



> Return address PO Box 320, 1110 AH Diemen

To the Minister of Medical Care
PO Box 20350
2500 EJ THE HAGUE

2024006550

Date 01 May 2024
Re: Package advice mavacamten (Camzyos®) for symptomatic
obstructive hypertrophic cardiomyopathy

**National Health Care
Institute**

Care
Medicinal Products
Willem Dudokhof 1
1112 ZA Diemen
PO Box 320
1110 AH Diemen
www.zorginstituutnederland.nl
info@zinl.nl

T +31 (0)20 797 85 55

Contact

Ms M.J.S. de Vries
warcg@zinl.nl

Our reference

2024006550

Dear Mrs Dijkstra,

This is a modified version of the package advice that was previously sent to you on 16 April 2024. An error in the List 2 condition has been corrected.

In a letter of 20 November 2023 [CIBG-23-06293], your predecessor requested the National Health Care Institute to carry out a substantive review of whether mavacamten (Camzyos®) is interchangeable with a product that is included in the Medicine Reimbursement System (GVS). The National Health Care Institute has now completed the substantive assessment. The considerations are set out in the reports in the annex.

Mavacamten is registered for the treatment of symptomatic (*New York Heart Association* (NYHA) class II-III) obstructive hypertrophic cardiomyopathy (oHCM) in adult patients.

Mavacamten is available in 2.5 mg, 5 mg, 10 mg or 15 mg capsules.

The marketing authorisation holder requests the inclusion in List 1B of the Health Insurance Regulation and claims added value compared to the standard medicinal treatment.

Outcome of the substantive assessment

Assessment of interchangeability

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

Therapeutic value

The marketing authorisation holder claims that mavacamten has an added value compared to the standard medicinal treatment. Standard treatment for this indication consists of symptomatic treatment with beta-blockers or non-dihydropyridine calcium antagonists. Mavacamten is the first licensed medicinal product that addresses the cause of oHCM (enlarged heart muscle).

According to the European Society of Cardiology (ESC) 2023 guideline,

mavacamten can be used in patients who have had an inadequate response, contraindication or intolerance to beta-blockers or non-dihydropyridine calcium antagonists, and who are treated with the standard treatment of a beta-blocker or a non-dihydropyridine calcium antagonist and before invasive procedures (SRT) are considered. The Dutch professional association supports this positioning and based on this, mavacamten (added to the standard treatment) was compared with the standard treatment alone (placebo) in this assessment.

**National Health Care
Institute**
Care
Medicinal Products

Date
01 May 2024

Our reference
2024006550

Two double-blind, randomised, placebo-controlled phase III studies investigated the effectiveness and safety of mavacamten in patients with oHCM. Based on these studies, it can be concluded that mavacamten is effective in treating the symptoms and improving the quality of life in the short term. However, the longer-term effectiveness on hard outcomes such as cardiovascular death and the prevention of heart failure and atrial fibrillation is still very uncertain.

To demonstrate a clinically relevant effect on cardiovascular mortality, a long study duration and a large patient population are required due to the low 1-year risk of CV mortality (1-2%). The National Health Care Institute currently sees mavacamten potentially as a last resort for patients who are not eligible for invasive treatment. Patients who are now eligible for invasive therapy may no longer need to be treated invasively as a result of mavacamten treatment.

There were very few intervention-related adverse effects in both the mavacamten and placebo arms, and the number of discontinuations due to adverse effects was low. Most adverse effects were mild to moderate. The *European Medicines Agency* (EMA) concluded that the cardiovascular safety of mavacamten is considered acceptable for now. However, the agency indicated that due to the very low number of events in the studies, there is uncertainty about the long-term safety of mavacamten, and that additional research into cardiovascular safety is necessary.

All in all, the National Health Care Institute concludes that mavacamten meets the established medical science and medical practice in adult patients with symptomatic (NYHA class II-III) obstructive hypertrophic cardiomyopathy (oHCM) who have not responded adequately to, or have a contraindication or intolerance to beta-blockers or non-dihydropyridine calcium antagonists.

Budget impact analysis

There is uncertainty about the number of patients with symptomatic oHCM. Therefore, the budget impact analysis used two different prevalence rates for its calculations. The professional association only sees a place for mavacamten for patients with LVEF \geq 55% (89%). This has been taken into account in the calculation of the patient number. The National Health Care Institute estimates that between 412 and 1,420 patients will be treated with mavacamten in the third year after market introduction. One whole year of treatment with mavacamten costs €17,488 per patient per year. Based on this, the total cost of treatment ranges between €7.2 million and €24.8 million in the third year after market introduction.

Since the overall group of patients with hypertrophic cardiomyopathy is significantly greater, there is a risk of wider (off-label) use of mavacamten with a significant financial impact.

Cost-effectiveness

The marketing authorisation holder reports a ICER of €15,019 per QALY gained, compared to the standard treatment. At a reference value of €50,000 per QALY, mavacamten plus the standard treatment is considered cost-effective compared to standard treatment only. The cost-effectiveness results appear to be representative for the short term, but for the long term, the results are uncertain and the calculated ICER may be too optimistic.

The National Health Care Institute concludes that the pharmaco-economic analysis is of sufficient quality and that the outcomes of the analysis are sufficient for decision-making. However, there is a short follow-up and there are important uncertainties in the hard, longer-term outcome parameters such as morbidity and mortality. This means that the results of the cost-effectiveness analysis must be interpreted very carefully.

There are currently several studies being conducted into the effects of mavacamten on hard, longer-term outcome parameters. These studies are likely to clarify these uncertainties. Should the results prove unsatisfactory, a reassessment of the (cost) effectiveness might be required.

Advice

Based on the above, we advise that you include mavacamten (Camzyos®) in List 1B. Given the risk of wider (off-label) use, we recommend that the List 2 conditions below are applied. The professional association is already in an advanced stage of drafting the treatment protocol for the indicated patients. Given the uncertainties surrounding the long-term (cost) effectiveness, and the risk that this may be less optimistic, the National Health Care Institute intends to monitor mavacamten in the context of cyclical package management.

Condition mavacamten

Only for an insured person with symptomatic (NYHA class II-III) obstructive hypertrophic cardiomyopathy (oHCM), who

- either despite optimal beta-blocker or calcium antagonist use has persistent symptoms (NYHA \geq II)
- or has a proven contraindication or intolerance to beta-blockers or non-dihydropyridine calcium antagonists.

The prescription must be prescribed by a centre of expertise.

Yours sincerely,

Sjaak Wijma
Chairperson of the Executive Board

**National Health Care
Institute**
Care
Medicinal Products

Date
01 May 2024

Our reference
2024006550