CAMZYOS® ▼ (mavacamten) Prescribing Information

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CAMZYOS® ▼ (mavacamten) PRESCRIBING INFORMATION
Great Britain

Consult Summary of Product Characteristics (SmPC) before prescribing.

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information.

PRESENTATION: Hard capsule (capsule); 2.5 mg, 5 mg, 10 mg, 15 mg mavacamten.

INDICATION: Treatment of symptomatic (New York Heart Association, NYHA, class II-III) obstructive hypertrophic cardiomyopathy (oHCM) in adult patients.

DOSAGE AND ADMINISTRATION: Treatment should be initiated under the supervision of a physician experienced in the management of patients with cardiomyopathy. Before treatment initiation, patients' left ventricular ejection fraction (LVEF) should be assessed by echocardiography. If LVEF is < 55%, treatment should not be initiated. Before initiation of treatment, females of childbearing potential must have a negative pregnancy test. Patients should be genotyped for Cytochrome P450 (CYP) 2C19 (CYP2C19) in order to determine appropriate mavacamten dose. Patients with CYP2C19 poor metaboliser phenotype may have increased mavacamten exposures (up to 3 times) that can lead to increased risk of systolic dysfunction compared to normal metabolisers. If treatment initiation occurs prior to determination of CYP2C19 phenotype, patients should follow dosing instructions for poor metabolisers until CYP2C19 phenotype is determined. *Posology*: The dose range is 2.5 mg to 15 mg (either 2.5 mg, 5 mg, 10 mg or 15 mg).

CYP2C19 poor metaboliser phenotype: The recommended starting dose is 2.5 mg orally once daily. The maximum dose is 5 mg once daily. The patient should be assessed for early clinical response by left ventricular outflow tract (LVOT) gradient with Valsalva manoeuvre 4 and 8 weeks after treatment initiation. *CYP2C19 intermediate, normal, rapid and ultra rapid metaboliser phenotype*: The recommended starting dose is 5 mg orally once daily. The maximum dose is 15 mg once daily. The patient should be assessed for early clinical response by LVOT gradient with Valsalva manoeuvre 4 and 8 weeks after treatment initiation.

Once an individualised maintenance dose is achieved, patients should be assessed every 12 weeks. If at any visit the patient's LVEF is < 50%, the treatment should be interrupted for 4 weeks and until LVEF returns to ≥ 50%. In patients experiencing an intercurrent illness such as serious infection or arrhythmia (including atrial fibrillation or other uncontrolled tachyarrhythmia) which may impair systolic function, LVEF assessment is recommended, and dose increases are not recommended until intercurrent illness is resolved. Consideration should be given to discontinue treatment in patients who have shown no response (e.g., no improvement in symptoms, quality of life, exercise capacity, LVOT gradient) after 4-6 months on the maximum tolerated dose. *Missed or delayed doses*: If a dose is missed, it should be taken as soon as possible, and the next scheduled dose should be taken at the usual time the following day. Two doses should not be taken on the same day. *Special populations*: *Elderly*: No dose adjustment to the standard dose and titration scheme is required for patients aged 65 years and older. *Renal impairment*: No dose adjustment to the standard dose and titration scheme is required for patients with mild (estimated glomerular filtration rate [eGFR] 60-89 mL/min/1.73m^2) to moderate (eGFR 30-59 mL/min/1.73m^2) renal impairment. No dose recommendation can be made for patients with severe (eGFR < 30 mL/min/1.73m^2) renal impairment because mavacamten has not been studied in patients with severe renal impairment. *Hepatic impairment*: The mavacamten starting dose should be 2.5 mg in all patients with mild (Child-Pugh class A) and moderate (Child-Pugh class B) hepatic impairment since mavacamten exposure is likely to be increased. No dose recommendation can be made for patients with severe hepatic impairment (Child-Pugh class C) because mavacamten has not been studied in patients with severe hepatic impairment. *Paediatric population*: The safety and efficacy of mavacamten in children and adolescents below 18 years have not been established. No data are available. Mavacamten should not be used in children less than 12 years because of potential safety concerns. *Method of administration*: For oral use. Treatment should be taken once daily with or without meals at about the same time each day. The capsule should be swallowed whole with water.

CONTRAINDICATIONS: Hypersensitivity to the active substance or to any of the excipients (refer to SmPC). During pregnancy and in females of childbearing potential not using effective contraception. Concomitant treatment with strong CYP3A4 inhibitors in patients with CYP2C19 poor metaboliser phenotype and undetermined CYP2C19 phenotype. Concomitant treatment with the combination of a strong CYP2C19 inhibitor and a strong CYP3A4 inhibitor. Refer to SmPC for further details.

WARNINGS AND PRECAUTIONS: *Systolic dysfunction defined as symptomatic LVEF < 50%**: Mavacamten reduces LVEF and may cause heart failure due to systolic dysfunction defined as symptomatic LVEF < 50%. Patients with a serious intercurrent illness such as infection or arrhythmia (including atrial fibrillation or other uncontrolled tachyarrhythmia), or those undergoing major cardiac surgery may be at greater risk of systolic dysfunction and progress to heart failure. New or worsening dyspnoea, chest pain, fatigue, palpitations, leg oedema or elevations in N-terminal pro-B-type natriuretic peptide (NT-proBNP) may be signs and symptoms of systolic dysfunction and should prompt an evaluation of cardiac function. LVEF should be measured prior to initiating treatment and closely monitored thereafter. Treatment interruption may be necessary to ensure that LVEF remains ≥ 50%. *Heart failure risk or loss of response to mavacamten due to interactions**: Mavacamten is primarily metabolised by CYP2C19 and to a lesser extent by CYP3A4 and mostly by CYP3A4 in CYP2C19 poor metabolisers, which may lead to the following interactions: Starting or increasing the dose of a strong or moderate CYP3A4 inhibitor or any CYP2C19 inhibitor may increase risk of heart failure due to systolic dysfunction. Stopping or decreasing dose of any inhibitor of CYP3A4 or CYP2C19 may lead to a loss of therapeutic response to mavacamten. Starting a strong CYP3A4 or strong CYP2C19 inducer may lead to a loss of therapeutic response to mavacamten. Stopping a strong CYP3A4 or strong CYP2C19 inducer may increase risk of heart failure due to systolic dysfunction. Prior to and during mavacamten treatment, the potential for interactions, including over the counter medicinal products (such as omeprazole or esomeprazole), should be considered. Concomitant treatment with strong CYP3A4 inhibitors in patients with CYP2C19 poor metaboliser phenotype and undetermined CYP2C19 phenotype is contraindicated. Concomitant treatment with the combination of a strong CYP2C19 inhibitor and a strong CYP3A4 inhibitor is contraindicated. Dose adjustment of

mavacamten and/or close monitoring may be required in patients initiating or discontinuing treatment with, or changing the dose of concomitant medicinal products that are inhibitors or inducers of CYP2C19 or CYP3A4. Intermittent administration of these medicinal products is not recommended. *Concomitant use of negative inotropes*: The safety of concomitant use of mavacamten with disopyramide, or use of mavacamten in patients taking beta blockers in combination with verapamil or diltiazem has not been established. Therefore, patients should be closely monitored when taking these concomitant medicinal products. *Embryo-foetal toxicity**: Based on animal studies, mavacamten is suspected to cause embryo-foetal toxicity when administered to a pregnant female. Due to risk to the foetus, mavacamten is contraindicated during pregnancy and in females of childbearing potential not using effective contraception. Before initiation of treatment, females of childbearing potential must be informed of this risk to the foetus, must have a negative pregnancy test and must use effective contraception during treatment and for 6 months after treatment discontinuation. *Sodium content*: This medicinal product contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'. Refer to SmPC section 4.5 for other drug-drug interactions.

*serious adverse drug reaction

PREGNANCY AND LACTATION: *Pregnancy*: There are no data from the use of mavacamten in pregnant females. Mavacamten is suspected to cause embryo-foetal toxicity when administered during pregnancy. Therefore, mavacamten is contraindicated during pregnancy. Mavacamten should be stopped 6 months before planning a pregnancy. If a patient becomes pregnant, mavacamten must be discontinued. Medical advice should be given regarding the risk of harmful effects to the foetus associated with treatment and ultrasonography examinations should be performed. *Breast-feeding*: It is unknown whether mavacamten or its metabolites are excreted in human milk. Because of the unknown adverse effects of mavacamten in breastfed newborns/infants, females must not breast-feed during treatment with mavacamten.

UNDESIRABLE EFFECTS*:* The most commonly reported adverse reactions with mavacamten are dizziness (17%), dyspnoea (12%), systolic dysfunction (5%) and syncope (5%). *Very common (≥ 1/10)*: Dizziness, Dyspnoea. *Common (≥ 1/100 to < 1/10)*: Syncope*, Systolic dysfunction (LVEF < 50% with or without symptoms)*. Refer to SmPC for full details on adverse reactions.

*serious adverse drug reaction

LEGAL CATEGORY: POM

MARKETING AUTHORISATION NUMBER and BASIC NHS PRICE: Carton of 28 hard capsules 2.5 mg (PLGB 15105/0180) £1073.20; Carton of 28 hard capsules 5 mg (PLGB 15105/0181) £1073.20; Carton of 28 hard capsules 10 mg (PLGB 15105/0182) £1073.20; Carton of 28 hard capsules 15 mg (PLGB 15105/0183) £1073.20.

MARKETING AUTHORISATION HOLDER: Bristol-Myers Squibb Pharma EEIG, Plaza 254, Blanchardstown Corporate Park 2, Dublin 15, D15 T867, Ireland

FOR FURTHER INFORMATION CONTACT:
medical.information@bms.com or 0800 731 1736 (Great Britain)

DATE OF PREPARATION: July 2024

ADDITIONAL INFORMATION AVAILABLE ON REQUEST

Approval code: 3500-GB-2400238

Adverse events should be reported. Reporting forms and information can be found at:
Great Britain - www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store;
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LEGAL CATEGORY: POM

MARKETING AUTHORISATION NUMBER and BASIC NHS PRICE: Carton of 28 hard capsules 2.5 mg (EU/1/23/1716/002) £1073.20; Carton of 28 hard capsules 5 mg (EU/1/23/1716/004) £1073.20; Carton of 28 hard capsules 10 mg (EU/1/23/1716/006) £1073.20; Carton of 28 hard capsules 15 mg (EU/1/23/1716/008) £1073.20.

MARKETING AUTHORISATION HOLDER: Bristol-Myers Squibb Pharma EEIG, Plaza 254, Blanchardstown Corporate Park 2, Dublin 15, D15 T867, Ireland

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DATE OF PREPARATION: June 2024

ADDITIONAL INFORMATION AVAILABLE ON REQUEST

Approval code: 3500-GB-2400239

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