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National Health Care Institute
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Our reference
2023030600

Date 17 August 2023
Re: Package advice tezepelumab (Tezspire®)

Dear Mr Kuipers,

In the letter of 2 April 2023 [CIBG-23-05284], you requested the National Health Care Institute to carry out a substantive review of whether the medicinal product tezepelumab (Tezspire®) is interchangeable with a product included in the health insurance package, in the context of an application for inclusion on List 1B of the Medicine Reimbursement System (GVS). You also requested an assessment of the therapeutic value for tezepelumab.

The National Health Care Institute, advised by the Scientific Advisory Board (WAR), has now completed this therapeutic value assessment.

Tezepelumab (Tezspire®) is indicated as an add-on maintenance treatment for adults and adolescents 12 years and older with severe asthma who are inadequately controlled despite high dose inhaled corticosteroids in combination with another medicinal product for maintenance treatment.

The conclusion was that tezepelumab meets the criteria of established medical science and medical practice for the aforementioned indication. However, the National Health Care Institute is still working on appropriate use agreements and the preparation of the List 2 conditions. An additional advice on the inclusion of tezepelumab on List 1B of the Health Insurance Act (Rzv) with indication conditions on List 2 of the Rzv will be issued shortly. Until then, patients may already start tezepelumab treatment in the hospital.

Below, I explain our findings.

Background
The biologicals for severe asthma have been considered inpatient care up till now. In recent years, subcutaneous formulations of these medicinal products have become available, allowing the patient to administer these products themselves at home. Tezepelumab is the first new medicinal product in this class to become readily available as a subcutaneous product. Based on the demarcation letter[1],

[1] Ministerie van Volksgezondheid, Welzijn en Sport (2014) Afbakening aanspraak Farmaceutische Zorg en aanspraak Geneeskundige Zorg met betrekking tot geneesmiddelen. Kenmerk: 183496-115412-GMT

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tezepelumab is considered an outpatient medicinal product. The current policy of the Ministry of Health, Welfare and Sport (VWS) does not allow this to be changed at this time.

Outcome of the substantive assessment

Assessment of interchangeability

Based on the criteria for interchangeability, tezepelumab is not interchangeable with other medicinal products included in the GVS. Based on this, tezepelumab cannot be placed on List 1A. Next, the National Health Care Institute assessed whether tezepelumab is eligible for inclusion on List 1B.

Therapeutic value

The assessment differentiated between patients with severe allergic asthma, severe eosinophilic asthma, severe type 2 asthma and severe non-evident type 2 asthma. The effectiveness of tezepelumab was investigated in a double-blind, multicentre randomized phase III study (NAVIGATOR). This study compared the effectiveness and safety of tezepelumab with placebo in patients with severe (uncontrolled) asthma. This study included all the aforementioned subtypes of asthma. This study shows that tezepelumab results in a clinically relevant reduction in asthma exacerbations compared to placebo, as well as a statistically significant improvement in asthma control and quality of life in patients with severe asthma. Based on various direct and indirect comparisons and network meta-analyses of clinical studies, the National Health Care Institute concludes that tezepelumab has a therapeutic value comparable with that of omalizumab, benralizumab, mepolizumab, reslizumab and dupilumab in patients with severe evident type 2 asthma and an added therapeutic value in comparison with placebo in patients with severe non-evident type 2 asthma.

As such, Tezepelumab meets the criteria of established medical science and medical practice as an add-on maintenance treatment for adults and adolescents 12 years and older with severe asthma who are inadequately controlled despite high dose inhaled corticosteroids in combination with another medicinal product for maintenance treatment. Tezepelumab is therefore eligible for inclusion on List 1B.

Budget impact analysis

The National Health Care Institute estimates that 887 patients will be treated with tezepelumab in the third year after market introduction: 720 patients with evident type 2 asthma and 167 patients with non-evident type 2 asthma. A whole year of treatment with tezepelumab costs €13,000 per patient per year, taking into account patient compliance. It is relevant to mention here that the treatment will be administered in the hospital for the first six months. The total cost of treatment with tezepelumab thus reaches €11.6 million in the third year after market introduction. The total additional costs for the use of tezepelumab, taking into account substitution of the other biologicals, amounts to €3.8 million in the third year after market introduction.
For the already available biologicals for severe asthma, price negotiations may have been made which reduce the actual expenditure on these.

Pharmaco-economic analysis

Given the comparable therapeutic value to the other biologicals for severe asthma that are already being reimbursed, and the estimated budget impact, a

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pharmaco-economic analysis is not relevant here. Since tezepelumab has a therapeutic comparable value, the net price of tezepelumab should not exceed that of the already available biologicals.

Reimbursement framework
Prior to and during the assessment, the Dutch Society of Pulmonology and Tuberculosis (NVALT) indicated several times that tezepelumab placement in the outpatient care system creates an uneven playing field compared to the other biologicals. They also indicated that it is of vital importance that tezepelumab, like the other biologicals for severe asthma, is administered in hospital, at least during the first 6 months, especially because of the risk of (severe) allergic reactions. On the basis of these arguments, the National Health Care Institute has agreed with the Association of Dutch Healthcare Insurers (ZN) that, in addition to any inclusion in the GVS, reimbursement should also be arranged via an add-on indication. This means that tezepelumab will receive double funding. Double funding of medicinal products is generally considered undesirable because it creates an uneven playing field within a group of medicinal products, which may, among other things, unfavourably affect the prescribing behaviour of physicians. In this case, ZN indicates that the inpatient costs of these medicinal products are likely to be lower, through price agreements, than the costs of this medicinal product in the GVS.

Further conditions
There are already inpatient care agreements in place for the appropriate use of biologicals for severe asthma. The National Health Care Institute considers it important that clear appropriate use agreements and in particular stop criteria are also determined for the use of tezepelumab. Discussions are currently ongoing with the physicians association and health care insurers on the alignment of these agreements. These agreements are also important for the formulation of List 2 conditions if tezepelumab is included on List 1B of the Rzv. As these discussions are still ongoing and the first 6 months of treatment should take place in the hospital, the National Health Care Institute does not yet provide advice on inclusion in the GVS. Additional advice on this matter will follow after these discussions have been concluded.

Advice
The National Health Care Institute concludes that tezepelumab (Tezspire®) meets the criteria of established medical science and medical practice as an add-on maintenance treatment for adults and adolescents 12 years and older with severe asthma who are inadequately controlled despite high dose inhaled corticosteroids in combination with another medicinal product for maintenance treatment, and is therefore considered insured care.

On the basis of this advice, the health care insurers agree that patients can start the first 6 months of treatment in hospital under the appropriate use arrangements already in place for the other biologicals for severe asthma. Additional advice on inclusion in the GVS and the List 2 conditions will follow as soon as possible and at least no later than 1 January 2024.

Yours sincerely,
Sjaak Wijma
Chairperson of the Executive Board