptinezumab (Vyepti®) has been determined to be comparable with the 3 *outpatient* CGRP inhibitors [erenumab (Aimovig®), fremanezumab (Ajovy®) & galcanezumab (Emgality®)], which are included in the GVS under specific conditions for the treatment of patients with treatment-resistant CM. These medicinal products are administered via subcutaneous injection *(SC)*. A patient can do this at home. Eptinezumab (Vyepti®) must be administered intravenously (IV) at the hospital. This will involve additional hospital costs. The National Health Care Institute recommends that you include the inpatient eptinezumab (Vyepti®) in the basic health care package, provided that the cost of treatment with eptinezumab (Vyepti®) does not exceed the average cost of treatment with any of the 3 *outpatient* CGRP inhibitors. I will explain the advice in more detail below.

General

At your request, the National Health Care Institute assesses whether new care should be part of the standard health insurance package from the perspective of the health insurance package from joint premiums. We consider this both in the scientific sense and in terms of public support, and also review the aspects of efficiency and transparency. The National Health Care Institute assessed eptinezumab (Vyepti®) on the basis of the four package criteria[1]: effectiveness[2], cost-effectiveness[3], necessity and feasibility. The National Health Care Institute is advised by its Scientific Advisory Board (WAR) for the review of data according to

[1] 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, Diemen. Via: www.zorginstituutnederland.nl

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

established medical science and medical practice. Stakeholders were also consulted in this context.

Integral weighting of package criteria
Established medical science and medical practice
Chronic migraine (CM) is defined as a minimum of 15 headache days per month over a period of more than 3 months, of which at least 8 monthly migraine days (MMD). The Dutch Society of Neurology (NVN) guideline *'Medical management of migraine and medication overuse headache'* is the starting point for the pharmacotherapeutic treatment of CM.

Eptinezumab (Vyepti®) is indicated for prophylaxis of migraine in adults who have at least four monthly migraine days. In the reimbursement application, the marketing registration holder claims that eptinezumab (Vyepti®) has a therapeutic value comparable tothe CGRP inhibitors, which are already reimbursed for CM prophylaxis. Eptinezumab (Vyepti®) should therefore be reimbursed under the same conditions. Eptinezumab (Vyepti®) was studied in 3 randomised, double-blind, placebo-controlled studies. The comparison of eptinezumab (Vyepti®) with the already reimbursed CGRP inhibitors is based on the same approach as in their assessment in 2021; *GVS advice CGRP inhibitors erenumab, fremanezumab, galcanezumab (Aimovig®, AJOVY®, Emgality®) for the treatment of patients with episodic and chronic migraine | Report | National Health Care Institute (zorginstituutnederland.nl)*. The pooling results of the relevant studies were compared with the results of the 3 pooled studies with eptinezumab (Vyepti®). The study results were then assessed using the same key outcome parameters, such as 'reduction in the number of monthly migraine days', 'reduction in the number of days with acute attack medication per month', and 'discontinuation due to undesirable effects'. The effects of eptinezumab (Vyepti®) are comparable to the effects of the 3 CGRP inhibitors, which are already reimbursed for CM prophylaxis. Like these 3 CGRP inhibitors, eptinezumab (Vyepti®) does not give rise to any more serious undesirable reactions or discontinuation due to undesirable reactions compared to placebo. As with the 3 already compensated CGRP inhibitors, cardiovascular undesirable reactions should be taken into consideration for eptinezumab (Vyepti®), based on its mechanism of action. Based on this analysis, the National Health Care Institute, advised by its Scientific Advisory Board (WAR), concludes that for prophylaxis of CM eptinezumab (Vyepti®) has an therapeutic value comparable with that of the 3 already reimbursed CGRP inhibitors; see PT report. Eptinezumab therefore meets the established medical science and medical practice.

Budget impact
The Scientific Advisory Board (WAR), the physicians' association and health care insurers expect that patients with treatment-resistant CM will, in general, (continue to) prefer treatment, due to the ease of use of self-administered subcutaneous administration, with the already reimbursed CGRP inhibitors over intravenous treatment with eptinezumab (Vyepti®) in a hospital. According to the physicians' association, quarterly administration does not sufficiently compensate for this disadvantage. Based on this broadly supported observation, the National Health Care Institute estimates that reimbursement of eptinezumab (Vyepti®) as medical care under exactly the same conditions (including equal net price) as the outpatient CGRP inhibitors will result in a very limited budget impact. For this reason, no BIA has been developed. Specifically, it should be considered that

inpatient treatment with eptinezumab (Vyepti®) in a hospital entails higher costs than outpatient treatment with a CGRP inhibitor, which a patient injects subcutaneously at home.

Cost-effectiveness
Because of the similarities in effectiveness (comparable therapeutic value) of eptinezumab (Vyepti®) and the CGRP inhibitors that are already being reimbursed, the National Health Care Institute has not carried out a cost-effectiveness analysis.

Additional conditions and appropriate-use agreements
In consultation with the physicians' association (NVN) and the Netherlands Headache Association (NHV), it was determined, in 2021, that the 3 outpatient CGRP inhibitors are reimbursed for the prophylaxis of CM in adults under the following conditions:

'*Only for an insured person 18 years and older with CM after exclusion or treatment of medication overuse headache and after failing prophylactic treatment with*
1) at least 2 months of topiramate or valproate in adequate doses and
2) at least 2 attempts with botulinum toxin A (6 months) in accordance with the PREEMPT protocol,
unless it is an insured person with CM who, prior to or on 17 September 2021, was already treated with a CGRP inhibitor under a managed access programme.

In addition, appropriate-use agreements (start-stopping criteria) have also been made between health insurance companies and the physicians' association (NVN) as conditions for reimbursement; see PT report, p. 12 - 13. In essence, determining the indication for the treatment of CM with CGRP inhibitors in this context is the responsibility of a neurologist with headache as an area of special interest. The NVN guideline *'Medical management of migraine and medication overuse headache'* is the starting point for the pharmacotherapeutic treatment. The treating neurologist monitors its effect using a headache diary prior to and during treatment. Treatment is evaluated 3-monthly for the first 6 months and at least annually thereafter. Treatment is discontinued in consultation with the patient if: a) after 6 months, there is no reduction in migraine days by at least 30% for at least half of the number of months or if the patient indicates insufficient benefit; or b) there are unacceptable side effects/safety risks.

Final conclusion
Eptinezumab (Vyepti®) has a therapeutic value comparable tothe CGRP inhibitors that are already being reimbursed for CM prophylaxis. It therefore meets the established medical science and medical practice. The National Health Care Institute therefore recommends that you include eptinezumab (Vyepti®) in the health insurance package for an equal net price (including hospital costs) and under exactly the same further conditions and appropriateness arrangements.

Yours sincerely,

Sjaak Wijma
Chairperson of the Executive Board