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Date 13 January 2021
Subject GVS advice mexiletine (Namuscla®)

Our reference
2020050860

Dear Ms van Ark,

In your letter of 14 July 2020 (CIBG-20-0673), you requested the National Health Care Institute to assess whether the product mexiletine 167 mg (Namuscla®) is interchangeable with another product that is included in the Medication Reimbursement System (GVS). The National Health Care Institute, advised by the Scientific Advisory Board (WAR) and the Insured Package Advisory Committee (ACP), has since completed this assessment.

Mexiletine (Namuscla®) is indicated for the symptomatic treatment of myotony in adult patients with non-dystrophic myotonic disorders.
Each capsule of Namuscla® contains 200 mg of mexiletine hydrochloride, corresponding to 167 mg (166.62 mg) of mexiletine.

The National Health Care Institute has concluded that mexiletine (Namuscla®) has a therapeutic added value compared to placebo. In addition, there are no differences in clinical effects between mexiletine (Namuscla®) and two other mexiletine preparations.
Currently, mexiletine is available in the Netherlands in the form of imported mexiletine and as a pharmacy preparation, at a much lower price than the registered mexiletine (Namuscla®). The National Health Care Institute notes that the pricing is not in proportion to the efforts to register mexiletine (Namuscla®).

Due to the unnecessarily high price, and from the point of view of solidarity which is the basic principle of our healthcare system, the National Health Care Institute advises you not to include mexiletine (Namuscla®) in List 1B of the GVS. To continue to guarantee the patient's access to mexiletine, the National Health Care Institute recommends that in this case, the pharmacy preparations be included in List 3 of the Health Insurance Scheme.

I would like to explain our findings and final conclusion below.

Recorded indication
Mexiletine (Namuscla®) is indicated for the symptomatic treatment of myotonia in adult patients with non-dystrophic myotonic disorders. It is available as a hard capsule and contains 200 mg of mexiletine hydrochloride, corresponding to 167

mg of mexiletine. The recommended starting dose is 167 mg of mexiletine per day. The maintenance treatment consists of 167 mg to 500 mg of mexiletine per day.

Background
Initially, mexiletine was used as an antiarrhythmic agent in cardiac arrhythmia, with mexiletine being commercially available under the brand name Mexitil® from 1975 to 2008. Typically, mexiletine is used in the treatment of ventricular tachycardia and ventricular fibrillation as the last treatment option for cardiac patients for whom no other treatment is available.

Since the 1980s, mexiletine has been used for the mentioned treatment, and since 2014, mexiletine has also been reimbursed for a subgroup within the patients with non-dystrophic myotonic disorder on the basis of rational pharmacotherapy.

Dutch patients currently use imported mexiletine preparations or pharmacy preparations.
These mexiletine preparations are reimbursed by health insurers for the treatment of non-dystrophic myotonic disorder (in adults and children) and for the treatment of cardiac arrhythmia.

Review of interchangeability
To determine the place of a medicinal product in the GVS, its interchangeability with medicinal products already included in the GVS must first be assessed.
No medication has been included in the GVS for the indication 'symptomatic treatment of myotonia in adults patients with non-dystrophic myotonic disorders'.

Therapeutic value
For the evaluation of therapeutic value, the National Health Care Institute has compared mexiletine (Namuscla®) to a placebo. In addition, the National Health Care Institute compared the clinical effects of mexiletine (Namuscla®) with two other mexiletine preparations.
It concluded that in the symptomatic treatment of myotonia in adult patients with non-dystrophic myotonic disorders, mexiletine has added value compared to placebo. The clinical effects of mexiletine (Namuscla®) are similar to those of the other mexiletine preparations.

Budget impact analysis
The Health Care and Youth Inspectorate (IGJ) has indicated that off-label use of a registered medicinal product always takes precedence over importing an unregistered medicinal product from abroad. In the case of mexiletine (Namuscla®), this means that importing from abroad is only possible if, for medical reasons, the registered alternative Namuscla® cannot be applied. In practice, this means that some of the cardiology patients will have to be given mexiletine (Namuscla®). Pharmacy preparation is currently increasingly used in the Netherlands, but pharmacy preparation could be delivered to patients who are actually registered with that (hospital) pharmacy.

The price of imported mexiletine hydrochloride 200 mg (corresponding to 167 mg mexiletine) is €285 per pack of 100 capsules, or €2.85 per capsule. The pharmacy purchasing price of the pharmacy preparation is €400 - €435 per pack of 60

capsules with 167 mg of mexiletine, or an average of €6.95 per capsule. The National Health Care Institute did not take into account that the price of pharmacy preparation (and thus the total cost per patient) could decrease if more patients were to be treated with the pharmacy preparation.

The initial purchasing price of mexiletine (Namuscla®) was €3,900 per pack of 100 capsules with 167 mg of mexiletine. The market authorisation holder has lowered this price to €2,339 per pack of 100 capsules with 167 mg of mexiletine, or an average of €23.39 per capsule. At the time when mexiletine was commercially available as Mexitil®, the pharmacy purchasing price was €0.23 per capsule.

Taking into account the different assumptions regarding patient numbers, the current treatment algorithm, market penetration, patient compliance and applied dosages, the inclusion of mexiletine (Namuscla®) for the symptomatic treatment of myotonia in adult patients with non-dystrophic myotonic disorders will mean additional costs charged to the pharmaceutical budget of between €6.1 and €7.6 million. Should mexiletine (Namuscla®) also be used in the treatment of ventricular tachycardia and ventricular fibrillation, the additional costs will increase by €1.0 to €1.3 million.

Pharmaco-economic analysis
Based on the estimated budget impact, the product is exempt from pharmaco-economic analysis. The National Health Care Institute notes that no exemption had been granted initially. The exemption was granted after the market authorisation holder reduced the pharmacy purchasing price by 40 percent, which resulted in an estimated budget impact below the €10 million threshold.

Other considerations
In addition to this indication, mexiletine is used for the symptomatic treatment of myotonia in children with non-dystrophic myotonic disorders and to treat cardiac arrhythmia in those for whom no other treatment is available. Health insurers will continue to reimburse mexiletine for these patients on the basis of rational pharmacotherapy.

Inclusion in the GVS fits your policy to minimize off-label usage and to prefer registered products.
However, the National Health Care Institute has reservations about the high price of this product. The main reason for this is that mexiletine was previously available in the Netherlands at a significantly lower price (for a different indication and under a different brand name). Besides, mexiletine is currently also available in the Netherlands in the form of imported mexiletine and as a pharmacy preparation, at a price much lower than the registered mexiletine (Namuscla®).

At the request of the National Health Care Institute, the market authorisation holder gave a justification for the requested price. The market authorisation holder has indicated that this price is based on the significant costs associated with marketing and making mexiletine (Namuscla®) available in accordance with current European standards. However, the National Health Care Institute notes that the pricing is not in proportion to the efforts to register mexiletine (Namuscla®).

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Innovation ensures that medicinal products are made available for rare diseases. The current (international) regulations offer manufacturers room for financial compensation for their investments and efforts. However, partly inspired by the National Health Care Institute's Insured Package Advisory Committee, I have observed that there are manufacturers who use this room in a way that conflicts with that purpose of the regulation. Very high prices are being charged for products that have already been proven in practice. The National Health Care Institute wishes to flag this up, so that you may, if you so wish, include it in the (international) evaluations of the regulations of orphan medicinal products that are currently ongoing.

A much higher price of a product already available (via import or pharmacy preparation) will take up a much larger and unnecessary part of the insured budget. This is at the expense of treatments for other patients or the premium payer. It is the opinion of the National Health Care Institute that this high price is irresponsible and also incompatible with the social values of health insurance. Such unnecessarily high pricing threatens our system that is based on solidarity.

Final conclusion
The National Health Care Institute has concluded that mexiletine (Namuscla®) has a therapeutic added value compared to a placebo, and that there are no differences in clinical effects between mexiletine (Namuscla®) and already available mexiletine preparations.

Due to the unnecessarily high price, and from the point of view of solidarity which is the basic principle of our healthcare system, the National Health Care Institute advises you not to include mexiletine (Namuscla®) in List 1B of the GVS. To continue to guarantee patient access to mexiletine, the National Health Care Institute recommends that the pharmacy preparations should be included in List 3 of the Health Insurance Scheme.

Yours sincerely,

Sjaak Wijma
Chair of the Executive Board