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2021029109

Our reference
2021029109

Date 11 August 2021
Subject GVS advice on the reassessment of tafamidis (Vyndaqel®)

Dear Ms van Ark,

As you requested on 20 April 2021 (CIBG-20-01735), the National Health Care Institute is advising you about tafamidis 61 mg free acid (Vyndaqel®) for the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy (ATTR-CM) and who are in NYHA class I or II. The reason for this is the manufacturer's request for a reassessment of tafamidis 61 mg free acid.

The National Health Care Institute advises that you should not include tafamidis 61 mg free acid on List 1B of the Medicine Reimbursement System (GVS) unless a price reduction of at least 50% can be negotiated and agreements can be made regarding appropriate and efficient use of the treatment.

General

At your request, the National Health Care Institute assesses whether new care should be part of the health insurance package, and makes a decision based on the health care package paid from joint premiums. The National Health Care Institute has assessed tafamidis 61 mg free acid for the said indication on the basis of the four package criteria[1] of effectiveness[2], cost-effectiveness[3], necessity and feasibility. We take into consideration the degree of certainty that this will be achieved, both in the scientific sense, as well as in terms of public support, and we consider the efficiency and transparency aspects. The National Health Care Institute is advised about package reviews by two independent committees:

- the Scientific Advisory Board for the review of data according to the established medical science and medical practice, and to determine the cost-effectiveness;
- the Insured Package Advisory Committee for the social assessment.

We also consulted stakeholders during the assessment process.

1 Real-world package management 3 (2013). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl

2 Established medical science and medical practice assessment: updated version (2015). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl

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

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Reassessment

At your request (CIBG-20-0120), the National Health Care Institute has previously advised you about the product tafamidis 61 mg free acid (Vyndaqel®)[4]. The manufacturer's cost-effectiveness analysis at that time was of insufficient methodological quality. The National Health Care Institute could not therefore provide a realistic estimate of cost-effectiveness, nor could it determine the price reduction required to be able to provide the treatment at a cost that will be acceptable to society. The National Health Care Institute therefore issued a negative recommendation about including tafamidis 61 mg free acid in the health insurance package. The manufacturer has now submitted a new dossier with a cost-effectiveness analysis that the National Health Care Institute deems to be sufficient in terms of methodological quality. The reassessment used the previous assessment of the therapeutic value of the drug; only the cost-effectiveness analysis has been assessed.

Integral weighting of package criteria

Patients with wild-type or hereditary transthyretin amyloidosis as adults with cardiomyopathy typically suffer from symptoms of heart failure such as dyspnoea, temporary loss of consciousness, arrhythmia and a reduced capacity to make physical efforts. Life expectancy in these patients is also reduced. Given the severity of the symptoms, the prognosis for the disorder and the impact it has on the patient (and their functioning and well-being), the disorder results in a severely compromised state of health for the patients and therefore to a high burden of disease (0.77).

Review of interchangeability
Tafamidis 61 mg free acid is not interchangeable with any medicinal products that are already included in the Medicine Reimbursement System, meaning that it is eligible for inclusion on List 1B.

Established medical science and medical practice
The National Health Care Institute has concluded that tafamidis 61 mg free acid has therapeutic added value compared to placebo in the treatment of wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy and who are in NYHA class I or II. This means that tafamidis 61 mg free acid complies with established medical science and medical practice for the subgroup in question. Tafamidis 61 mg free acid ensures that the patient's condition deteriorates less rapidly, leads to a better quality of life and reduces the risk of mortality.

Budget impact
The number of patients is estimated to be between 4,905 and 7,296. This large spread is due to uncertainty in the expected number of patients who have not been diagnosed at the present time and in the proportion of them who might be eligible for tafamidis 61 mg free acid. The total additional costs charged to the pharmaceutical budget are estimated at €172 to €421 million in the third year after inclusion in the package.

Cost-effectiveness
In the reassessment, the National Health Care Institute has concluded that the

[4] https://www.zorginstituutnederland.nl/werkagenda/publicaties/adviezen/2020/12/03/gvs-advies-tafamidis-vyndaqel

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cost-effectiveness analysis for tafamidis 61 mg free acid in the treatment of patients with wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy and who are in NYHA class I or II is sufficient in terms of methodological quality. Given the high burden of disease (0.77), the National Health Care Institute has adopted a reference value of €80,000 per QALY. The incremental cost-effectiveness ratio (ICER) has been determined as €151,050 per QALY. This means that treatment with tafamidis 61 mg free acid is not cost-effective and the price would have to decrease by at least 50% for it to fall below the reference value of €80,000 per QALY.

Furthermore, the National Health Care Institute would like to point out that this is an existing medicine for which an expansion of the indication is currently being investigated. The National Health Care Institute has no evidence that the manufacturer has had to make any major investments to get this drug on the market. The National Health Care Institute therefore believes that a discount of substantially more than 50% would be appropriate. Additionally, new drugs for this indication may become available in due course. The National Health Care Institute recommends that you should take these two aspects into account during the price negotiations.

Final conclusion
The National Health Care Institute has concluded that tafamidis 61 mg free acid (Vyndaqel®) is not interchangeable with another product included in the Medicine Reimbursement System (GVS), meaning that it is eligible for inclusion on List 1B. Tafamidis 61 mg free acid complies with established medical science and medical practice for the treatment of patients with wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy and who are in NYHA class I or II. However, the National Health Care Institute also concludes that tafamidis 61 mg free acid (Vyndaqel®) cannot be provided at socially acceptable costs. The National Health Care Institute therefore recommends that you do not include tafamidis 61 mg free acid (Vyndaqel®) on List 1B of the GVS unless the following conditions are met:

- a substantial price reduction (at least 50%) of tafamidis 61 mg free acid, given the very high budgetary impact and the unfavourable cost-effectiveness ratio;
- agreement about the appropriateness (in an orphan drug arrangement) for effective use of the treatment. The National Health Care Institute is already involved in discussions with stakeholders responsible for providing treatment about how arrangements for appropriate use can be made.

Orphan drug arrangement
If it is included in the health care package, the National Health Care Institute will set up an orphan drug arrangement with the stakeholders. This will contain agreements about the starting and stopping criteria, a committee for indications, and a register for collecting and evaluating data. The various parties have already taken the first steps for this. The National Health Care Institute will continue to guide this process. The National Health Care Institute would like to point out here that it is important that centres of excellence have sufficient resources to meet the commitments made and to be able to follow the practice properly. The results of the orphan drug arrangement will be published annually in the *Orphan Drugs in Practice Monitor*. In the context of the treatment landscape, the National Health Care Institute takes the following points into consideration:

- the initial estimate of the number of patients versus the actual number

treated;
- the cost development compared to the original cost estimate;
- the realisation of an orphan drug arrangement and compliance with that arrangement.

If the application of tafamidis 61 mg free acid is included in the health care package after a successful price negotiation, the National Health Care Institute recommends the following reimbursement condition:

Condition for tafamidis 61 mg free acid (Vyndaqel®):
Only for insured parties aged eighteen or older with wild-type or hereditary transthyretin amyloidosis in adult patients with cardiomyopathy and who are in NYHA class I or II.

Yours sincerely,

Sjaak Wijma
Chair of the Executive Board

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