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

DOSING AND ADMINISTRATION GUIDE[1]

INDICATION

CAMZYOS® (mavacamten) 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.

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:

- **Strong CYP2C19 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.

CONTRAINDICATIONS

CAMZYOS is contraindicated with concomitant use of:

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

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

The CAMZYOS® Risk Evaluation and Mitigation Strategy (REMS) Program Is Designed to Help Support Closer Care and Monitor Patient Safety

1 Capsule a Day

2 Echos a Year*[1]

For eligible† patients in the Maintenance Phase

Enroll once. Treat many.

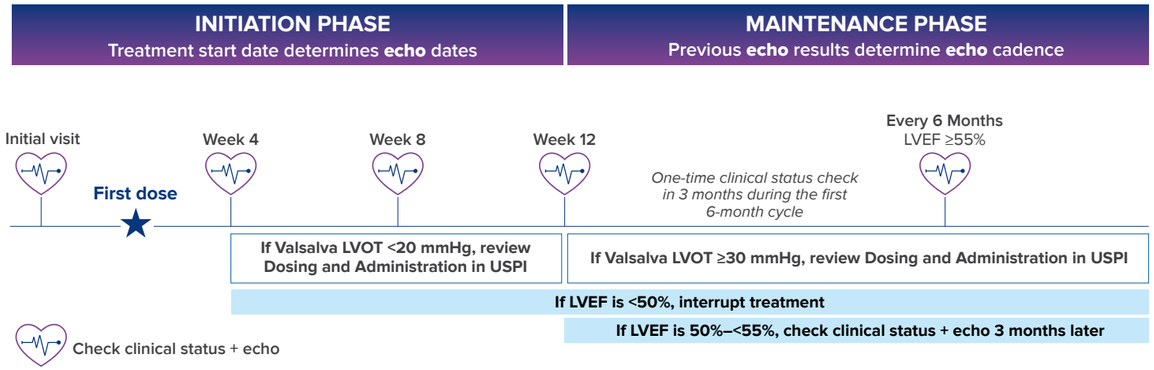
Prescribers must be certified by enrolling in the REMS program

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

For more information, visit CAMZYOSREMS.com or call 833-628-7367



*Additional echos may be needed after a change in the dose of CAMZYOS, treatment interruption, and/or after starting certain medications that are known to affect CAMZYOS (eg, weak to moderate CYP2C19 or moderate to strong CYP3A4 inhibitors).[1]

†Patients in the Maintenance Phase with LVEF ≥55% and Valsalva LVOT gradient <30 mmHg (or Valsalva LVOT ≥30 mmHg without up-titration).[1,2]

A simplified visualization of the number of echos required for treatment with CAMZYOS is captured above. Please see the detailed guidance on dosing and administration in the USPI.

See detailed dosing guidance for CAMZYOS on the following pages

CYP=cytochrome P450; echo=echocardiogram; LVEF=left ventricular ejection fraction; LVOT=left ventricular outflow tract.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS

Heart Failure

CAMZYOS reduces systolic contraction and can cause heart failure or significantly reduce ventricular function. Patients who experience a serious intercurrent illness (eg, serious infection) or arrhythmia (eg, 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 increase the risk of left ventricular systolic dysfunction and heart failure symptoms and clinical experience is limited.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

CYP450 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.

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

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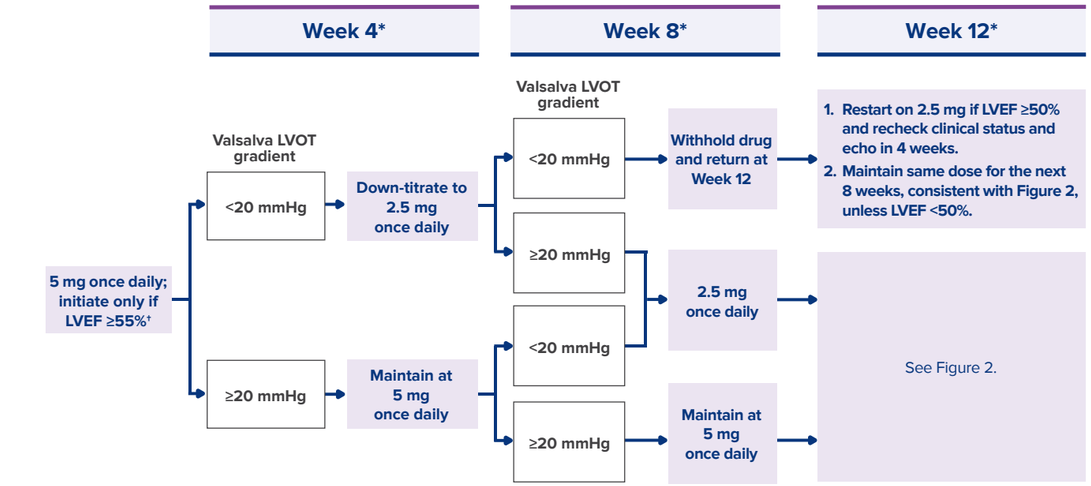
Detailed Dosing for CAMZYOS: Initiation Phase

Prior to initiation

- Assess LVEF by echo. Do not initiate treatment if LVEF <55%
- Confirm absence of pregnancy and advise females of reproductive potential to use effective contraception until 4 months after the last dose. Use a contraceptive not affected by CYP450 enzyme induction or add nonhormonal contraception
- Consider contraindications and drug interactions prior to and throughout treatment
- Consider assessment of post-exercise LVOT gradient in symptomatic patients with normal or near-normal Valsalva LVOT gradients prior to initiating treatment

Figure 1: Initiation Phase



*Interrupt treatment if LVEF is <50% at any clinic visit; restart treatment after 4 weeks if LVEF is ≥50%. See Figure 3.

†Patients initiating CAMZYOS on stable therapy with a moderate CYP2C19 inhibitor or a strong CYP3A4 inhibitor. See USPI Section 2.2 for dosing instructions.

In patients who are on stable therapy with a moderate CYP2C19 inhibitor or a strong CYP3A4 inhibitor, initiate CAMZYOS at 2.5 mg orally once daily. Interrupt CAMZYOS treatment if Valsalva LVOT gradient is <20 mmHg at Week 4 or Week 8. Treatment may be resumed after 4 weeks at 2.5 mg once daily if LVEF is ≥50%. If treatment is resumed at Week 12, recheck clinical status, Valsalva LVOT gradient, and LVEF in 4 weeks, and maintain the current dose for the next 8 weeks unless LVEF is <50%.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

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. Combined hormonal contraceptives (CHCs) containing a combination of ethinyl estradiol and norethindrone may be used with CAMZYOS. However, CAMZYOS may reduce the effectiveness of certain other CHCs. If these CHCs are used, advise patients to add nonhormonal contraception (such as condoms) during concomitant use and for 4 months after the last dose of CAMZYOS.

ADVERSE REACTIONS

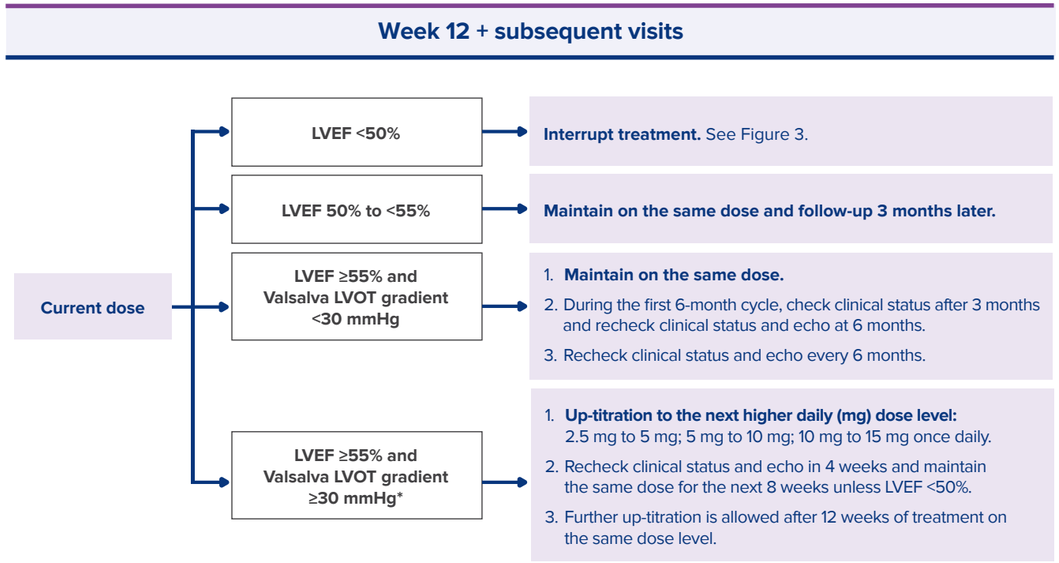
In the EXPLORER-HCM trial, adverse reactions occurring in >5% of patients and more commonly in the CAMZYOS group than in the placebo group were dizziness (27% vs 18%) and syncope (6% vs 2%). There were no new adverse reactions identified in VALOR-HCM.

Detailed Dosing for CAMZYOS: Maintenance Phase

Following initiation

- Assess patient response to treatment, including Valsalva LVOT gradient and LVEF, at Week 12 and every 3–6 months thereafter
  - —Adjust the dose based on Figures 2–3
- Patients may develop heart failure while taking CAMZYOS. Regular LVEF and Valsalva LVOT gradient assessment is required for careful dose titration to achieve an appropriate target Valsalva LVOT gradient while maintaining LVEF ≥50%

Figure 2: Maintenance Phase



*For patients with normal or near-normal Valsalva LVOT gradient (approximately 30 mmHg) prior to initiating treatment with CAMZYOS, if LVEF is ≥55% and post-exercise LVOT gradient is ≥30 mmHg, the dose may be increased to the next higher daily (mg) dose level if symptoms persist.

In patients who initiate a weak to moderate CYP2C19 inhibitor or a moderate to strong CYP3A4 inhibitor, reduce the dosage of CAMZYOS to the next lower daily (mg) dose level (ie, 15 mg to 10 mg; 10 mg to 5 mg; or 5 mg to 2.5 mg). Schedule clinical and echocardiographic assessment 4 weeks after inhibitor initiation, and do not up-titrate to the next higher daily (mg) dose level of CAMZYOS until 12 weeks after inhibitor initiation. Avoid initiation of concomitant weak to moderate CYP2C19 and moderate to strong CYP3A4 inhibitors in patients who are on stable treatment with 2.5 mg of CAMZYOS because a lower dose is not available [see Dosage and Administration (2.1), Drug Interactions (7.1) in the USPI].

IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS (cont'd)

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.

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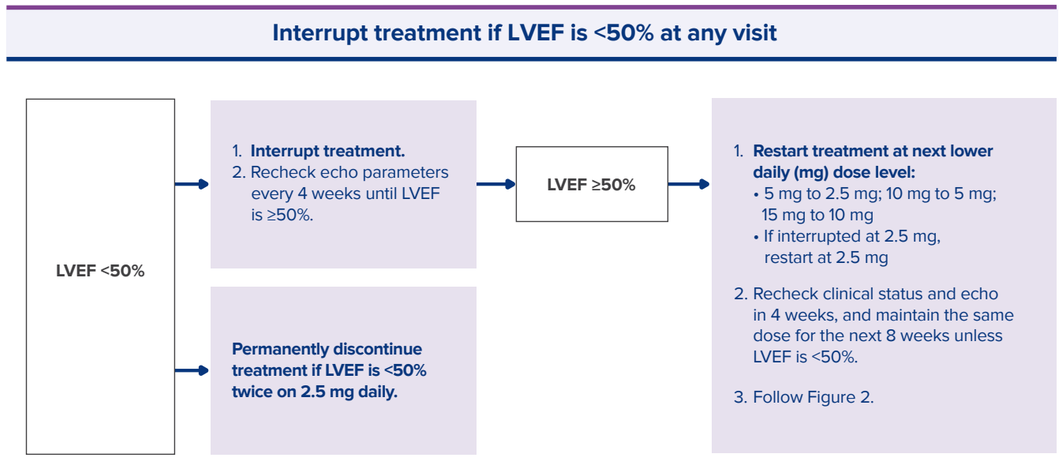
Detailed Dosing for CAMZYOS: Treatment Interruption

- Delay dose increases when there is intercurrent illness (eg, serious infection) or arrhythmia (eg, atrial fibrillation or other uncontrolled tachyarrhythmia) that may impair systolic function. Consider interruption of CAMZYOS in patients with an intercurrent illness
- CAMZYOS may be taken without regard to food. 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. Exact timing of dosing during the day is not essential, but two doses should not be taken on the same day. Swallow capsules whole. Do not break, open, or chew the capsules

Figure 3: Treatment Interruption at Any Clinic Visit if LVEF <50%



For short-term use (eg, 1 week), interrupt CAMZYOS for the duration of treatment with a weak to moderate CYP2C19 inhibitor or a moderate to strong CYP3A4 inhibitor. CAMZYOS may be reinitiated at the previous dose immediately upon discontinuation of concomitant therapy.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

Impact of Other Drugs on CAMZYOS:

- Strong CYP2C19 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 (ie, 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. For short-term use (eg, 1 week), interrupt CAMZYOS for the duration of treatment with a weak inhibitor of CYP2C19 or a moderate inhibitor of CYP3A4. CAMZYOS may be reinitiated at the previous dose immediately on discontinuation of concomitant therapy

IMPORTANT SAFETY INFORMATION (cont'd)

DRUG INTERACTIONS (cont'd)

- Moderate CYP2C19 Inhibitors or Strong CYP3A4 Inhibitors: Concomitant use with a moderate CYP2C19 inhibitor or strong CYP3A4 inhibitor increases CAMZYOS exposure, which may increase the risk of adverse drug reactions. Discontinuing use of a moderate CYP2C19 inhibitor or strong CYP3A4 inhibitor after long-term concomitant use may decrease CAMZYOS exposure, which may reduce CAMZYOS' efficacy. Initiate CAMZYOS at a starting dosage of 2.5 mg orally once daily in patients who are on a stable therapy with a moderate CYP2C19 inhibitor or a strong CYP3A4 inhibitor. Reduce dose of CAMZYOS by one level (ie, 15 to 10 mg, 10 to 5 mg, or 5 to 2.5 mg) in patients who are on CAMZYOS and intend to initiate a moderate CYP2C19 inhibitor or a strong CYP3A4 inhibitor. Avoid initiation of concomitant moderate CYP2C19 and strong CYP3A4 inhibitors in patients who are on a stable treatment with 2.5 mg of CAMZYOS because a lower dose is not available. An increase in dose of CAMZYOS may be needed if the moderate inhibitor of CYP2C19 or strong inhibitor of CYP3A4 is discontinued after long-term concomitant use. Monitor for new or worsening symptoms. For short-term use (ie, when CAMZYOS dose modification is not feasible), interrupt CAMZYOS for the duration of treatment with a weak inhibitor of CYP2C19 or a moderate inhibitor of CYP3A4. CAMZYOS may be reinitiated at the previous dose immediately on discontinuation of concomitant therapy

Potential for CAMZYOS to Affect Plasma Concentrations of Other Drugs

CAMZYOS is an inducer of CYP3A4, CYP2C9, and CYP2C19. Concomitant use with CYP3A4, CYP2C9, or CYP2C19 substrates may reduce plasma concentration of these drugs. Closely monitor when CAMZYOS is used with concomitant CYP3A4, CYP2C9, or CYP2C19 substrates unless otherwise recommended in the Prescribing Information.

Certain Combined Hormonal Contraceptives (CHCs): Progestin and ethinyl estradiol are CYP3A4 substrates. Concomitant use of CAMZYOS may decrease exposures of certain progestins, which may lead to contraceptive failure. CHCs containing a combination of ethinyl estradiol and norethindrone may be used with CAMZYOS, but if other CHCs are used, advise patients to add nonhormonal contraception (such as condoms) or use an alternative contraceptive method that is not affected by CYP450 enzyme induction (eg intrauterine system) 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 in patients on disopyramide, ranolazine, verapamil with a beta blocker, or diltiazem with a beta blocker as these medications and combinations increase the risk of left ventricular systolic dysfunction and heart failure symptoms and clinical experience is limited.

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. CHCs containing a combination of ethinyl estradiol and norethindrone may be used with CAMZYOS. However, CAMZYOS may reduce the effectiveness of certain other CHCs. If these CHCs are used, advise patients to add nonhormonal contraception (such as condoms) or use an alternative contraceptive method during concomitant use and for 4 months after the last dose of CAMZYOS.

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REMS Monitoring Support

With Convenient Online Tools and Resources

The CAMZYOS Interactive Dosing Guide is an interactive online guide to assist in determining the appropriate dose at key points during treatment. Access it at CAMZYOShcp.com/dosing-guide.

The CAMZYOS Imaging Scheduling Tool is an online scheduler to help you and your staff estimate dates for your patients' required imaging tests and can be found at CAMZYOShcp.com/echo-scheduler-tool.

Visit CAMZYOShcp.com for more on dosing, monitoring, and supporting your patients on CAMZYOS

References

1. CAMZYOS [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2025.
2. CAMZYOS REMS. Patient Status Form. Accessed April 18, 2025. https://www.camzyosrems.com/assets/commercial/us/camzyosrems/en/pdf/Camzyos-Patient-Status-Form.pdf

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