אוגוסט 2025

<u>קמזיוס 2.5 מ"ג – Camzyos 2.5 mg</u>
<u>קמזיוס 5 מ"ג – Camzyos 5 mg</u>
<u>קמזיוס 10 מ"ג – Camzyos 10 mg</u>
<u>קמזיוס 15 מ"ג – Camzyos 15 mg</u>
<u>(mavacamten)</u>
<u>במוסות Capsules</u>

רופא/ה ,רוקח/ת יקר/ה,

חברת בריסטול-מאיירס סקוויב (ישראל) מבקשת להודיע על עדכונים בעלון לרופא של התכשירים שבנדון.

להלן התוויית התכשירים כפי שמאושרת ע"י משרד-הבריאות:

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.

המרכיב הפעיל: mavacamten 2.5mg or 5mg or 10mg or 15mg per capsule

השינויים בעלון לרופא משוקפים בעמודים הבאים.

תוספת טקסט מסומנת בקו תחתון, מחיקת טקסט בקו חוצה.

למידע מלא על התרופה יש לעיין בעלון לרופא ובעלון לצרכן כפי שאושרו על ידי משרד-הבריאות.

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד-הבריאות וניתן לקבלו וכן את העלון לצרכן, מודפסים על ידי פנייה לבעל הרישום בריסטול-מאיירס סקוויב (ישראל) בע"מ.

בברכה,

אדר הופמן
רוקחת ממונה
בריסטול-מאיירס סקוויב (ישראל)

שינויים עיקריים בעלון לרופא:

FULL PRESCRIBING INFORMATION

…

5 WARNINGS AND PRECAUTIONS

5.1 Heart Failure

CAMZYOS reduces systolic contraction and can cause heart failure or ~~totally block~~ significantly reduce 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 *[see Clinical Trial Experience (6.1)]*.

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7 DRUG INTERACTIONS

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7.2 Potential for CAMZYOS to Affect Plasma Concentrations of Other Drugs

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Certain Combined Hormonal Contraceptives ~~(CHC)~~

Progestin and ethinyl estradiol are CYP3A4 substrates. Concomitant use of CAMZYOS may decrease exposures of certain progestins *[see Clinical Pharmacology (12.3)]*, which may lead to contraceptive failure. Combined hormonal contraceptives (CHCs) containing a combination of ethinyl estradiol and norethindrone may be used with mavacamten, 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 (e.g., intrauterine system) during concomitant use and for 4 months after the last dose of CAMZYOS.

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8 USE IN SPECIFIC POPULATIONS

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8.3 Females and Males of Reproductive Potential

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Contraception

Females

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 ~~mavacamten~~CAMZYOS. However, CAMZYOS may reduce the effectiveness of certain other ~~Combined hormonal contraceptives (~~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 *[see Drug Interactions (7.2)]*.

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12 CLINICAL PHARMACOLOGY

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12.3 Pharmacokinetics

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Drug Interactions

Clinical Studies and Model-Informed Approaches

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Strong CYP3A4 Inhibitors: Concomitant use of mavacamten (15 mg) with ketoconazole 400 mg once daily in CYP2C19 poor metabolizers is predicted to increase mavacamten AUC_{0-24} and C_{max} up to 130% and 90%, respectively.

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13 NONCLINICAL TOXICOLOGY

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~~13.2 Animal Toxicology and/or Pharmacology~~

~~The safety of mavacamten has been evaluated in rats and dogs at multiple dose levels (0.06 to 10 mg/kg/day) orally. Noted toxicities, including echocardiographic findings, reduction in systolic function, cardiac dilation, and death, as well as increased heart weights in rats, were consistent with mavacamten's mechanism of action and primary pharmacological activity. Other findings included cardiac osseous metaplasia in rats and QTc prolongation in dogs. Plasma exposures (AUC) at the NOAEL in rats and dogs were 0.1 and 0.3 times, respectively, human exposure (AUC) at the MRHD.~~

14 CLINICAL STUDIES

EXPLORER-HCM

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Figure 4: Subgroup Analysis of the Primary Composite Functional Endpoint

Subgroup	n Patients Meeting Primary Endpoint / N of Patients (%) Mavacamten	Placebo	Mean percentage difference (95% CI)
Age, years			
≤49	10/27 (37%)	6/25 (24%)	13% (-11.7 to 37.8)
50-64	21/51 (41%)	13/63 (21%)	21% (3.7 to 37.3)
≥65	14/45 (31%)	3/40 (8%)	24% (7.8 to 39.4)
Sex			
Female	19/57 (33%)	5/45 (11%)	22% (6.9 to 37.5)
Male	26/66 (39%)	17/83 (21%)	19% (4.3 to 33.6)
Body-mass index, kg/m^2			
<30	35/77 (46%)	16/77 (21%)	25% (10.3 to 39.0)
≥30	10/46 (22%)	6/51 (12%)	10% (-4.9 to 24.8)
LVEF at baseline			
<75%	25/69 (36%)	11/70 (16%)	21% (6.3 to 34.7)
≥75%	20/54 (37%)	11/58 (19%)	18% (1.7 to 34.4)
NYHA class at baseline			
II	29/88 (33%)	16/95 (17%)	16% (3.7 to 28.5)
III	16/35 (46%)	6/33 (18%)	28% (6.4 to 48.6)
β blocker usage at baseline			
Yes	28/94 (30%)	20/95 (21%)	9% (-3.6 to 21.1)
No	17/29 (59%)	2/33 (6%)	53% (32.9 to 72.2)
NT-proBNP at baseline, ng/L			
≤ median of 710 ng/L	18/55 (33%)	13/68 (19%)	14% (-1.9 to 29.1)
> median of 710 ng/L	24/65 (37%)	9/58 (16%)	21% (6.4 to 36.4)