For patients with NYHA Class II–III obstructive HCM,

Checklist for Prescribing CAMZYOS™[1,2]

Start with identifying an appropriate patient and counseling them on safety

IDENTIFY an appropriate patient

- ☐ Confirm absence of pregnancy and usage of effective contraception in females of reproductive potential
- ☐ Assess the patient's cardiovascular status and confirm with an echocardiogram (echo) that their LVEF is ≥55%. (Do not initiate CAMZYOS in patients with LVEF <55%)
- ☐ Review the patient's medications (prescription and over-the-counter) and supplements, and confirm there are no drug interactions or contraindications. For a complete list, see Sections 2, 4, and 7 in the US Full Prescribing Information here

COUNSEL your patient on the appropriate use of CAMZYOS

- ☐ Counsel your patient using the REMS Patient Brochure and the Medication Guide for CAMZYOS
- ☐ Inform your patient of the risks associated with treatment with CAMZYOS and that they must consult their HCP or seek medical attention immediately if they experience signs and symptoms of heart failure, including new or worsening shortness of breath, chest pain, fatigue, leg swelling, palpitations, or rapid weight gain
- ☐ Advise your patient about the potential risk of embryo-fetal toxicity with exposure to CAMZYOS. For patients using CHCs, advise them to use an alternative contraceptive method or add nonhormonal contraception during treatment with CAMZYOS and for 4 months after the last dose
- ☐ Counsel your patient on how to take CAMZYOS and what action to take in case of missed or delayed doses
- ☐ Counsel your patient about the risk of drug-drug interactions with CYP2C19 or CYP3A4 inhibitors and inducers. Advise them to inform their HCP of all the medications and supplements they take (prescription and over-the-counter) and to not stop or change the dose of a current medication or start a new medication without talking to their HCP

Prescribing checklist continued on the next page.

CHC=combined hormonal contraceptive; CYP=cytochrome P450; HCM=hypertrophic cardiomyopathy; HCP=healthcare provider; LVEF=left ventricular ejection fraction; NYHA=New York Heart Association; REMS=Risk Evaluation and Mitigation Strategy.

INDICATION

CAMZYOS is indicated for the treatment of adults with symptomatic New York Heart Association (NYHA) Class II–III obstructive hypertrophic cardiomyopathy (HCM) to improve functional capacity and symptoms.

SELECT IMPORTANT SAFETY INFORMATION

WARNING: RISK OF HEART FAILURE

CAMZYOS reduces left ventricular ejection fraction (LVEF) and can cause heart failure due to systolic dysfunction.

Echocardiogram assessments of LVEF are required prior to and during treatment with CAMZYOS. Initiation of CAMZYOS in patients with LVEF <55% is not recommended. Interrupt CAMZYOS if LVEF is <50% at any visit or if the patient experiences heart failure symptoms or worsening clinical status.

Concomitant use of CAMZYOS with certain cytochrome P450 inhibitors or discontinuation of certain cytochrome P450 inducers may increase the risk of heart failure due to systolic dysfunction; therefore, the use of CAMZYOS is contraindicated with the following:

- **Moderate to strong CYP2C19 inhibitors or strong CYP3A4 inhibitors**
- **Moderate to strong CYP2C19 inducers or moderate to strong CYP3A4 inducers**

Because of the risk of heart failure due to systolic dysfunction, CAMZYOS is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the CAMZYOS REMS PROGRAM.

Please see additional Important Safety Information, including **Boxed WARNING**, throughout and US Full Prescribing Information for CAMZYOS here.

CAMZYOS™ (mavacamten) 2.5, 5, 10, 15 mg capsules

Checklist for Prescribing CAMZYOS™[1,2] (cont'd)

After you have identified an appropriate patient for CAMZYOS, follow the steps below

1. ENROLL in the CAMZYOS REMS program*

- ☐ Before you can prescribe, you must be certified and enrolled in the CAMZYOS REMS program. Visit **CAMZYOSREMS.com** or by calling 833-628-7367 to complete REMS enrollment

*You may designate a member of your staff who is a licensed medical professional to be your REMS Designee. This person can perform REMS activities for you in the CAMZYOS REMS. You are responsible for all information entered and activities performed in the CAMZYOS REMS by the Designee. Initial and subsequent prescriptions for CAMZYOS must be written by a certified HCP.

2. EDUCATE your patient about the CAMZYOS REMS requirements and help them enroll in the program†

- ☐ Review the REMS Patient Brochure with your patient
- ☐ Enroll your patient in the CAMZYOS REMS program
- ☐ Complete and submit the REMS Patient Enrollment Form

†Forms for the CAMZYOS REMS program are available at CAMZYOSREMS.com or by calling 833-628-7367 for assistance.

3. DISCUSS the MyCAMZYOS™ program with your patient (optional)

- ☐ Inform your patient about the optional **MyCAMZYOS** access and support program
- ☐ If your patient would like to enroll in the program, help them complete and sign the **MyCAMZYOS** Enrollment Form in your office. (Program information and enrollment form are available at **CAMZYOShcp.com/MyCAMZYOS**)

4. PRESCRIBE CAMZYOS to appropriate patients (initial prescription)

- ☐ If your patient enrolls in **MyCAMZYOS**, the **MyCAMZYOS** Enrollment Form serves as the initial prescription. No additional prescription required
- ☐ If your patient does not want to enroll in **MyCAMZYOS**, complete and submit a prescription to your patient's insurance-mandated specialty pharmacy
- ☐ If needed, complete and submit a letter of medical necessity and/or a prior authorization form

5. SCHEDULE the required follow-up echos‡

- ☐ Once you receive confirmation that CAMZYOS has shipped, **consider scheduling the patient's echos at 4, 8, and 12 weeks from treatment start**. (Be sure to schedule the echos earlier in the week so that the specialty pharmacy is able to authorize the prescription)
- ☐ Remind your patient of the importance of maintaining their echo schedule

‡If dose interruption or a dose change occurs, the echo schedule will be impacted, and the next follow-up should be 4 weeks later. Please refer to the US Full Prescribing Information (Section 2) for the full echo requirements related to dosage and administration and information on managing treatment interruption.

6. REFILL CAMZYOS for appropriate patients (all subsequent prescriptions)

- ☐ Submit all subsequent prescriptions to the patient's insurance-mandated specialty pharmacy
- ☐ Be sure to submit a Patient Status Form within three days of the echo to ensure the timely dispense of medication. This form is located in the REMS portal at **CAMZYOSREMS.com** or by calling 833-628-7367 for assistance

SELECT IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

CAMZYOS is contraindicated with concomitant use of:

- Moderate to strong CYP2C19 inhibitors or strong CYP3A4 inhibitors
- Moderate to strong CYP2C19 inducers or moderate to strong CYP3A4 inducers

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SELECT IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Heart Failure

CAMZYOS™ reduces systolic contraction and can cause heart failure or totally block ventricular function. Patients who experience a serious intercurrent illness (e.g., serious infection) or arrhythmia (e.g., atrial fibrillation or other uncontrolled tachyarrhythmia) are at greater risk of developing systolic dysfunction and heart failure.

Assess the patient's clinical status and LVEF prior to and regularly during treatment and adjust the CAMZYOS dose accordingly. New or worsening arrhythmia, dyspnea, chest pain, fatigue, palpitations, leg edema, or elevations in N-terminal pro-B-type natriuretic peptide (NT-proBNP) may be signs and symptoms of heart failure and should also prompt an evaluation of cardiac function.

Asymptomatic LVEF reduction, intercurrent illnesses, and arrhythmias require additional dosing considerations.

Initiation of CAMZYOS in patients with LVEF <55% is not recommended. Avoid concomitant use of CAMZYOS in patients on disopyramide, ranolazine, verapamil with a beta blocker, or diltiazem with a beta blocker as these medications and combinations were excluded from EXPLORER-HCM. Concomitant use of CAMZYOS with disopyramide in combination with verapamil or diltiazem has been associated with left ventricular systolic dysfunction and heart failure symptoms in patients with obstructive HCM.

CYP 450 Drug Interactions Leading to Heart Failure or Loss of Effectiveness

CAMZYOS is primarily metabolized by CYP2C19 and CYP3A4 enzymes. Concomitant use of CAMZYOS and drugs that interact with these enzymes may lead to life-threatening drug interactions such as heart failure or loss of effectiveness.

Advise patients of the potential for drug interactions, including with over the counter medications (such as omeprazole, esomeprazole, or cimetidine). Advise patients to inform their healthcare provider of all concomitant products prior to and during CAMZYOS treatment.

CAMZYOS Risk Evaluation and Mitigation Strategy (REMS) Program

CAMZYOS is only available through a restricted program called the CAMZYOS REMS Program because of the risk of heart failure due to systolic dysfunction. Notable requirements of the CAMZYOS REMS Program include the following:

- Prescribers must be certified by enrolling in the REMS Program.
- Patients must enroll in the REMS Program and comply with ongoing monitoring requirements.
- Pharmacies must be certified by enrolling in the REMS Program and must only dispense to patients who are authorized to receive CAMZYOS.
- Wholesalers and distributors must only distribute to certified pharmacies.

Further information is available at www.CAMZYOSREMS.com or by telephone at 1-833-628-7367.

Embryo-Fetal Toxicity

CAMZYOS may cause fetal toxicity when administered to a pregnant female, based on animal studies. Confirm absence of pregnancy in females of reproductive potential prior to treatment and advise patients to use effective contraception during treatment with CAMZYOS and for 4 months after the last dose. CAMZYOS may reduce the effectiveness of combined hormonal contraceptives (CHCs). Advise patients using CHCs to use an alternative contraceptive method that is not affected by CYP 450 enzyme induction or to add nonhormonal contraception. Advise females of reproductive potential about the potential risk to the fetus with maternal exposure to CAMZYOS during pregnancy.

ADVERSE REACTIONS

In the EXPLORER-HCM trial, adverse reactions occurring in >5% of patients and more commonly in the CAMZYOS group than in the placebo group were dizziness (27% vs 18%) and syncope (6% vs 2%).

Effects on Systolic Function

In the EXPLORER-HCM trial, mean (SD) resting LVEF was 74% (6) at baseline in both treatment groups. Mean (SD) absolute change from baseline in LVEF was -4% (8) in the CAMZYOS group and 0% (7) in the placebo group over the 30-week treatment period. At Week 38, following an 8-week interruption of trial drug, mean LVEF was similar to baseline for both treatment groups. In the EXPLORER-HCM trial, 7 (6%) patients in the CAMZYOS group and 2 (2%) patients in the placebo group experienced reversible reductions in LVEF <50% (median 48%: range 35-49%) while on treatment. In all 7 patients treated with CAMZYOS, LVEF recovered following interruption of CAMZYOS.

DRUG INTERACTIONS

Potential for Other Drugs to Affect Plasma Concentrations of CAMZYOS

CAMZYOS is primarily metabolized by CYP2C19 and to a lesser extent by CYP3A4 and CYP2C9. Inducers and inhibitors of CYP2C19 and moderate to strong inhibitors or inducers of CYP3A4 may affect the exposures of CAMZYOS.

SELECT IMPORTANT SAFETY INFORMATION

DRUG INTERACTIONS (cont'd)

Impact of Other Drugs on CAMZYOS™:

- Moderate to Strong CYP2C19 Inhibitors or Strong CYP3A4 Inhibitors: Concomitant use increases CAMZYOS exposure, which may increase the risk of heart failure due to systolic dysfunction. Concomitant use is contraindicated.
- Moderate to Strong CYP2C19 Inducers or Moderate to Strong CYP3A4 Inducers: Concomitant use decreases CAMZYOS exposure, which may reduce CAMZYOS' efficacy. The risk of heart failure due to systolic dysfunction may increase with discontinuation of these inducers as the levels of induced enzyme normalizes. Concomitant use is contraindicated.
- Weak CYP2C19 Inhibitors or Moderate CYP3A4 Inhibitors: Concomitant use with a weak CYP2C19 inhibitor or a moderate CYP3A4 inhibitor increases CAMZYOS exposure, which may increase the risk of adverse drug reactions. Initiate CAMZYOS at the recommended starting dose of 5 mg orally once daily in patients who are on stable therapy with a weak CYP2C19 inhibitor or a moderate CYP3A4 inhibitor. Reduce dose of CAMZYOS by one level (i.e., 15 to 10 mg, 10 to 5 mg, or 5 to 2.5 mg) in patients who are on CAMZYOS treatment and intend to initiate a weak CYP2C19 inhibitor or a moderate CYP3A4 inhibitor. Schedule clinical and echocardiographic assessment 4 weeks after inhibitor initiation, and do not up-titrate CAMZYOS until 12 weeks after inhibitor initiation. Avoid initiation of concomitant weak CYP2C19 and moderate CYP3A4 inhibitors in patients who are on stable treatment with 2.5 mg of CAMZYOS because a lower dose is not available.

Potential for CAMZYOS to Affect Plasma Concentrations of Other Drugs

CAMZYOS is an inducer of CYP3A4, CYP2C9, and CYP2C19. Concomitant use with CYP3A4, CYP2C19, or CYP2C9 substrates may reduce plasma concentration of these drugs. Closely monitor when CAMZYOS is used in combination with CYP3A4, CYP2C19, or CYP2C9 substrates where decreases in the plasma concentration of these drugs may reduce their activity.

Hormonal Contraceptives: Progestin and ethinyl estradiol are CYP3A4 substrates. Concomitant use of CAMZYOS may decrease exposures of ethinyl estradiol and progestin, which may lead to contraceptive failure or an increase in breakthrough bleeding. Advise patients to use a contraceptive method that is not affected by CYP 450 enzyme induction (e.g., intrauterine system) or add nonhormonal contraception (such as condoms) during concomitant use and for 4 months after the last dose of CAMZYOS.

Drugs That Reduce Cardiac Contractility

Expect additive negative inotropic effects of CAMZYOS and other drugs that reduce cardiac contractility. Avoid concomitant use of CAMZYOS with disopyramide in combination with verapamil or diltiazem. If concomitant therapy with a negative inotrope is initiated, or if the dose of a negative inotrope is increased, monitor LVEF closely until stable doses and clinical response have been achieved.

SPECIFIC POPULATIONS

Pregnancy

CAMZYOS may cause fetal harm when administered to a pregnant female. Advise pregnant females about the potential risk to the fetus with maternal exposure to CAMZYOS during pregnancy. There is a pregnancy safety study for CAMZYOS. If CAMZYOS is administered during pregnancy, or if a patient becomes pregnant while receiving CAMZYOS or within 4 months after the last dose of CAMZYOS, healthcare providers should report CAMZYOS exposure by contacting Bristol Myers Squibb at 1-800-721-5072 or www.bms.com.

Lactation

The presence of CAMZYOS in human or animal milk, the drug's effects on the breastfed infant, or the effects on milk production are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for CAMZYOS and any potential adverse effects on the breastfed child from CAMZYOS or from the underlying maternal condition.

Females and Males of Reproductive Potential

Confirm absence of pregnancy in females of reproductive potential prior to initiation of CAMZYOS. Advise females of reproductive potential to use effective contraception during treatment with CAMZYOS and for 4 months after the last dose. Use of CAMZYOS may reduce the effectiveness of CHCs. Advise patients using CHCs to use an alternative contraceptive method or add nonhormonal contraception.

Please see US Full Prescribing Information, including **Boxed WARNING**.

References

1. U.S. Food and Drug Administration. Risk Evaluation and Mitigation Strategy (REMS) document. Accessed May 4, 2022. https://www.accessdata.fda.gov/drugsatfda_docs/rems/Camzyos_2022_04_28_REMS_Document.pdf **2.** CAMZYOS [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2022.