

U.S. Food and Drug Administration Approves Camzyos™ (mavacamten) for the Treatment of Adults With Symptomatic New York Heart Association Class II-III Obstructive Hypertrophic Cardiomyopathy (HCM) to Improve Functional Capacity and Symptoms

04/28/2022

CATEGORY: [Corporate/Financial News](#)

Camzyos is the first and only FDA-approved cardiac myosin inhibitor that specifically targets the source of obstructive HCM

Approval based on groundbreaking Phase 3 EXPLORER-HCM trial demonstrating benefit in patients receiving Camzyos versus placebo

PRINCETON, N.J.--(BUSINESS WIRE)-- [Bristol Myers Squibb](#) (NYSE: BMY) today announced that the U.S. Food and Drug Administration (FDA) approved *Camzyos*™ (mavacamten, 2.5 mg, 5 mg, 10 mg, 15 mg capsules) for the treatment of adults with symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy (obstructive HCM) to improve functional capacity and symptoms. *Camzyos* is the first and only FDA-approved allosteric and reversible inhibitor selective for cardiac myosin that targets the underlying pathophysiology of obstructive HCM.

This press release features multimedia. View the full release here: <https://www.businesswire.com/news/home/20220428006368/en>

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

CAMZYOS Logo, Bristol Myers Squibb

"This is a first-in-class medicine specifically for patients living with symptomatic obstructive HCM," said Milind Desai, M.D., MBA, director of the Hypertrophic Cardiomyopathy Center and director of clinical operations in Cleveland Clinic's Heart Vascular & Thoracic Institute. "With this FDA approval, U.S. cardiologists now have a new pharmacological option for eligible patients that targets the underlying pathophysiology of the disease."

The full U.S. Prescribing Information for *Camzyos* includes a **Boxed WARNING** for the 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 moderate to strong CYP2C19 inhibitors or strong CYP3A4 inhibitors, and 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** below.

"This approval builds on decades of cardiovascular leadership and reflects our steadfast commitment to people impacted by cardiovascular disease," said Samit Hirawat, M.D., executive vice president and chief medical officer, Global Drug Development, Bristol Myers Squibb. "We are proud to bring this first-of-its kind medicine to patients, which may help to address an unmet need in the U.S. in the symptomatic NYHA class II-III obstructive HCM treatment landscape."

This approval is based on data from the Phase 3 EXPLORER-HCM trial. At baseline, approximately 73% of the randomized patients were NYHA class II and 27% were NYHA class III. The mean LVEF was 74%, and the mean Valsalva left ventricular outflow tract (LVOT) gradient was 73 mmHg. The baseline mean Kansas City Cardiomyopathy Questionnaire-23 (KCCQ-23) Clinical Summary Score (CSS) was 71. At Week 30, 37% (n=45/123) of patients taking *Camzyos* achieved the composite primary endpoint, defined as the proportion of patients who achieved either improvement of mixed venous oxygen tension (pVO₂) by ≥1.5 mL/kg/min plus improvement in NYHA class by at least 1 or improvement of pVO₂ by ≥3.0 mL/kg/min plus no worsening in NYHA class, versus 17% (n=22/128) treated with placebo. The difference was 19% (95% CI: 9, 30; p=0.0005). Additionally at Week 30, patients receiving *Camzyos* had greater improvement compared to placebo group across all secondary endpoints, including:

- Mean change from baseline post-exercise LVOT peak gradient [-47 mmHg vs -10 mmHg; -35 difference (95% CI: -43, -28; p<0.0001)]
- Mean change from baseline in pVO₂ [1.4 mL/kg/min vs -0.1 mL/kg/min; 1.4 difference (95% CI: 0.6, 2.1; p<0.0006)]
- Number (%) of patients with improvement of NYHA class ≥ 1 [80 (65%) vs 40 (31%); difference of 34% (95% CI: 22%, 45%; p<0.0001)]

- Mean change from baseline in KCCQ-23 [†] CSS [14 vs 4; difference of 9 (95% CI: 5, 13); $p < 0.0001$]
 - Mean change in baseline in KCCQ-23 Total Symptom Score (TSS) (12 vs 5)
 - Mean change in baseline in KCCQ-23 Physical Limitations (PL) (15 vs 4)

[†] The KCCQ-23 CSS is derived from the Total Symptom Score (TSS) and the Physical Limitations (PL) score of the KCCQ-23. The CSS ranges from 0 to 100 with higher scores representing less severe symptoms and/or physical limitations.

Missing data were not imputed to summarize the baseline and change from baseline to Week 30 values. Difference in mean change from baseline between treatment groups was estimated using a mixed model for repeated measures.

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%). 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. Additionally, 7 (6%) patients in the *Camzyos* group and 2 (2%) patients in the placebo group experienced reversible reductions in LVEF to <50% (median 48%; range 35-49%) while on treatment. In all 7 patients treated with *Camzyos*, LVEF recovered following interruption of *Camzyos*.

"The approval of *Camzyos* represents a significant milestone for appropriate symptomatic obstructive HCM patients and their families, who have long awaited a new treatment option for this chronic and progressive disease," said Anjali T. Owens, MD, Medical Director of the Center for Inherited Cardiac Disease and an Assistant Professor of Medicine at the Perelman School of Medicine at the University of Pennsylvania. "As a lead U.S. investigator on the EXPLORER-HCM study, I'm grateful to the patients and their families whose participation in the trial played a key role in this approval."

Bristol Myers Squibb offers various programs and resources to address the needs of patients and caregivers, and provide support that allows for access to therapies, including *Camzyos*. For additional information, call 855-*Camzyos* (855-226-9967) 8 am to 11 pm ET, Monday through Friday.

About EXPLORER-HCM

The EXPLORER-HCM Phase 3 trial was a double-blind, randomized, placebo-controlled, parallel group trial that enrolled a total of 251 adult patients with symptomatic (NYHA class II or III), obstructive hypertrophic cardiomyopathy. All participants had measurable left ventricular ejection fraction (LVEF) $\geq 55\%$ and left ventricular outflow tract (LVOT) peak gradient (resting and/or provoked) ≥ 50 mmHg at baseline. Patients on dual therapy with beta blocker and calcium channel blocker treatment or monotherapy with disopyramide or ranolazine were excluded. Patients with a known infiltrative or storage disorder causing cardiac hypertrophy that mimicked obstructive HCM, such as Fabry disease, amyloidosis, or Noonan syndrome with left ventricular hypertrophy, were also excluded. Patients were randomized in a 1:1 ratio to receive either a starting dose of 5 mg of *Camzyos* or placebo once daily for 30 weeks. The dose was periodically adjusted to optimize patient response (decrease in LVOT gradient with Valsalva maneuver) and maintain LVEF $\geq 50\%$. Treatment assignment was stratified by baseline disease severity NYHA functional class (NYHA class II-III), baseline use of beta blockers (yes or no), and type of ergometer (treadmill or exercise bicycle). The majority of patients in both arms of EXPLORER-HCM were on background therapy including 75% on beta blockers, and 17% on calcium channel blockers.

The primary endpoint for EXPLORER-HCM was a composite functional endpoint, assessed at 30 weeks, and was defined as the proportion of patients who achieved either improvement of mixed venous oxygen tension (pVO_2) by ≥ 1.5 mL/kg/min plus improvement in NYHA class by at least 1 or improvement of pVO_2 by ≥ 3.0 mL/kg/min plus no worsening in NYHA class. A greater proportion of patients met the primary endpoint at Week 30 in the *Camzyos* group compared to the placebo group (37% vs 17%, respectively, difference of 19% (95% CI: 9, 30; $p = 0.0005$). The treatment effects of *Camzyos* on LVOT obstruction, functional capacity, and health status were assessed by change from baseline through Week 30 in post-exercise LVOT peak gradient, change in pVO_2 , proportion of patients with improvement in NYHA class, Kansas City Cardiomyopathy Questionnaire-23 (KCCQ-23) Clinical Summary Score (CSS), and Hypertrophic Cardiomyopathy Symptom Questionnaire (HCMSQ) Shortness of Breath (SoB) domain score. At Week 30, patients receiving *Camzyos* had greater improvement compared to placebo group across all secondary endpoints.

About *Camzyos*™ (mavacamten)

Camzyos™ (mavacamten) is the first and only cardiac myosin inhibitor approved by the U.S. Food and Drug Administration (FDA) 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. *Camzyos* is an allosteric and reversible inhibitor selective for cardiac myosin. *Camzyos* modulates the number of myosin heads that can enter "on actin" (power-generating) states, thus reducing the probability of force-producing (systolic) and residual (diastolic) cross-bridge formation. Excess myosin actin cross-bridge formation and dysregulation of the super-relaxed state are mechanistic hallmarks of HCM. *Camzyos* shifts the overall myosin population towards an energy-sparing, recruitable, super-relaxed state. In HCM patients, myosin inhibition with *Camzyos* reduces dynamic LVOT obstruction and improves cardiac filling pressures.

About *Camzyos* 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 *Camzyos* 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 by telephone at 1-833-628-7367.

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:

- 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.

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

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 (NT)-pro hormone 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 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*.

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 10mg, 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 U.S. Full [Prescribing Information](#), including **Boxed WARNING** and [Medication Guide](#).

About Bristol Myers Squibb

Bristol Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol Myers Squibb, visit us at BMS.com or follow us on [LinkedIn](#), [Twitter](#), [YouTube](#), [Facebook](#) and [Instagram](#).

Cautionary Statement Regarding Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 regarding, among other things, the research, development and commercialization of pharmaceutical products. All statements that are not statements of historical facts are, or may be deemed to be, forward-looking statements. Such forward-looking statements are based on current expectations and projections about our future financial results, goals, plans and objectives and involve inherent risks, assumptions and uncertainties, including internal or external factors that could delay, divert or change any of them in the next several years, that are difficult to predict, may be beyond our control and could cause our future financial results, goals, plans and objectives to differ materially from those expressed in, or implied by, the statements. These risks, assumptions, uncertainties and other factors include, among others, whether *Camzyos*[™] (mavacamten) for the indication described in this release will be commercially successful, any marketing approvals, if granted, may have significant limitations on their use, and that continued approval of such product candidate for such indication described in this release may be contingent upon verification and description of clinical benefit in confirmatory trials. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many risks and uncertainties that affect Bristol Myers Squibb's business and market, particularly those identified in the cautionary statement and risk factors discussion in Bristol Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2021, as updated by our subsequent Quarterly Reports on Form 10-Q, Current Reports on Form 8-K and other filings with the Securities and Exchange Commission. The forward-looking statements included in this document are made only as of the date of this document and except as otherwise required by applicable law, Bristol Myers Squibb undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, changed circumstances or otherwise.

References

1. *Camzyos* Prescribing Information. *Camzyos* U.S. Product Information. Last updated: April 2022. Princeton, NJ: Bristol-Myers Squibb Company.

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Dr. Desai is a paid consultant for Bristol Myers Squibb.

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