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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Mavacamten for treating symptomatic obstructive hypertrophic cardiomyopathy

Final scope

Final 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. Most people with HCM may initially have few or no symptoms. However, the disease is progressive, and symptoms may develop or worsen at any age. 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 (ESC) 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. If beta-blockers are ineffective or contraindicated, non-dihydropyridine calcium channel blockers (such as verapamil and diltiazem) are suitable alternatives. Disopyramide, alone or in combination with either beta-blockers or non-dihydropyridine calcium channel blockers, can also be considered. If severe symptoms persist despite maximally tolerated medical therapy, people may be offered surgical myectomy or non-surgical reduction of the myocardial septum (NICE interventional procedures guidance 40). For people with obstructive HCM who progress to heart failure, the only ESC guideline recommended treatment options are those recommended to manage left ventricular outflow obstruction. People with HCM, regardless of the presence of obstruction, should undergo clinical risk assessment for sudden cardiac death risk. In cases where individuals are considered to be at high risk of arrhythmias and sudden cardiac death, implanted devices such as a pacemaker or an implantable cardioverter defibrillator may be used.

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The technology

Mavacamten (brand name unknown, Bristol-Myers Squibb) is a small molecule that binds selectively to cardiac myosin ATPase which changes the heart muscle's ability to contract. It is administered orally.

Mavacamten does not currently have a marketing authorisation in the UK for symptomatic obstructive hypertrophic cardiomyopathy. It has been studied with individually optimised standard care in randomised controlled trials compared with placebo in adults with symptomatic obstructive HCM (NYHA class II-III) who had left ventricular ejection fraction of 55% or higher.

Intervention(s)	Mavacamten in combination with standard care
Population(s)	Adults with symptomatic obstructive hypertrophic cardiomyopathy (NYHA class II-III)

Comparators	• Individually optimised standard care without mavacamten
	• Standard care is defined as:
	  ○ Beta-blockers
	  ○ Non-dihydropyridine calcium channel blockers
	  ○ Disopyramide, alone or in combination with either beta-blockers or non-dihydropyridine calcium channel blockers.

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

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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	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. Related Guidelines: Chronic heart failure in adults: diagnosis and management (2018). NICE guideline 106. 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 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)

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	NHS England (2013) 2013/14 NHS Standard Contract For Cardiology: Cardiac Magnetic Resonance Imaging(Cmr) (Adult)

References

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

2 Cardiomyopathy. NHS. Accessed May 2021.