

# Mavacamten for treating symptomatic obstructive hypertrophic cardiomyopathy

Technology appraisal guidance  
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[www.nice.org.uk/guidance/ta913](https://www.nice.org.uk/guidance/ta913)

## Your responsibility

The recommendations in this guidance represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance is at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the [Yellow Card Scheme](#).

Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the NHS Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should [assess and reduce the environmental impact of implementing NICE recommendations](#) wherever possible.

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# 1 Recommendations

- 1.1 Mavacamten is recommended as an option for treating symptomatic obstructive hypertrophic cardiomyopathy in adults who have a New York Heart Association class of 2 to 3. It is recommended only if:
- it is an add-on to individually optimised standard care that includes beta-blockers, non-dihydropyridine calcium-channel blockers or disopyramide, unless these are contraindicated, and
  - the company provides it according to the [commercial arrangement](#).
- 1.2 This recommendation is not intended to affect treatment with mavacamten that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

## Why the committee made these recommendations

Treatment for obstructive hypertrophic cardiomyopathy aims to manage its symptoms. Standard care is either beta-blockers or non-dihydropyridine calcium-channel blockers and if symptoms persist then disopyramide may be added. Some people with uncontrolled symptoms may choose to have surgery. Mavacamten is the first treatment that specifically treats the condition rather than the symptoms. For this evaluation, the company asked for mavacamten to be considered only as an add-on treatment for people having optimised standard care. This is a narrower population that does not include everyone covered by mavacamten's marketing authorisation.

Clinical trial evidence suggests that mavacamten plus standard care is more effective than standard care alone, and that it may avoid or delay the need for invasive surgery.

The most likely cost-effectiveness estimate for mavacamten is within the range that NICE considers an acceptable use of NHS resources. So mavacamten is recommended.

## 2 Information about mavacamten

### Marketing authorisation indication

- 2.1 Mavacamten (Camzyos, Bristol-Myers Squibb) is indicated for 'the treatment of symptomatic (New York Heart Association, NYHA, class II-III) obstructive hypertrophic cardiomyopathy (oHCM) in adult patients'.

### Dosage in the marketing authorisation

- 2.2 The dosage schedule is available in the [summary of product characteristics for mavacamten](#).

### Price

- 2.3 Mavacamten has a list price of £1,073.20 per pack of 28 2.5-mg, 5-mg, 10-mg or 15-mg capsules (company submission).
- 2.4 The company has a [commercial arrangement](#). This makes mavacamten available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

## 3 Committee discussion

The [evaluation committee](#) considered evidence submitted by Bristol-Myers Squibb, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the [committee papers](#) for full details of the evidence.

### The condition

#### Obstructive hypertrophic cardiomyopathy

3.1 Cardiomyopathies are chronic diseases of the heart muscle that alter its structure and impair its function. The pathophysiology of hypertrophic cardiomyopathy (HCM) is complex. HCM is characterised by excessive heart muscle contraction (hypercontractility), ventricular hypertrophy and impaired ventricular relaxation. It is known that genetic mutations in the cardiac sarcomere, the contractile unit of muscle in the heart, are associated with approximately 50% of HCM cases. Obstructive HCM represents approximately two thirds of total HCM cases. The obstructive form of HCM is characterised by an additional feature known as left ventricular outflow tract (LVOT) obstruction. This is when the peak pressure gradient of the LVOT is equal to or greater than 30 mmHg. In people without a sarcomere mutation, it is thought that LVOT obstruction may be related to anatomical factors and is not driven by the hypercontractility of the cardiac sarcomere alone. But, this is uncertain. Regardless of the cause, obstructive HCM causes progressive structural and functional changes that ultimately presents as a range of pathologies in addition to LVOT obstruction. These include diastolic dysfunction, myocardial ischaemia, heart valve dysfunction and arrhythmias. Obstructive HCM is also associated with a higher risk of heart failure and mortality.

#### Measuring symptom severity

3.2 Heart failure is usually classified according to the severity of the symptoms people experience. The clinical expert explained that the most

commonly used classification system is the New York Heart Association (NYHA) Functional Classification. It places people in 1 of 4 categories based on how much they are limited during physical activity. Class 1 is the least severe class of symptoms, with no limitations on physical activity. Class 4 is the most severe class of symptoms, with people unable to do any physical activity without discomfort. People in this most severe class will also experience symptoms of heart failure at rest. The committee noted the clinical expert's view that NYHA classes can be quite subjective, but concluded that it was the most widely used symptom classification for the condition. The committee therefore agreed it was an appropriate way to quantify symptom severity.

## Effects on quality of life

- 3.3 Obstructive HCM impacts on all aspects of life, with physical symptoms frequently leading to psychological, social and economic impacts. The patient experts explained that frequent episodes of breathlessness and exhaustion are the most common symptoms that impact on quality of life. Obstructive HCM is a progressive disease and without effective treatment symptoms typically get worse over time. The disease may develop at any age and can occur in younger people who may have previously had very active lifestyles. The patient experts described how the reduced ability to participate in everyday activities such as sports, walking more than short distances, or socialising was a substantial burden that was difficult to come to terms with. Daily activities such as childcare, cooking, bathing and dressing become very challenging, or even impossible to complete without assistance. The patient support group representative explained that people with the condition often experience loss of confidence, anxiety, depression, and social isolation. They may also experience feelings similar to bereavement for the aspects of their former life that have been lost. In addition, they explained how physical symptoms can often impact on people's ability to work. As a result, it is also common for people with the condition to have financial worries. Because there is sometimes a genetic factor, people with obstructive HCM may have family members who have the condition or are at risk of developing it. The committee concluded that obstructive HCM is a disease with a very large and wide-ranging impact on quality of life.

## Clinical management

### Treatment options

- 3.4 There are currently no disease-specific treatments for obstructive HCM. The aim of treatment is therefore to manage the symptoms associated with LVOT obstruction. Non-vasodilating beta-blockers are usually first-line treatment for obstructive HCM and can reduce the LVOT pressure gradient and associated symptoms. But these treatments have highly variable effectiveness and are associated with side effects. Non-dihydropyridine calcium-channel blockers, such as verapamil and diltiazem, are recommended when beta-blockers are contraindicated, ineffective or not tolerated. But non-dihydropyridine calcium-channel blockers are also associated with side effects, tolerability issues and variable efficacy. The committee noted that beta-blockers in combination with non-dihydropyridine calcium-channel blockers is not considered standard care in the UK. Disopyramide is a sodium channel blocker. It can be used as a second-line therapy in combination with a beta-blocker or non-dihydropyridine calcium-channel blocker if symptoms remain after beta-blocker or a non-dihydropyridine calcium-channel blocker monotherapy. Disopyramide can be effective in controlling some of the symptoms of LVOT obstruction. But, it is also associated with side effects, such as dry eyes and mouth, urinary hesitancy or retention, and constipation. If medical treatments are not effective in controlling symptoms, some people may choose to have invasive surgery called septal reduction therapy (SRT). But the patient experts explained that people with the condition usually want to avoid these treatments for as long as possible due to their uncertain efficacy, associated risks and long recovery times. The committee agreed that the available treatments for obstructive HCM are not disease specific but offer potential benefits for some people. However, they are also associated with side effects that can impact on quality of life. The committee concluded that there is a substantial need for new disease-specific treatments that alter the course of obstructive HCM. They noted that such treatments would offer greater hope to people with this condition.



## Proposed positioning of mavacamten and comparators

3.5 The company's proposed position for mavacamten in the treatment pathway is as a second-line adjunctive therapy when beta-blocker or non-dihydropyridine calcium-channel blocker monotherapy has not controlled symptoms. The committee noted that the proposed pathway does not include combination therapy with disopyramide or with beta-blockers plus non-dihydropyridine calcium-channel blockers, due to safety concerns. The company explained that it had deviated from the decision problem and excluded disopyramide based on the opinions of clinical experts it had consulted. It stated that the low rate of usage was largely due to the side effect profile, the risk of tachyphylaxis (where successive doses of a drug can give a rapidly diminishing response), and problems in obtaining the drug. At technical engagement, the company provided analyses of disopyramide use in the NHS using data from the Clinical Practice Research Datalink and the linked Hospital Episode Statistics datasets. This analysis showed that disopyramide use was relatively low (the exact numbers are deemed to be academic in confidence and cannot be reported here). The EAG commented that this data was highly uncertain because of a lack of clarity in the data extraction protocol used, and because it was unclear whether the data included secondary care prescriptions. Furthermore, the data included people in NYHA class 1, who are not part of the company's decision problem. The clinical expert agreed with the company that disopyramide use is highly variable. This is because larger centres tend to have senior clinical staff who are more likely to have sufficient experience of using disopyramide, and are therefore more comfortable using it. The clinical expert also agreed that there are ongoing problems with its availability in the NHS, and that it is used considerably less than beta-blockers and non-dihydropyridine calcium-channel blockers. But the clinical expert also explained that although disopyramide might only be used in approximately 5% to 10% of people with obstructive HCM in UK clinical practice, this figure is not necessarily representative of the people who would be using mavacamten. Because mavacamten is being positioned as a second-line adjunctive treatment after symptoms have not been sufficiently controlled with beta-blockers or non-dihydropyridine calcium-channel blockers, people at this point in the pathway are those who would also be more likely to have disopyramide. The clinical expert

explained that in this group of people with ongoing symptoms, disopyramide use would be approximately 30%. If symptoms remain uncontrolled at this stage in the pathway, the only remaining option is SRT, which people are often keen to avoid for as long as possible (see [section 3.4](#)). The EAG suggested that comparators should accurately reflect current practice in the NHS. The EAG explained that its clinical experts confirmed that for some people disopyramide is effective, well tolerated and can be used for decades. But, the EAG also explained that the company's systematic literature review identified no good-quality studies that could provide comparative efficacy evidence for disopyramide for use in the economic evaluation. The committee noted the limitation in the evidence base, but concluded that it would have preferred to see analysis that included disopyramide as a comparator, based on its use in UK clinical practice.

## Clinical effectiveness

### Data sources

- 3.6 Evidence for the efficacy and safety of mavacamten with standard care compared with standard care alone is primarily from the company's pivotal trial, EXPLORER-HCM. EXPLORER-HCM is a phase 3, double-blind, randomised, placebo-controlled, multicentre study of 251 people with obstructive HCM. Longer-term safety data comes from the EXPLORER-LTE cohort of 231 people previously enrolled in EXPLORER-HCM who continued into the long-term extension study MAVA-LTE. The primary endpoint in EXPLORER-HCM was a composite endpoint. This endpoint was intended to incorporate both a physiological measure of exercise capacity measured by peak oxygen consumption and a physician-assessed component measuring symptoms using NYHA class. The clinical expert explained that peak oxygen consumption was used to establish the extent to which a person's breathlessness is because of their heart condition and not other factors, such as their level of fitness. The change in NYHA class is also meaningful because it measures symptom burden in terms of activities that can be completed. But, the clinical expert cautioned that this measure does also have limitations, particularly because it can be quite subjective. The committee noted that

people in the trial could reach the primary endpoint in 1 of 2 ways: either an increase of at least 1.5 ml/kg per minute in their peak oxygen consumption with at least 1 NYHA class improvement, or an increase of at least 3.0 ml/kg per minute in peak oxygen consumption with no worsening of NYHA class. EXPLORER-HCM met its primary endpoint, with mavacamten demonstrating clinically meaningful improvements in NYHA class and peak oxygen consumption. More people in the mavacamten arm reached the primary endpoint compared with those in the placebo arm (37% versus 17%, respectively;  $p=0.0005$ ). But the committee also noted that most people in the mavacamten group (63%) did not achieve the primary outcome. Analysis of people who met both component parts of the composite primary endpoint showed that 20% of those in the mavacamten arm had an increase of at least 3.0 ml/kg per minute in peak oxygen consumption and at least 1 NYHA class improvement, but only 8% in the placebo arm had both. Clinically meaningful and statistically significant improvements were also observed across all secondary endpoints in EXPLORER-HCM. Additional data supporting the efficacy of mavacamten in preventing the need for SRT is available from VALOR-HCM. This is a phase 3 multicentre randomised placebo-controlled trial of 112 people with symptomatic obstructive HCM who were eligible for SRT. The primary outcome in VALOR-HCM was the proportion of people who remained guideline eligible for SRT or chose to undergo SRT at 16 weeks. After 16 weeks, a statistically significant greater proportion of people in the placebo group remained guideline eligible or chose to undergo SRT compared with the mavacamten group (76.8% and 17.9%, respectively;  $p<0.001$ ). The company explained that the results of this trial support the view that mavacamten has a role in preventing or postponing the need for people to undergo invasive SRT in order to control the symptoms associated with obstructive HCM. The committee agreed that the selected endpoints are clinically relevant and that mavacamten demonstrates meaningful improvements over placebo for people with obstructive HCM.

## Efficacy by sarcomere mutation status

- 3.7 The company explained that the mechanism of action of mavacamten is not dependent on the presence or absence of sarcomere gene mutations. This is because it acts on the hypercontractility of the cardiac

muscle, irrespective of the cause of the hypercontractility. The company also suggested that the results of EXPLORER-HCM demonstrate that mavacamten is effective across all prespecified subgroups, including mutation status. The EAG cautioned that the results of subgroup analyses in EXPLORER-HCM could suggest that mavacamten efficacy may differ between people with or without a sarcomere mutation. However, the small sample sizes included in this analysis means that these results lack statistical significance, and are therefore uncertain. The EAG also explained that the differences in efficacy observed across the different trial outcomes sometimes favoured mavacamten and sometimes favoured the comparator. This suggests that the results are highly uncertain, and that further subgroup analysis according to mutation status might not be appropriate. The clinical expert explained that it is possible that there might be a difference in efficacy, and that mavacamten could be more effective in people with a sarcomere mutation. They explained that this could partially explain why 63% of people in the mavacamten arm of EXPLORER-HCM did not reach the primary endpoint (see [section 3.6](#)). The clinical expert believed that there is not yet enough evidence to determine the impact of sarcomere mutations on treatment effect. This is because the pathophysiology of obstructive HCM is complex and, in people without mutations, LVOT obstruction may be driven less by hypercontractility and be more related to anatomical factors. However, this remains highly uncertain. The patient experts suggested that while the availability of genetic testing is improving, results are not rapidly available and can take up to 6 months. In addition to regional variability, the need for genetic testing could potentially present a barrier to access for people with obstructive HCM. The committee noted that the cost effectiveness of mavacamten could be impacted by any difference in efficacy between people with or without a sarcomere mutation. It concluded that while economic analysis by sarcomere mutation subgroup would be desirable, this analysis would be difficult given the very small sample sizes, and would likely be highly uncertain.

## Safety monitoring

- 3.8 Studies of mavacamten highlighted the potential risk of heart failure from systolic dysfunction, meaning that the heart pump function decreases

too much in some people. Because of this risk, the summary of product characteristics (SPC) provides a minimum level of safety monitoring that should be implemented if the drug is used in clinical practice (this document is currently confidential and so the specific monitoring requirements cannot be reported here). Echocardiography is the primary method for diagnosis and monitoring of HCM, and for assessment of left ventricle wall thickness. It is also used to detect and monitor LVOT obstruction, which is important for managing symptoms and the risk of sudden cardiac death. The EAG explained that while it understood the need for the intensive monitoring protocol specified in the SPC, it was unsure whether this level of monitoring would be feasible in the NHS. This was because of a lack of trained echocardiographers and associated long waiting times for these services in the NHS. The company suggested that, based on feedback from clinical experts, the frequency of echo monitoring may reduce over time. At technical engagement, after further consultation with clinical experts, the company suggested an initial intensive monitoring protocol in the model, with a slightly less intensive protocol over the remaining time horizon. The clinical expert confirmed that resource limitations were a problem, and that it was likely that monitoring would be less frequent than stipulated in the SPC. They suggested that this is not an issue that is unique to mavacamten, and that monitoring could begin at an intensive level but then taper, most likely after 2 years. But the EAG suggested that the limited availability of echocardiographic services in the NHS was not necessarily a strong justification to assume a lower level of safety monitoring in the economic model. For this reason, the EAG restated its preference for the safety monitoring protocol specified in the SPC. But it also produced a range of scenarios to explore how varying the intensity of safety monitoring impacts the cost-effectiveness analysis. The committee noted that the impact on the incremental cost-effectiveness ratio (ICER) was relatively small. The NHS England national clinical lead stated that they would not recommend less frequent monitoring than provided in the SPC recommendations. The committee therefore agreed with the EAG that the most conservative assumption, as per the protocol specified in the SPC, was most appropriate and concluded that this should be included in the company's base case.

## Economic model

### Effect of treatment on mortality

3.9 In its base case, the company modelled mortality using estimates of an association between NYHA class and mortality derived from analyses of US electronic medical record data. Death rates in NYHA class 1 were assumed to be the same as for people of the same age and sex in the general population. Death rates for NYHA class 2 to 4 were then adjusted relative to NYHA class 1 using analysis of 3,322 medical records of people with obstructive HCM (Wang et al. 2022). At technical engagement the company provided additional analysis that added another US electronic medical record dataset to the original analysis. The company also did 2 other scenarios, adjusted and unadjusted, using analyses of 2,495 medical records from the international SHaRe registry database. The EAG cautioned that this approach has been criticised because the observed relationship between NYHA class and mortality has not been proven to be causal. There is also currently no evidence that treatments for reducing the symptoms of obstructive HCM increase survival of people with the condition. The company agreed that the relationship may not be causal, but suggested that the lack of direct evidence is the reason why a proxy analysis must be used for modelling mortality. The EAG also commented that survival benefits have not been presumed for the treatments that are used to control the symptoms of obstructive HCM. It said that for these reasons, it was unsure of the appropriateness of including a mortality benefit in the economic model. The EAG offered 2 alternative scenarios. The committee noted that the first of these, where each NYHA class has a mortality hazard ratio of 1, was not clinically plausible but was included to show the extent of the impact on cost effectiveness of this assumption. The second scenario assigned a pooled hazard ratio (derived from the company's electronic medical record analysis) across all NYHA classes to reflect the fact that people with obstructive HCM have a higher risk of death than the general population. This latter scenario does not assume any causal link between a change in NYHA class and mortality. The clinical expert confirmed that there is no direct evidence for a link between NYHA class and mortality, and that this is also the case for all other treatments for obstructive HCM, including SRT. The assumed clinical benefit for all these treatments



is that they are used to improve quality of life rather than to reduce mortality. The NHS England national clinical lead commented that although there is no evidence for a causal relationship, it did not seem clinically plausible that the risk of death would be similar across all NYHA classes, and that therefore the EAG's scenario for a pooled hazard ratio is likely not appropriate. The EAG commented that the hazard ratio would be more likely to increase as NYHA class increases, but that the extent to which the hazard ratio would change across each NYHA class was very uncertain. The committee considered the lack of direct evidence proving a causal link between NYHA class and mortality, and the EAG's second scenario using a pooled hazard ratio across the different NYHA classes. It agreed that the company's analysis showed a correlation, but that the question of whether this was a causal relationship was currently unknown. On balance, it concluded that the hazard ratios from the company's updated analysis were appropriate for decision making but were highly uncertain.

## Long-term rates of progression

3.10 Obstructive HCM is a progressive disease in which symptoms will worsen in the absence of effective treatment. In its original base case the company had assumed no disease progression (reduction in NYHA class) as a conservative assumption. But it also did a scenario analysis using the rate of 4.55% progression for all treatments, taken from a cohort study (Maron et al. 2016). The EAG said it preferred this rate of progression for all treatments to the company's original assumption because it is clinically plausible, based on clinical expert opinion. At technical engagement, the company presented additional clinical expert opinion on the rate of disease progression seen in clinical practice. These clinical experts did not disagree with the value of 4.55%, and so the company used this value in its revised base case, aligning with the EAG's preference. The EAG explained that while it agreed with the rate of 4.55%, this was derived from a single source, and that the lack of additional sources of data make this rate highly uncertain. It also commented that it was uncertain whether mavacamten should have a lower rate of progression than other treatments, and it had done a scenario to explore this assumption. The committee agreed that there were no alternative estimates to consider, but that it was better to

include disease progression in the model than to assume no progression. It concluded that the assumption of a rate of progression of 4.55% for all treatments was suitable for decision making but was uncertain.

## Imbalance in transition probabilities

3.11 The main measure of clinical effectiveness in the model is change in NYHA class over time. Transitions between the 4 NYHA class health states are governed by transition probabilities: short-term transition probabilities for the first 30 weeks and long-term transition probabilities thereafter. The EAG commented that it thought the methods used to estimate short-term transition probabilities from EXPLORER-HCM NYHA class data were reasonable. However, after week 30, the company assume no further transitions between NYHA classes in the mavacamten arm. This same assumption is also applied to the beta-blocker or non-dihydropyridine calcium-channel blocker monotherapy comparator arm, but only after week 46. The EAG also explained that between week 30 and week 46, NYHA transition probabilities for the comparator arm were estimated using weeks 30 and 38 of the EXPLORER-HCM trial, and the week 46 baseline assessment of the EXPLORER-LTE extension cohort. The company stated that it preferred this different approach for each treatment arm because it represented the longest continuous data available. The EAG explained that it was likely that using different methods to model transition probabilities between weeks 30 and 46 in the mavacamten and comparator arms would have introduced bias. Instead the EAG's preferred assumption was to model the comparator arm in the same way as the mavacamten arm after week 30. The company explained that doing this would disregard the trial data showing a diminishing effect on NYHA class in the comparator arm after week 30. However, the EAG restated its concerns on the potential for bias because of different durations of follow up for the treatment arms. It is also possible that bias could be introduced if there are differences in how people move from each arm of the randomised trial into the EXPLORER-LTE study. Because the changes between week 30 and 46 in the comparator arm are carried forward through the remaining time horizon of the model, and because the number of transition events that govern changes in NYHA class are low, bias may have been introduced. The committee considered the relative merits of each approach. They



agreed that the EAG's preference for applying the approach for the mavacamten arm to both arms after week 30 was more appropriate for decision making because of the risk of bias and concluded that this assumption should be applied.

## Cost-effectiveness estimates

### Acceptable ICER

3.12 The committee considered the extent of the uncertainty in the modelling assumptions used to calculate the company and EAG base case ICERs. In particular, it recalled the uncertainty in the key issues with the largest potential impact on cost effectiveness: the effect of treatments on mortality, the rate of disease progression, and the risk of bias from the imbalance in follow up for transition probabilities. The committee concluded that there was high uncertainty associated with each of these assumptions, and so the maximum acceptable ICER would be at the lower end of the range normally considered a cost-effective use of NHS resources (that is, £20,000 per quality-adjusted life year [QALY] gained).

### Company and EAG cost-effectiveness estimates

3.13 The company made several changes to its base case at technical engagement. Its original base case ICER for mavacamten with standard care compared with standard care alone was £30,139 per QALY gained. The company's revised base case ICER for mavacamten with standard care compared with standard care alone was £19,401 per QALY gained. For its revised base case the company adopted the following changes:

- a rate of progression of 4.55%, in alignment with the EAG (see [section 3.10](#))
- an adjustment of its preferred assumption about safety monitoring based on clinical expert opinion (see [section 3.8](#))
- an update to the mortality modelling using additional electronic medical record data (see [section 3.9](#))
- proportional capping of utilities at general population norms for age, in

alignment with the EAG.

The EAG maintained its preference for a safety monitoring protocol in line with that stipulated in the SPC. It also maintained its preference for the same modelling approach for long-term transition probabilities in both arms after week 30. These assumptions increase the company's base case ICER of £19,401 per QALY gained to an EAG base case ICER of £37,088 per QALY gained. The committee agreed that it preferred the assumptions in the EAG base case. Following the appraisal committee meeting, the company revised its commercial arrangement. The updated discount reduced the EAG base case ICER to £19,997 per QALY gained. Because of uncertainty in the economic modelling and from the exclusion of disopyramide as a relevant comparator (see [section 3.5](#)), the committee concluded that mavacamten could be considered cost-effective only if it is an add-on to individually optimised standard care including beta-blockers, non-dihydropyridine calcium-channel blockers or disopyramide, unless these are contraindicated.

## Other factors

### Equality issues

- 3.14 No equality or social value issues were identified.
- 3.15 NICE's advice about conditions with a high degree of severity did not apply.

### Innovation

- 3.16 The company considered mavacamten to be innovative because it directly targets the underlying disease process, and so represents a step change in the treatments available for people with obstructive HCM. The patient and clinical experts highlighted the lack of effective pharmacological management for obstructive HCM, the importance of slowing down disease progression and of managing the debilitating symptoms associated with LVOT obstruction. They also highlighted the potential for mavacamten to avoid or delay the need for invasive SRT, especially in the context of long NHS waiting lists for these procedures.

The committee acknowledged the new benefits offered by mavacamten as an additional treatment option for obstructive HCM. However, it concluded that it had not been presented with evidence of any additional benefits that were not captured in the QALY measurements.

## Conclusion

### **Mavacamten is recommended for routine use in the NHS**

3.17 The committee agreed that there was a high degree of uncertainty in the clinical evidence and economic modelling for mavacamten. Using the committee's preferred assumptions, and taking into consideration the company's revised commercial arrangement, the ICER for mavacamten with standard care compared with standard care alone was within the range that NICE considers to be a cost-effective use of NHS resources. So, mavacamten is recommended for symptomatic obstructive HCM in adults, only if it is an add-on to individually optimised standard care including beta-blockers, non-dihydropyridine calcium-channel blockers or disopyramide, unless these are contraindicated.

## 4 Implementation

- 4.1 Section 7 of the National Institute for Health and Care Excellence (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 3 months of its date of publication.
- 4.2 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final draft guidance.
- 4.3 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has symptomatic obstructive hypertrophic cardiomyopathy and the doctor responsible for their care thinks that mavacamten is the right treatment, it should be available for use, in line with NICE's recommendations.

## 5 Evaluation committee members and NICE project team

### Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by [committee C](#).

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The [minutes of each evaluation committee meeting](#), which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

### Chair

**Stephen O'Brien**

Chair, technology appraisal committee C

### NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser and a project manager.

**Luke Cowie**

Technical lead

**Sally Doss**

Technical adviser

**Celia Mayers**

Project manager

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