NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Mavacamten for treating symptomatic obstructive hypertrophic cardiomyopathy

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of mavacamten within its marketing authorisation for treating symptomatic obstructive hypertrophic cardiomyopathy.

Background

Hypertrophic cardiomyopathy (HCM) is a genetic condition that is most often caused by a change or fault (or mutation) in one or more genes and is characterised by the thickening of the muscular wall of the heart (the myocardium). Thickening of the septum (the dividing wall between the left and the right side of the heart), resulting in reduced or restricted blood flow is classified as obstructive HCM. Common symptoms of HCM include shortness of breath, chest pain, palpitations, light headedness, and fainting. People with obstructive HCM can develop serious complications such as atrial fibrillation, heart failure, malignant ventricular arrhythmias, and sudden cardiac death.

HCM is the most common genetic cardiovascular disease and has a prevalence of around 1 in 500 people in the general population. However, most people with HCM have few, if any, symptoms[1].The disease most commonly presents in the second or third decade of life but may present at any age. HCM is the most common cause of sudden unexpected death in childhood and in young athletes[2].

There is no curative treatment for HCM. Treatment approaches vary depending on symptoms and risk of sudden disease. People with HCM often need to make lifestyle changes, such as limiting their activity, to adjust for their disease. European Society of Cardiology Guidelines on hypertrophic cardiomyopathy recommend that people with symptomatic disease, predominately with left ventricular outflow tract obstruction, receive beta-blockers to reduce symptoms and obstruction. Verapamil, disopyramide in addition to beta-blockers or diuretics may also be considered. In cases where individuals are considered to be at high risk of sudden cardiac death, implanted devices such as a pacemaker or an implantable cardioverter defibrillator (ICD) may be used (NICE technology appraisal guidance 314). If severe symptoms persist, people may have surgical myectomy. Alternatively, non-surgical reduction of the myocardial septum may be offered (NICE interventional procedures guidance 40). For people who progress to heart failure, treatment may include beta-blockers, ACE inhibitors, angiotensin-receptor blockers, or mineralocorticoid receptor antagonists. Other treatment options for chronic heart failure may include ivabradine or sacubitril valsartan (NICE guideline 106). Dapagliflozin may also be considered (NICE technology appraisal guidance TA679).

The technology

Mavacamten (brand name unknown, Bristol-Myers Squibb) is a small molecule that binds selectively to cardiac myosin ATPase reducing contractility of the heart muscle. It is administered orally once a day.

Mavacamten does not currently have a marketing authorisation in the UK for obstructive hypertrophic cardiomyopathy. It has been studied in clinical trials compared with placebo in adults with obstructive HCM.

Intervention(s)	Mavacamten
Population(s)	Adults with symptomatic obstructive hypertrophic cardiomyopathy

Comparators	• Established clinical management including:
	  ○ beta-blockers
	  ○ verapamil
	  ○ disopyramide
	  ○ ACE inhibitors
	  ○ angiotensin-receptor blockers
	  ○ ivabradine
	  ○ dapagliflozin
	  ○ mineralocorticoid receptor antagonists
	  ○ sacubitril valsartan
	• Implanted devices (including ICD and pacemakers)
	• Surgical myectomy
	• Non-surgical reduction of the myocardial septum

Outcomes	The outcome measures to be considered include: • response rates • mortality • cardiovascular mortality • exercise capacity • oxygen consumption • symptom severity • change in NYHA class • change in left ventricular ejection fraction • adverse effects of treatment • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.
Other considerations	If the evidence allows the following subgroups will be considered: • people eligible for septal replacement therapy. The availability and cost of biosimilar and generic products should be taken into account. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure (2014). NICE Technology Appraisal 314. Terminated appraisals: None. Appraisals in development (including suspended appraisals): None. Related Guidelines: Chronic heart failure in adults: diagnosis and management (2018). NICE guideline 106. Guidelines in development: None. Related Interventional Procedures: Non-surgical reduction of the myocardial septum (2004) NICE interventional procedures guidance 40.

	Related Quality Standards: Chronic heart failure in adults (2011) NICE quality standard 9 Related NICE Pathways: Chronic heart failure (2019) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2, 3 and 4. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 NHS England (2013) 2013/14 NHS Standard Contract For Cardiology: Inherited Cardiac Conditions (All Ages) NHS England (2013) 2013/14 NHS Standard Contract For Cardiology: Cardiac Magnetic Resonance Imaging(Cmr) (Adult)

Questions for consultation

Have all relevant comparators for mavacamten been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for obstructive hypertrophic cardiomyopathy?

Are there any comparators included which are not considered relevant?

Where do you consider mavacamten will fit into the existing treatment pathway?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom mavacamten is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which mavacamten will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider mavacemten to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of mavacamten can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1 Hypertrophic cardiomyopathy. British Heart Foundation. Accessed May 2021.

2 Cardiomyopathy. NHS. Accessed May 2021.