HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ETCAMAH safely and effectively. See full prescribing information for ETCAMAH.

ETCAMAH® (camizestrant) tablets, for oral use
Initial U.S. Approval: 2026

WARNING: ARRHYTHMIA RISK WITH CONCOMITANT USE OF QTc INTERVAL PROLONGING DRUGS

See full prescribing information for complete boxed warning.

- **ETCAMAH in combination with ribociclib, a QTc interval prolonging drug and a strong CYP3A inhibitor, or in combination with other QTc interval prolonging drugs, can increase the risk of Torsades de Pointes, other ventricular arrhythmias, and sudden death (5.1, 5.2, 7.1).**
- **Avoid concomitant use of ETCAMAH with products (other than ribociclib) known to prolong the QTc interval and/or have a known risk of Torsades de Pointes. If concomitant use with other products cannot be avoided, monitor the QTc interval more frequently (5.1, 7.3).**
- **Obtain ECG prior to initiation and monitor heart rate and QTc interval during treatment. Assess and correct electrolyte abnormalities prior to initiation and during treatment. Withhold ETCAMAH until resolution of QTc interval prolongation and resume or permanently discontinue ETCAMAH based on severity (2.2, 2.4).**

---------- INDICATIONS AND USAGE ----------
ETCAMAH is an estrogen receptor antagonist indicated:
- in combination with a CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib) for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer upon detection of *ESR1* mutation during aromatase inhibitor and CDK4/6 inhibitor therapy, based on an FDA-authorized test. (1, 2.1)

  This indication is approved under accelerated approval based on progression-free survival as measured from detection of *ESR1* mutation. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). (1)

---------- DOSAGE AND ADMINISTRATION ----------
- Select patients for treatment with ETCAMAH based on the detection of *ESR1* mutation during aromatase inhibitor and CDK4/6 inhibitor therapy. (2.1)
- Recommended Dosage: 75 mg orally once daily with or without food. (2.3)
- See Full Prescribing Information for dosage modifications for adverse reactions (2.4).
- Recommended dosage for patients with hepatic impairment differs depending on the CDK4/6 inhibitor used in combination with ETCAMAH. (2.5)

---------- DOSAGE FORMS AND STRENGTHS ----------
Tablets: 75 mg. (3)

---------- CONTRAINDICATIONS ----------
None. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Bradycardia: Monitor heart rate more frequently during the first 30 days. Avoid concomitant use of ETCAMAH with other products known to cause bradycardia. Withhold or permanently discontinue ETCAMAH based on severity. (2.2, 2.4, 5.2, 7.4)
- Embryo-Fetal Toxicity: ETCAMAH can cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception. (5.3, 8.1, 8.3)

---------- ADVERSE REACTIONS ----------
The most common adverse reactions (≥ 20%), including laboratory abnormalities, with ETCAMAH in combination with a CDK4/6 inhibitor were decreased neutrophils, decreased leukocytes, decreased hemoglobin, decreased lymphocytes, decreased platelets, visual disturbances, and fatigue. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact AstraZeneca at 1-800-236-9933 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------
- CYP3A Inhibitors: Monitor for increased adverse reactions to ETCAMAH with strong CYP3A inhibitors and modify the dosage as recommended. (7.1)
- CYP3A Inducers: Avoid concomitant use of strong and moderate CYP3A inducers. If concomitant use with a moderate CYP3A inducer cannot be avoided, dose adjustment is needed when ETCAMAH is given in combination with abemaciclib or palbociclib. (2.6, 7.1)
- CYP2C9 and/or CYP2C19 Substrates: Avoid concomitant use of ETCAMAH with CYP2C9 substrates or CYP2C19 substrates during treatment with ETCAMAH and at least 2 weeks after the last dose of ETCAMAH, unless otherwise recommended in the Prescribing Information of the CYP2C9 substrate or CYP2C19 substrate. (7.2)
- CYP3A Substrates: Refer to the Prescribing Information for CYP3A substrates where minimal increases in the concentration may lead to serious adverse reactions. (7.2)

---------- USE IN SPECIFIC POPULATIONS ----------
Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 09/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: ARRHYTHMIA RISK WITH CONCOMITANT USE OF QTc INTERVAL PROLONGING DRUGS

ETCAMAH in combination with ribociclib, a QTc interval prolonging drug and a strong CYP3A inhibitor, or in combination with other QTc interval prolonging drugs, can increase the risk of Torsades de Pointes, other ventricular arrhythmias, and sudden death (5.1, 5.2, 7.1).

Avoid concomitant use of ETCAMAH with products (other than ribociclib) known to prolong the QTc interval and/or have a known risk of Torsades de Pointes. If concomitant use with other products cannot be avoided, monitor the QTc interval more frequently (5.1, 7.3).

Obtain ECG prior to initiation and monitor heart rate and QTc interval during treatment. Assess and correct electrolyte abnormalities prior to initiation and during treatment. Withhold ETCAMAH until resolution of QTc interval prolongation and resume or permanently discontinue ETCAMAH based on severity (2.2, 2.4).

1 INDICATIONS AND USAGE

ETCAMAH in combination with a CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib) is indicated for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer upon detection of *ESR1* mutation during aromatase inhibitor and CDK4/6 inhibitor therapy, based on an FDA-authorized test *[see Dosage and Administration (2.1)]*.

This indication is approved under accelerated approval based on progression-free survival as measured from detection of *ESR1* mutation *[see Clinical Studies (14)]*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Select patients with HR-positive, HER2-negative locally advanced or metastatic breast cancer who have received at least 6 months of an aromatase inhibitor and CDK4/6 inhibitor therapy for treatment with ETCAMAH in combination with a CDK4/6 inhibitor based on the presence of an *ESR1* mutation in plasma specimens, using an FDA-authorized test performed every 3 months until an *ESR1* mutation has been detected *[see Indications and Usage (1) and Clinical Studies (14)]*.

Information on FDA-authorized tests for the detection of an *ESR1* mutation in breast cancer is available at: http://www.fda.gov/CompanionDiagnostics.

2.2 Recommended Cardiac Evaluation

Perform an electrocardiogram (ECG) prior to initiating ETCAMAH, then every week for the first 2 weeks of treatment, and periodically during treatment as clinically indicated *[see Warnings and Precautions (5.1)]*.

Monitor heart rate more frequently during the first 30 days of treatment with ETCAMAH in patients with bradycardia (resting heart rate less than 60 bpm) at baseline and those on concomitant medications known to lower heart rate (e.g., beta-blockers) *[see Warnings and Precautions (5.2)]*.

2.3 Recommended Dosage and Administration

The recommended dosage of ETCAMAH is 75 mg orally once daily, with or without food, until disease progression or unacceptable toxicity *[see Clinical Pharmacology (12.3)]*.

Administer ETCAMAH in combination with a CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib). Continue the CDK4/6 inhibitor at the same dosage as when the *ESR1* mutation was detected. Refer to the Prescribing Information of the CDK4/6 inhibitor for additional dosing information *[see Clinical Studies (14)]*.

Take ETCAMAH at approximately the same time each day.

Swallow tablets whole. Do not cut, crush, or chew tablets prior to swallowing. Do not take broken, cracked, or otherwise not intact tablets.

If a dose is missed within 6 hours, take the missed dose. If a dose of ETCAMAH is missed for more than 6 hours, skip the dose for the day and take the next dose at the usual time.

If a dose is vomited, do not take an additional dose and take the next dose at the usual time.

2.4 Dosage Modifications for Adverse Reactions

The recommended dosage modifications for ETCAMAH for adverse reactions are provided in Table 1. No dose reductions of ETCAMAH are recommended.

Table 1. Recommended Dosage Modifications for ETCAMAH

Adverse Reaction	Severity[a]	ETCAMAH Dosage Modifications
QTc Interval Prolongation *[see Warnings and Precautions (5.1)]*	QTc > 500 msec or QTc > 480 msec and prolongation from baseline > 60 msec	Withhold ETCAMAH. If other contributing causes are identified, then treat or correct the contributing causes. Resume ETCAMAH when QTc returns to < 480 msec. Re-assess ECGs weekly for the first 2 weeks of treatment, and periodically during treatment as clinically indicated. Permanently discontinue ETCAMAH if QTc interval prolongation is either > 500 msec or > 60 msec change from baseline AND associated with any of the following: Torsades de Pointes, polymorphic ventricular tachycardia, syncope, or signs/symptoms of serious arrhythmia.
Bradycardia[b] *[see Warnings and Precautions (5.2)]*	Symptomatic, Grade 2 or above	Withhold ETCAMAH until symptoms resolve. Obtain ECG to evaluate etiology of symptomatic bradycardia. If a contributing concomitant medication is identified, modify the dosage or discontinue this medication as appropriate until bradycardia symptoms resolve and then resume ETCAMAH. Consider reassessing the heart rate after restart of ETCAMAH. Permanently discontinue ETCAMAH for persistent symptomatic bradycardia.
Visual Disturbances[c] *[see Adverse Reactions (6.1)]*	Grade 2 or above/limiting instrumental ADLs	Withhold ETCAMAH until symptoms resolve to Grade 1 or below. Refer patients to an eye care professional for an ophthalmic examination and treatment. Reassess visual disturbances at the next visit.
Other Adverse Reactions *[see Adverse Reactions (6.1)]*	Grade 3 or higher	Withhold ETCAMAH until resolution to Grade 2 or below, then resume ETCAMAH. Permanently discontinue ETCAMAH for recurrence of Grade 3 or higher adverse reactions.

ADL = Activities of daily living; CTCAE = Common Terminology Criteria for Adverse Events; NCI = National Cancer Institute.
[a] Severity as defined by NCI CTCAE version 5.0.
[b] Bradycardia includes bradycardia and sinus bradycardia.
[c] Visual disturbances include: photopsia, blurred vision, visual field defect, decreased visual acuity, visual impairment, diplopia, photophobia and visual perseveration.

Refer to the Prescribing Information for the co-administered CDK4/6 inhibitor for dosage modification guidelines related to adverse reactions, organ impairment, and drug-drug interactions.

2.5 Dosage in Patients with Hepatic Impairment

The recommended dosage for patients with hepatic impairment differs depending on the CDK4/6 inhibitor used in combination with ETCAMAH.

For patients with severe (Child-Pugh C) hepatic impairment who are receiving ETCAMAH in combination with ribociclib, the recommended dosage of ETCAMAH is 75 mg once every other day.

For patients with severe (Child-Pugh C) hepatic impairment who are receiving ETCAMAH in combination with abemaciclib or palbociclib, no dosage modification of ETCAMAH is recommended.

Monitor patients with moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment receiving ETCAMAH in combination with any CDK4/6 inhibitor for increased adverse reactions and modify the dosage as recommended *[see Dosage and Administration (2.4)]*.

2.6 Dosage Modifications for Strong and Moderate CYP3A Inducers

Avoid concomitant use of strong CYP3A inducers.

Dosage modifications for concomitant use of moderate CYP3A inducers differ depending on the CDK4/6 inhibitor used in combination with ETCAMAH.

Avoid concomitant use of moderate CYP3A inducers for patients who are receiving ETCAMAH in combination with abemaciclib or palbociclib. If concomitant use of a moderate CYP3A inducer cannot be avoided, increase the ETCAMAH dosage from 75 mg once daily to 150 mg once daily for patients who are receiving ETCAMAH in combination with abemaciclib or palbociclib *[see Drug Interactions (7.1)]*. After the moderate CYP3A inducer has been discontinued for at least 14 days, resume the ETCAMAH dosage used prior to initiation of the moderate CYP3A inducer.

For patients who are receiving ETCAMAH in combination with ribociclib concomitantly with a moderate CYP3A inducer, no ETCAMAH dosage modification is recommended.

3 DOSAGE FORMS AND STRENGTHS

75 mg tablets: beige, round, bi-convex, film-coated tablets debossed with ‘CM’ above ‘75’ on one side and plain on the reverse.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 QTc Interval Prolongation

ETCAMAH in combination with a CDK4/6 inhibitor is associated with QTc interval prolongation *[see Clinical Pharmacology (12.2)]*.

When ETCAMAH is used in combination with ribociclib, a CDK4/6 inhibitor that causes QTc interval prolongation and is a strong CYP3A inhibitor, there is potential for an increased risk of Torsades de Pointes, other ventricular arrhythmias, and sudden death. One case of Torsades de Pointes was observed in a dose-finding trial when ETCAMAH was used with ribociclib *[see Drug Interactions (7.1, 7.3) and Clinical Pharmacology (12.2)]*.

In SERENA-6, QTc interval prolongation occurred in 2.6% of patients treated with ETCAMAH in combination with a CDK4/6 inhibitor. QTc interval prolongation led to dose interruption of ETCAMAH in 0.6% of patients. ETCAMAH also causes bradycardia, which increases the risk of QTc interval prolongation. *[see Warnings and Precautions (5.2)]*.

Perform an ECG prior to initiating ETCAMAH, then every week for the first 2 weeks of treatment, and periodically during treatment as clinically indicated *[see Dosage and Administration (2.2)]*.

Obtain serum electrolytes at baseline and during treatment as clinically indicated, and correct electrolyte abnormalities.

Avoid concomitant use of ETCAMAH in combination with a CDK4/6 inhibitor with products that can cause QTc interval prolongation, are strong CYP3A inhibitors, and/or drugs known to lower heart rate *[see Warnings and Precautions (5.2) and Drug Interactions (7.1, 7.3, 7.4)]*.

Withhold or permanently discontinue ETCAMAH based on severity *[see Dosage and Administration (2.4)]*.

5.2 Bradycardia

ETCAMAH causes a decrease in heart rate. Bradycardia increases the risk for life-threatening arrhythmias and sudden death when concomitant QTc interval prolongation is present, such as when ETCAMAH is used in combination with ribociclib, both a QTc interval prolonging product and a strong CYP3A inhibitor *[see Warnings and Precautions (5.1) and Drug Interactions (7.1, 7.3)]*.

In SERENA-6, bradycardia adverse events occurred in 8% of patients treated with ETCAMAH. The mean heart rate decrease from baseline was approximately 13 beats per minute (bpm) with ETCAMAH with the maximum decrease observed on Day 15. The median time to onset of adverse reaction was 17 days (range 13 to 283) after starting ETCAMAH. Bradycardia led to dose interruption of ETCAMAH in 3.9% of patients. The safety of ETCAMAH has not been established in patients with a baseline resting heart rate less than 55 bpm as these patients were excluded from SERENA-6.

Monitor heart rate more frequently during the first 30 days of treatment with ETCAMAH in patients with bradycardia (heart rate less than 60 bpm) at baseline and those on concomitant medications known to lower heart rate (e.g., beta-blockers) *[see Dosage and Administration (2.2), and Drug Interactions (7.4)]*.

Withhold or permanently discontinue ETCAMAH based on severity *[see Dosage and Administration (2.4)]*.

5.3 Embryo-Fetal Toxicity

Based on findings in animals and its mechanism of action, ETCAMAH can cause fetal harm when administered to a pregnant woman *[see Clinical Pharmacology (12.1)]*. In animal reproduction studies, oral administration of camizestrant to rats during pregnancy resulted in adverse developmental outcomes including embryo-fetal/neonatal mortality and alterations to growth at maternal exposures below the human AUC at the recommended dose.

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective non-hormonal contraception during treatment with ETCAMAH and for 4 weeks after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ETCAMAH and for 1 week after the last dose *[see Use in Specific Populations (8.1, 8.3)]*.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

The following clinically significant adverse reactions are described elsewhere in the labeling:

- QTc interval prolongation *[see Warnings and Precautions (5.1)]*
- Bradycardia *[see Warnings and Precautions (5.2)]*

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

HR-positive, HER2-negative Locally Advanced or Metastatic Breast Cancer

The safety of ETCAMAH was evaluated in 155 patients with HR-positive, HER2-negative locally advanced or metastatic breast cancer with detectable *ESR1* mutation without disease progression during first line treatment with an aromatase inhibitor (AI) in combination with a CDK4/6 inhibitor in SERENA-6 *[see Clinical Studies (14)]*. Patients received ETCAMAH 75 mg orally once daily in combination with a CDK4/6 inhibitor (N = 157) or AI in combination with a CDK4/6 inhibitor (N = 158).

The median duration of exposure to ETCAMAH in combination with a CDK4/6 inhibitor was 10.1 months.

Serious adverse reactions occurred in 10% of patients who received ETCAMAH in combination with a CDK4/6 inhibitor. Serious adverse reactions in > 1% of patients included urinary tract infection, pneumonia, and osteonecrosis of jaw

(1.3% each). Fatal adverse reactions occurred in 1.3% of patients who received ETCAMAH in combination with a CDK4/6 inhibitor, including acute respiratory distress syndrome and sudden death (0.6% each).

Permanent discontinuation of ETCAMAH due to adverse reactions occurred in 1.3% of patients. Adverse reactions that resulted in permanent discontinuation of ETCAMAH included gastroesophageal reflux disease, cholestasis and hepatic cytolysis (0.6% each).

Dosage interruption of ETCAMAH due to adverse reactions occurred in 22% of patients. Adverse reactions which required dosage interruption of ETCAMAH in ≥ 2% of patients included bradycardia (3.9%) and visual disturbances (2.6%).

The most common (≥ 20%) adverse reactions, including laboratory abnormalities, were decreased neutrophils, decreased leukocytes, decreased hemoglobin, decreased lymphocytes, decreased platelets, visual disturbances, and fatigue.

Tables 2 and 3 summarize the adverse reactions and laboratory abnormalities, respectively, in SERENA-6.

Table 2. Adverse Reactions in ≥ 10% (All Grades) of Patients with HR-positive, HER2-negative Locally Advanced or Metastatic Breast Cancer Who Received ETCAMAH in SERENA-6[*]

Adverse Reaction	ETCAMAH with a CDK4/6 Inhibitor N = 155		Aromatase Inhibitor with a CDK4/6 Inhibitor N = 155	
	All Grades (%)	Grade 3 or 4 (%)	All Grades (%)	Grade 3 or 4 (%)
Eye Disorders				
Visual disturbances[†]	34	0.6	16	0
Dry eye	12	0	7	0
General Disorders and Administration Site Conditions				
Fatigue[‡]	23	0	19	0.6
Musculoskeletal and Connective Tissue Disorders				
Arthralgia	16	0	17	0.6
Back pain	10	0.6	10	0
Gastrointestinal Disorders				
Nausea	10	0	14	0.6

[*] Graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.
[†] Visual disturbances include: photopsia, blurred vision, visual field defect, decreased visual acuity, visual impairment, diplopia, photophobia, and visual perseveration.
[‡] Fatigue includes: fatigue and asthenia.

Clinically relevant adverse reactions (< 10%) in patients who received ETCAMAH included: vitreous floaters, bradycardia, and QTc prolongation.

Table 3. Select Laboratory Abnormalities ≥ 10% that Worsened from Baseline in Patients with HR-positive, HER2-negative Locally Advanced or Metastatic Breast Cancer Who Received ETCAMAH in SERENA-6[*, †]

Laboratory Abnormality	ETCAMAH with a CDK4/6 Inhibitor N = 155		Aromatase Inhibitor with a CDK4/6 Inhibitor N = 155	
	All Grades (%)	Grade 3 or 4 (%)	All Grades (%)	Grade 3 or 4 (%)
Hematology				
Neutrophils decreased	68	42	66	39
Leukocytes decreased	66	23	58	17
Hemoglobin decreased	47	3.9	38	5
Lymphocyte decreased	39	9	37	8
Platelets decreased	36	2.6	30	1.3
Chemistry				
Aspartate aminotransferase increased	17	2.6	29	1.3
Corrected calcium decreased	17	0	12	0.7
Creatinine increased	16	0.6	20	1.3
Gamma glutamyl transferase increased	12	2.7	23	8

Laboratory Abnormality	ETCAMAH with a CDK4/6 Inhibitor N = 155		Aromatase Inhibitor with a CDK4/6 Inhibitor N = 155	
	All Grades (%)	Grade 3 or 4 (%)	All Grades (%)	Grade 3 or 4 (%)
Alanine aminotransferase increased	12	1.3	20	0
Creatine kinase increased	12	0	6	0
Alkaline phosphatase increased	10	0.7	22	0.7

[*] Graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.
[†] Includes patients with at least one baseline and one post-baseline result.

Patient-Reported Outcomes

Patient-reported blurred vision was assessed using the Patient-Reported Outcomes Common Terminology Criteria for Adverse Events (PRO-CTCAE) at baseline, every week through Week 12, and then every 8 weeks until treatment discontinuation.

For post-baseline time points, completion rates for the patient-reported symptom of blurred vision (severity) ranged between 65% to 80% for patients on ETCAMAH in combination with a CDK4/6 inhibitor and 58% to 72% for patients on AI in combination with a CDK4/6 inhibitor up to Week 52. PRO-CTCAE blurred vision (severity) results are summarized in Table 4.

Table 4 Patient-Reported Symptom of Blurred Vision Assessed by PRO-CTCAE

Number of Patients[*]	ETCAMAH in combination with a CDK4/6 inhibitor (N = 102)		AI in combination with a CDK4/6 inhibitor (N = 88)			
Symptoms	Any symptoms before study treatment (%)[†]		Any Worsening on treatment (%)[‡]		Any Worsening to Score 3 or 4 (%)[§]	
	ETCAMAH in combination with a CDK4/6 inhibitor (%)	AI in combination with a CDK4/6 inhibitor (%)	ETCAMAH in combination with a CDK4/6 inhibitor (%)	AI in combination with a CDK4/6 inhibitor (%)	ETCAMAH in combination with a CDK4/6 inhibitor (%)	AI in combination with a CDK4/6 inhibitor (%)
Blurred Vision (Severity)	31	25	69	50	10	4.5

[*] The number of patients with score before study treatment and at least one on treatment up to week 52
[†] The percentage of patients whose symptom score at baseline assessment (before study treatment) was 1-4
[‡] The percentage of patients whose symptom score increased with respect to their score at baseline assessment (before study treatment)
[§] The percentage of patients whose symptom score increased to 3 or 4 with respect to their score at baseline assessment (before study treatment)
The symptom attribute scoring for severity is defined as a score of 0 = ‘none’; 1 = ‘mild’; 2 = ‘moderate’; 3 = ‘severe’; 4 = ‘very severe’.

Patient-reported overall impact of visual disturbances was assessed using the Visual Symptom Assessment Questionnaire [VSAQ]. The VSAQ was assessed at baseline, in Weeks 2, 6 and 24, and then every 12 weeks. For post-baseline timepoints, completion rates ranged from 69% to 81% for patients on ETCAMAH in combination with a CDK4/6 inhibitor and 60% to 73% for patients on AI in combination with a CDK4/6 inhibitor.

Among patients who reported experiencing a visual disturbance and completed a baseline and at least one post baseline assessment, 12% of patients on ETCAMAH in combination with a CDK4/6 inhibitor versus 13% of patients on AI in combination with a CDK4/6 inhibitor reported “I am bothered by visual disturbances from my cancer treatment”. With respect to baseline, the proportion of patients with VSAQ responses of "quite a bit" or "extremely" bothered was 4.9% of patients on ETCAMAH in combination with a CDK4/6 inhibitor and 1.2% of patients on AI in combination with a CDK4/6 inhibitor.

Among patients who reported experiencing a visual disturbance while receiving ETCAMAH in combination with a CDK4/6 inhibitor, episodes were typically < 1 minute and occurred < 3 days per week.

Patient-reported overall side-effect burden was assessed using the single-item Patient Global Impression of Treatment Tolerability (PGI-TT) questionnaire at baseline, every week through Week 12, and then every 8 weeks until treatment discontinuation. For post-baseline timepoints, the completion rate for patients on ETCAMAH in combination with a CDK4/6 inhibitor ranged from 67% to 81% and for patients on AI in combination with a CDK4/6 inhibitor ranged from 59% to 73% in the first 52 weeks.

In the PGI-TT questionnaire patients provided a response to "In the last 7 days, how bothered were you by the side effects of your cancer treatment?" The proportion of patients with PGI-TT responses of "not at all" bothered was > 30% across all timepoints for patients on ETCAMAH in combination with a CDK4/6 inhibitor and > 40% across all timepoints for patients on AI in combination with a CDK4/6 inhibitor.

7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on ETCAMAH

Table 5 describes drug interactions where concomitant use of another drug affects ETCAMAH.

Table 5. Drug Interactions involving ETCAMAH and Other Drug Products

Strong CYP3A Inhibitors	
Prevention or Management	• Monitor for increased adverse reactions to ETCAMAH and modify the dosage as recommended *[see Dosage and Administration (2.4)]*.
Mechanism and Clinical Effect	• Camizestrant is a CYP3A substrate. Concomitant use with strong CYP3A inhibitors increases camizestrant plasma concentrations *[see Clinical Pharmacology (12.3)]*, which may increase the risk of adverse reactions related to ETCAMAH. • ETCAMAH is indicated to be used in combination with CDK4/6 inhibitors, including ribociclib, which is a strong CYP3A inhibitor and can prolong the QT interval *[see Warnings and Precautions (5.1) and Drug Interactions (7.3)]*.
Strong and Moderate CYP3A Inducers	
Prevention or Management	• Avoid concomitant use of strong CYP3A inducers. • The co-administration of ETCAMAH and a moderate CYP3A inducer is allowed with caution. • The dosage recommendations for concomitant use of moderate CYP3A inducers differ depending on the CDK4/6 inhibitor used in combination with ETCAMAH. o Avoid concomitant use of moderate CYP3A inducers for patients who are receiving ETCAMAH in combination with abemaciclib or palbociclib. If concomitant use cannot be avoided, increase the ETCAMAH dosage from 75 mg once daily to 150 mg once daily for patients who are receiving ETCAMAH in combination with abemaciclib or palbociclib *[see Dosage and Administration (2.6)]*. After the moderate CYP3A inducer has been discontinued for at least 14 days, resume the ETCAMAH dosage used prior to initiation of the moderate CYP3A inducer. o For patients who are receiving ETCAMAH in combination with ribociclib concomitantly with a moderate CYP3A inducer, no ETCAMAH dosage modification is recommended.
Mechanism and Clinical Effect	• Camizestrant is a CYP3A substrate. Concomitant use with strong or moderate CYP3A inducers decreases camizestrant plasma concentrations *[see Clinical Pharmacology (12.3)]* which may reduce ETCAMAH effectiveness.

7.2 Effect of ETCAMAH on Other Drugs

Table 6 describes drug interactions where concomitant use of ETCAMAH affects another drug.

Table 6. Drug Interactions involving ETCAMAH and Other Drug Products

CYP2C9 Substrates or CYP2C19 Substrates

Prevention or Management	• Avoid concomitant use of ETCAMAH with CYP2C9 substrates or CYP2C19 substrates during treatment with ETCAMAH and at least 2 weeks after the last dose of ETCAMAH, unless otherwise recommended in the Prescribing Information of the CYP2C9 substrate or CYP2C19 substrate.
Mechanism and Clinical Effect	• ETCAMAH is a strong CYP2C9 inhibitor and a strong CYP2C19 inhibitor. • ETCAMAH is predicted to increase the exposure of both CYP2C9 substrates and CYP2C19 substrates *[see Clinical Pharmacology (12.3)]*, which may increase the risk of adverse reactions related to these substrates.
Certain CYP3A Substrates	
Prevention or Management	• Refer to the Prescribing Information for CYP3A substrates where minimal increases in the concentration may lead to serious adverse reactions.
Mechanism and Clinical Effect	• ETCAMAH is a CYP3A inhibitor. • ETCAMAH increases exposure of CYP3A substrates *[see Clinical Pharmacology (12.3)]*, which may increase the risk of adverse reactions related to these substrates.

7.3 Drugs That Prolong the QTc Interval

ETCAMAH is indicated in combination with a CDK4/6 inhibitor and there is increased risk of QTc interval prolongation with ribociclib, a strong CYP3A inhibitor that can prolong the QTc interval *[see Drug Interactions (7.1)]*. Refer to the ribociclib prescribing information for dosage modifications.

Avoid concomitant use of ETCAMAH with products (other than ribociclib) known to prolong the QTc interval and/or have a known risk of Torsades de Pointes. If concomitant use with other products cannot be avoided, monitor the QTc interval more frequently *[see Warnings and Precautions (5.1)]*.

ETCAMAH in combination with a CDK4/6 inhibitor is associated with QTc interval prolongation *[see Clinical Pharmacology (12.2)]*.

7.4 Drugs That Cause Bradycardia

Avoid concomitant use of ETCAMAH with other products known to cause bradycardia. Monitor for signs and symptoms of bradycardia if concomitant use cannot be avoided *[see Warnings and Precautions (5.2)]*.

ETCAMAH causes decreases in heart rate that are dose and baseline heart rate dependent *[see Clinical Pharmacology (12.2)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings in animals and its mechanism of action, ETCAMAH can cause fetal harm when administered to a pregnant woman *[see Clinical Pharmacology (12.1)]*. There are no available human data on ETCAMAH use in pregnant women to inform the drug-associated risk. In animal reproduction studies, oral administration of camizestrant to rats during pregnancy resulted in adverse developmental outcomes including embryo-fetal/neonatal mortality and alterations to growth at maternal exposures below the human AUC at the recommended dose *(see Data)*. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2%-4% and 15%-20%, respectively.

Data

Animal Data

In an embryo-fetal development study with pre- and post-natal assessments, female rats received camizestrant at doses of 0.1 mg/kg from gestation Day (GD) 2 to 20, doses up to 0.091 mg/kg from GD 6 to 16, or doses of 0.075 and 0.75 mg/kg from GD 6 to lactation day (LD) 6. Administration of 0.1 mg/kg camizestrant during GD 2 to 20 resulted in no pregnancies. Camizestrant at doses ≥ 0.075 mg/kg administered from GD 6 to LD 6 resulted in increased length of

gestation, dystocia, and decreased pup survival and pup weight. At all doses, maternal exposures were below the human AUC at the recommended dose.

8.2 Lactation

Risk Summary

There are no data on the presence of camizestrant or its metabolites in human milk, its effects on milk production, or on the breastfed child. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with ETCAMAH and for 1 week after the last dose.

8.3 Females and Males of Reproductive Potential

ETCAMAH can cause fetal harm when administered to pregnant women *[see Use in Specific Populations (8.1)]*.

Pregnancy Testing

Verify pregnancy status of females of reproductive potential prior to initiating ETCAMAH treatment.

Contraception

Females

Advise females of reproductive potential to use effective non-hormonal contraception during treatment with ETCAMAH and for 4 weeks after the last dose.

Males

Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ETCAMAH and for 1 week after the last dose.

Refer to the Prescribing Information of the CDK4/6 inhibitor palbociclib, if used in combination with ETCAMAH, for contraception information. Advise patients to use effective contraception during treatment and for the longest post-treatment duration as recommended in the Prescribing Information.

Infertility

Based on findings from animal studies, ETCAMAH may impair fertility in females and males of reproductive potential. Findings in female animals were reversible. The reversibility of effects on male fertility in animals is unknown *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

The safety and effectiveness of ETCAMAH have not been established in pediatric patients.

8.5 Geriatric Use

Of the 155 patients who received ETCAMAH in SERENA-6, 62 (39%) patients were ≥ 65 years of age and 5 (3.2%) patients were ≥ 75 years of age *[see Clinical Studies (14)]*. No overall differences in safety and effectiveness were observed between patients ≥ 65 years of age and younger patients. There are insufficient number of patients ≥ 75 years of age to assess differences in safety or effectiveness.

8.6 Hepatic Impairment

The recommended dosage for patients with hepatic impairment differs depending on the CDK4/6 inhibitor used in combination with ETCAMAH.

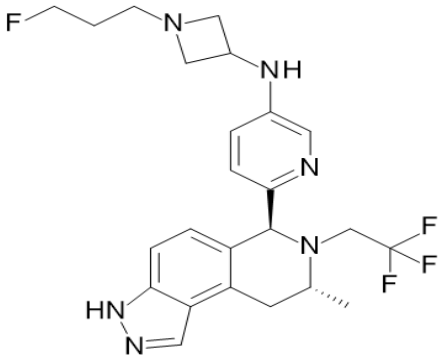
Reduce the dosing frequency of ETCAMAH for patients with severe (Child-Pugh C) hepatic impairment who are receiving ETCAMAH in combination with ribociclib *[see Dosage and Administration (2.5) and Clinical Pharmacology (12.3)]*.

No dosage modification of ETCAMAH is recommended for patients with mild or moderate (Child-Pugh A or B) hepatic impairment who are receiving ETCAMAH in combination with ribociclib or for patients with mild, moderate, or severe (Child-Pugh A, B, or C) hepatic impairment who are receiving ETCAMAH in combination with abemaciclib or palbociclib.

Monitor patients with moderate or severe hepatic impairment receiving ETCAMAH in combination with any CDK4/6 inhibitor for increased adverse reactions and modify the dosage as recommended *[see Dosage and Administration (2.4)]*.

11 DESCRIPTION

ETCAMAH tablets contain camizestrant, an estrogen receptor antagonist for oral use. The chemical name is *N*-[1-(3-fluoropropyl)-3-azetidinyl]-6-[(6*S*,8*R*)-8-methyl-7-(2,2,2-trifluoroethyl)-6,7,8,9-tetrahydro-3*H*-pyrazolo[4,3-*f*]isoquinolin-6-yl]-3-pyridinamine. Camizestrant is white to brown powder. The molecular formula for camizestrant is $C_{24}H_{28}F_4N_6$ and the molecular weight is 476.51 g/mol. The chemical structure for camizestrant is shown below:



Each ETCAMAH tablet contains 75 mg camizestrant and the following inactive ingredients: anhydrous dibasic calcium phosphate, magnesium stearate, microcrystalline cellulose, and sodium starch glycolate. The tablet film-coating consists of ferric oxide red, ferric oxide yellow, ferrosoferric oxide, polyethylene glycol 3350, polyvinyl alcohol, talc and titanium dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Camizestrant is an estrogen receptor (ER) antagonist. In vitro, camizestrant binds to the ligand binding domain of ERα, antagonizing the activity of ERα encoded by both wild-type *ESR1* and mutated *ESR1* and inducing proteasome-dependent degradation of ERα, without agonizing ERα.

Camizestrant demonstrated anti-tumor activity in ER-positive cell lines, in vitro, and patient derived xenograft (PDX) models, in vivo, including those with wild-type or mutated *ESR1* genes. Treatment with camizestrant and CDK4/6 inhibitors (abemaciclib, palbociclib, or ribociclib) demonstrated greater anti-tumor activity than single agent treatment in ER-positive cell lines and PDX models.

12.2 Pharmacodynamics

Exposure-Response Relationships

The exposure-response relationships for efficacy of camizestrant in combination with CDK4/6 inhibitors (abemaciclib, palbociclib, and ribociclib) have not been fully characterized.

Higher exposure to camizestrant was associated with increased incidence of bradycardia and visual disturbance over the dose range of 25 mg (0.3 times the recommended dose) to 450 mg (6 times the recommended dose).

Cardiac Electrophysiology

There is insufficient information to fully characterize the effect size of camizestrant on the QTc interval *[see Warnings and Precautions (5.1)]*.

12.3 Pharmacokinetics

Camizestrant pharmacokinetics were observed at steady state in patients with breast cancer at the approved recommended dosage and are presented as mean (CV%), unless otherwise specified.

Camizestrant total systemic exposure (AUC) is 1,115 ng·h/mL (40.8%) and maximum concentration (C_{max}) is 73.6 ng/mL (40.2%). Camizestrant steady-state AUC and C_{max} increase by approximately 2-fold when administered in combination with ribociclib (*see Drug Interaction Studies)*. Camizestrant AUC and C_{max} increase in a greater than dose proportional manner over the dosage range of 25 mg to 450 mg (0.3 to 6 times the approved recommended dosage) once daily.

Camizestrant steady state is reached by Day 5. Accumulation was observed after multiple dosing with an accumulation ratio of 1.4 for C_{max} and 1.8 for AUC.

Absorption

Camizestrant absolute oral bioavailability is 43%. Camizestrant median time to maximum concentration (T_{max}) is 3 to 4 hours.

Effect of Food

No clinically significant differences in camizestrant pharmacokinetics were observed following administration of a high-fat meal (951 calories, 58% fat) in healthy postmenopausal women.

Distribution

Camizestrant apparent volume of distribution is 1,888 L (29.3%).

Camizestrant plasma protein binding is 0.75 and is not concentration-dependent in vitro. The blood-to-plasma concentration ratio is 0.99.

Elimination

Camizestrant terminal half-life is approximately 23 hours with an apparent clearance of 69 L/h (40.6%).

Metabolism

Camizestrant is primarily metabolized by CYP3A and UGT1A4.

Excretion

Following a single oral 75 mg dose of radiolabeled camizestrant to healthy subjects, 65% of the total radioactivity was recovered in feces (14.5% unchanged) and 17% in urine (4.8% unchanged).

Specific Populations

No clinically significant differences in the pharmacokinetics of camizestrant were observed based on age (29 – 89 years), body weight (34 – 150 kg), race (86% White, 9% Asian, and 1.3% Black), and creatinine clearance (CLcr) 30 mL/min to < 90 mL/min (calculated using the modified Cockcroft-Gault equation). The effect of CLcr 15 to < 30 mL/min and end-stage renal disease (CLcr < 15 mL/min) on camizestrant pharmacokinetics is unknown.

Patients with Hepatic Impairment

Camizestrant C_{max} and AUC increased in patients with moderate (Child-Pugh B) and severe (Child-Pugh C) hepatic impairment compared to patients with normal hepatic function following a single 75 mg dose. Camizestrant steady state C_{max} and AUC are predicted to increase in patients with mild (Child-Pugh A), moderate (Child-Pugh B), and severe (Child-Pugh C) hepatic impairment compared to patients with normal hepatic function. Table 7 summarizes observed systemic exposure of camizestrant in patients with hepatic impairment following a single dose and predicted systemic exposures at steady-state.

Table 7. Observed and Predicted Systemic Exposure of Camizestrant in Patients with Hepatic Impairment

PK Parameter	Mild (Child-Pugh A) Hepatic Impairment	Moderate (Child-Pugh B) Hepatic Impairment	Severe (Child-Pugh C) Hepatic Impairment
Single Dose			
C_{max}	N/A	2.7-fold increase	3.1-fold increase
AUC	N/A	2.4-fold increase	3.8-fold increase
Steady-State			
C_{maxss}	1.4-fold increase	2.1-fold increase	3.4-fold increase
AUC_{ss}	1.4-fold increase	2.2-fold increase	4.2-fold increase

N/A = not available.

When camizestrant 75 mg once daily is coadministered with ribociclib 400 mg once daily in patients with severe hepatic impairment (Child-Pugh C), compared to patients with normal hepatic function, the steady-state camizestrant AUC was predicted to increase approximately 6-fold.

Drug Interaction Studies

Clinical Studies and Model-Informed Approaches

Strong CYP3A Inhibitors: Camizestrant C_{max} increased 1.4-fold and AUC 1.9-fold following concomitant administration of itraconazole (strong CYP3A inhibitor) 200 mg twice daily on day 1 followed by 200 mg once daily for 5 days.

Camizestrant C_{max} and AUC increased approximately 2-fold when administered concomitantly with ribociclib (strong CYP3A inhibitor) 400 or 600 mg once daily.

Strong CYP3A Inducers: Camizestrant C_{max} decreased to 41% and AUC decreased to 30% following concomitant administration of carbamazepine (strong CYP3A inducer) 100 mg once daily for 3 days, followed by 200 mg once daily for 3 days and then 300 mg once daily for 6 days.

Camizestrant C_{max} is predicted to decrease to 38% and AUC to 30% following concomitant administration of rifampicin (strong CYP3A inducer) 600 mg once daily for 17 days.

Moderate CYP3A Inducers: Camizestrant C_{max} is predicted to decrease to 58% and AUC to 43% following concomitant administration of phenobarbital (moderate CYP3A inducer) 100 mg once daily for 17 days. Phenobarbital or efavirenz (moderate CYP3A inducer) is predicted to have minimal effects on camizestrant AUC and C_{max} when camizestrant is given in combination with 400 mg or 600 mg ribociclib.

CYP2C9 Substrates: Warfarin (sensitive CYP2C9 substrate) C_{max} is predicted to increase 1.1-fold and AUC 13-fold following concomitant administration with camizestrant.

Siponimod (moderately sensitive CYP2C9 substrate) C_{max} is predicted to increase 1.1-fold and AUC 5.3-fold following concomitant administration with camizestrant.

CYP2C19 Substrates: Omeprazole (sensitive CYP2C19 substrate) C_{max} is predicted to increase 3.3-fold and AUC 8.5-fold and lansoprazole (moderately sensitive CYP2C19 substrate) C_{max} is predicted to increase 1.5-fold and AUC 5.7-fold following concomitant administration with camizestrant.

CYP3A Substrates: Midazolam (sensitive CYP3A substrate) C_{max} increased 1.5-fold and AUC 2-fold following concomitant administration with camizestrant.

In Vitro Studies

CYP450 Enzymes: Camizestrant is a reversible inhibitor of CYP2B6 and CYP2D6, but does not inhibit CYP1A2, CYP2A6, CYP2C8, and CYP2E1. Camizestrant can induce CYP1A2 and CYP2B6.

UGT Enzymes: Camizestrant inhibits UGT1A1 and UGT2B7.

Transporter Systems: Camizestrant is a substrate of P-gp, but not a substrate of BCRP, OATP1B1, or OATP1B3.

Camizestrant can inhibit P-gp, BCRP and OATP1B1. Camizestrant does not inhibit OATP1B3, OCT2, OAT1, OAT3, MATE1, and MATE2K.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Carcinogenicity studies have not been conducted with camizestrant.

Mutagenesis

Camizestrant was not mutagenic in the bacterial reverse mutation (Ames) assay. Camizestrant was not genotoxic in an in vitro mouse lymphoma micronucleus assay or an in vivo rat bone marrow micronucleus test.

Impairment of Fertility

In a fertility and early embryofetal development study, daily oral administration of camizestrant to female rats for 2 weeks prior to and during mating, and up to gestation day 6 led to altered estrous cycles and mating behavior, decreased number

of pregnancies and live embryos, and increased pre- and post-implantation loss. Effects on fertility were reversible following a 4 week treatment-free period prior to mating. Additional findings in repeat dose studies in rats included atrophy in the uterus/cervix and ovarian cysts at ≥ 0.1 mg/kg in rats (below the human AUC at the recommended dose), atrophy in the vagina at ≥ 1 mg/kg (below the human AUC at the recommended dose), and ovarian atrophy at ≥ 25 mg/kg in rats (≥ 10 times the human AUC at the recommended dose). Atrophy in the uterus/cervix and vagina, and ovarian cysts were observed at ≥ 5 mg/kg in dogs (≥ 3 times the human AUC at the recommended dose).

In a repeat dose toxicity study, daily oral administration of camizestrant to male rats resulted in lower spermatid/sperm counts at ≥ 10 mg/kg, increased sperm abnormalities and lower mating rate at 25 mg/kg (≥ 6 times the human AUC at the recommended dose) and lower sperm motility, and pregnancy rate at 75 mg/kg (25 times the human AUC at the recommended dose) when mated with untreated female rats. Additional findings in repeat dose studies in rats and dogs included atrophy in the prostate, seminal vesicles, and testis and decrease sperm cellularity in epididymis of rats at ≥ 10 mg/kg (≥ 2 times the human AUC at the recommended dose), and cellular debris in epididymis at ≥ 5 mg/kg (≥ 4 times the human AUC at the recommended dose) of dogs.

13.2 Animal Toxicology and/or Pharmacology

In repeat dose studies, daily oral administration of camizestrant resulted in hyperplasia in the ovary, in female rats at ≥ 5 mg/kg (≥ 0.5 times the human AUC at the recommended dose) and Leydig cells of testis in male dogs at ≥ 5 mg/kg (≥ 4 times the human AUC at the recommended dose), as well as benign tumors including ovarian granulosa cell in female rats at 75 mg/kg and dogs at ≥ 5 mg/kg (57 times (rats) and ≥ 2 times (dog) the human AUC at the recommended dose), and Leydig cell adenoma in a male dog at 10 mg/kg (14 times the human AUC at the recommended dose).

In dogs, combination dosing of camizestrant with atropine resulted in a significant increase in plasma and brain exposure of atropine considered to be due to inhibition of atropine metabolism.

14 CLINICAL STUDIES

The efficacy of ETCAMAH was evaluated in adult patients with ER-positive, HER2-negative, locally advanced or metastatic breast cancer with detectable *ESR1* mutations in SERENA-6 (NCT04964934), a randomized, double-blind, placebo-controlled, multicenter, ctDNA-guided trial to assess the switching to ETCAMAH in combination with a CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib) versus continuing aromatase inhibitor (AI) (anastrozole or letrozole) in combination with a CDK4/6 inhibitor. The *ESR1* mutation status was assessed by ctDNA testing during first-line treatment with an AI in combination with a CDK4/6 inhibitor. All patients were required to be currently receiving treatment of an AI in combination with a CDK4/6 inhibitor for ≥ 6 months as the initial endocrine-based treatment with no evidence of disease progression as per investigator assessment. Patients could have received one prior line of chemotherapy before the start of AI in combination with a CDK4/6 inhibitor treatment. Patients with a baseline heart rate less than 55 beats per minute were excluded from the trial. Patients were tested every 2-3 months for *ESR1* mutations using the Guardant360 CDx assay. A total of 3256 patients had at least one ctDNA test. Randomization occurred once *ESR1* mutations were detected.

Of the enrolled patients, 315 patients were randomized (1:1) to receive either:

- ETCAMAH 75 mg orally once daily and a placebo in combination with a CDK4/6 inhibitor (N = 157) or
- AI (anastrozole 1 mg or letrozole 2.5 mg) orally once daily and a placebo in combination with a CDK4/6 inhibitor (N = 158).

The choice of CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib) and its dosage remained the same at the time of randomization for both arms of treatment. Randomization was stratified by visceral disease (yes vs. no), *ESR1* mutation detection (first test vs. subsequent ctDNA tests), time from initiation of AI in combination with a CDK4/6 inhibitor to randomization (< 18 months vs. ≥ 18 months), and CDK4/6 inhibitor (abemaciclib vs. palbociclib vs. ribociclib). Pre-/peri-menopausal female patients and male patients taking concomitant gonadotropin-releasing hormone (GnRH) agonist continued to receive it after randomization. Treatment with ETCAMAH in combination with a CDK4/6 inhibitor continued until disease progression or unacceptable toxicity.

The primary efficacy outcome measure was investigator-assessed progression-free survival (PFS) per RECIST v1.1. An additional efficacy outcome measure included overall survival (OS).

Of the 315 patients randomized, the median age was 61 years (range 29 to 89 years); female (99%); White (63%), Asian (23%), Black (1.9%), other (1%), and not reported (11%); Hispanic or Latino (3%), not Hispanic or Latino (95%), and

missing (2%). Eastern Cooperative Oncology Group (ECOG) performance status 0 (65%) or 1 (33%). Of the female patients, 79% were post-menopausal and 20% were pre-/peri-menopausal. Of the patients, 57% had non-visceral disease, 63% had received ≥ 18 months of AI plus CDK4/6 inhibitor, and 53% had an *ESR1* mutation detected on the first ctDNA test. The percentage of patients on palbociclib was 76%, ribociclib was 15%, and abemaciclib was 10%.

SERENA-6 demonstrated a statistically significant improvement in PFS for patients receiving ETCAMAH in combination with a CDK4/6 inhibitor compared to patients receiving AI in combination with a CDK4/6 inhibitor. At the time of the PFS analysis, overall survival data were not mature with 39 (12% maturity) events.

Efficacy results are summarized in Table 8 and Figure 1.

Table 8: Efficacy Results in SERENA-6

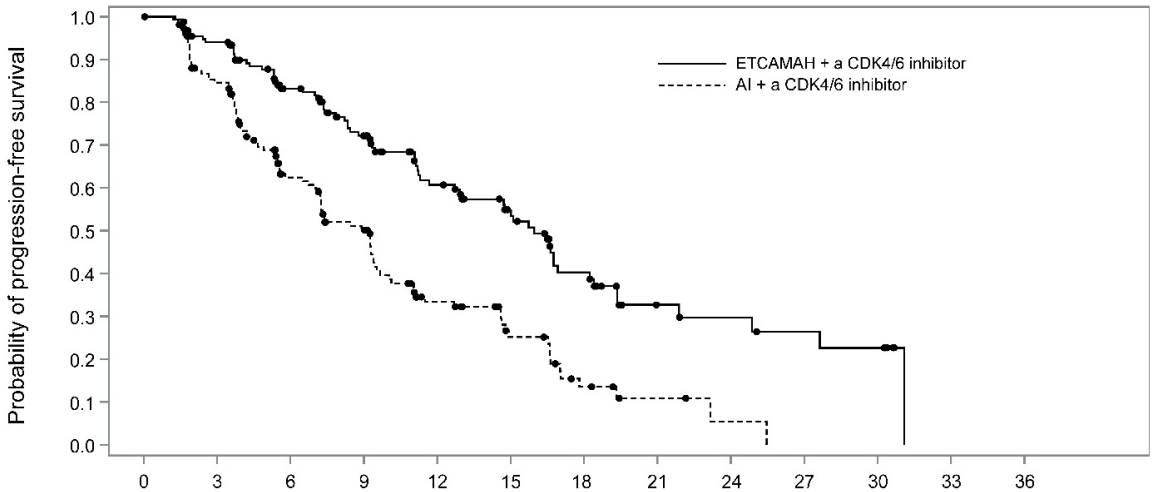
	ETCAMAH plus a CDK4/6 inhibitor N = 157	**AI plus a CDK4/6 inhibitor N = 158**
Progression-Free Survival		
Number of events (%)	71 (45)	100 (63)
Median, months[*] (95% CI)	16.0 (12.7, 18.2)	9.2 (7.2, 9.5)
Hazard ratio (95% CI)[†]	0.44 (0.31, 0.60)	
p-value[‡]	< 0.00001	

[*] Based on the Kaplan-Meier method.

[†] Based on a stratified Cox proportional hazards model. A hazard ratio < 1 favors ETCAMAH plus a CDK4/6 inhibitor treatment arm.

[‡] Based on the stratified log-rank test.

Figure 1: Kaplan Meier Plot of PFS by Investigator Assessment in SERENA-6



Number of patients at risk

Month	00	03	06	09	12	15	18	21	24	27	30	33
ETCAMAH + a CDK4/6 inhibitor	157	138	105	82	55	41	26	11	9	7	6	0
AI + a CDK4/6 inhibitor	158	124	73	55	29	17	7	3	1	0	0	0

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Package Size	Contents	NDC Number
28-count bottle	Bottle containing 28 tablets with desiccant 75 mg tablets: beige, round, bi-convex film-coated tablets debossed with 'CM' above '75' on one side and plain on the reverse	0310-0075-01

Storage and Handling

Store ETCAMAH at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

Store and dispense ETCAMAH tablets in the original bottle with desiccant to protect from moisture.

Alternatively, dispense ETCAMAH tablets in a USP equivalent tight container and discard after 30 days **if stored without desiccant**.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA approved patient labeling (Patient Information).

QTc Interval Prolongation

Inform patients ETCAMAH is indicated to be used in combination with a CDK4/6 inhibitor and there is potential risk of additional QTc interval prolongation when combined with ribociclib and/or products that can cause QTc interval prolongation, which may increase the risk of Torsades de Pointes, other ventricular arrhythmias, and sudden death. Advise patients that ECG will be monitored before treatment and thereafter. Advise patients or caregivers to seek immediate medical attention if they suspect or develop signs or symptoms associated with clinical consequences of QTc interval prolongation. Instruct patients to consult with their healthcare provider prior to taking other drugs that cause QTc interval prolongation with ETCAMAH *[see Warnings and Precautions (5.1) and Drug Interactions (7.1, 7.3)]*.

Bradycardia

Inform patients ETCAMAH causes decrease in heart rate. Advise patients that heart rate will be monitored more frequently during the first 30 days of treatment with ETCAMAH in patients with bradycardia (heart rate less than 60 bpm) at baseline and those on concomitant medications known to lower heart rate. Advise patients to report any symptoms of bradycardia and to inform their healthcare provider about the use of any heart and blood pressure medications *[see Warnings and Precautions (5.2) and Drug Interactions (7.4)]*.

Embryo-Fetal Toxicity

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions (5.3) and Use in Specific Populations (8.1)]*.

Advise females of reproductive potential to use effective non-hormonal contraception during treatment with ETCAMAH and for 4 weeks after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ETCAMAH and for 1 week after the last dose *[see Use in Specific Populations (8.3)]*.

For male patients with female partners of reproductive potential, refer to the Prescribing Information of the CDK4/6 inhibitor palbociclib if used in combination with ETCAMAH for contraception information. Advise patients to use effective contraception during treatment and for the longest post-treatment duration as recommended in the Prescribing Information.

Lactation

Advise women not to breastfeed during treatment with ETCAMAH and for 1 week after the last dose *[see Use in Specific Populations (8.2)]*.

Infertility

Advise males and females of reproductive potential that ETCAMAH may impair fertility *[see Use in Specific Populations (8.3)]*.

Drug Interactions

Advise patients to inform their healthcare provider(s) of all the concomitant medications that will be taken with ETCAMAH, including prescription medicines, over-the-counter medicines, vitamins, and herbal products *[see Drug Interactions (7)]*.

Distributed by:

AstraZeneca Pharmaceuticals LP

Wilmington, DE 19850

PATIENT INFORMATION
ETCAMAH® (et kam' ah)
(camizestrant)
tablets, for oral use

What is the most important information I should know about ETCAMAH?

ETCAMAH can cause serious side effects including:

- **Changes in electrical activity of your heart (QTc interval prolongation)**. Taking ETCAMAH in combination with ribociclib or other QTc interval prolonging drugs may cause life-threatening heart rhythm problems and may lead to death. Before starting and during treatment with ETCAMAH, your healthcare provider will do an electrocardiogram (ECG) to check the electrical activity of your heart and do blood tests to check the blood levels of your body salts (electrolytes). Your healthcare provider will treat abnormal electrolyte levels.
- **Slow heart rate (bradycardia).** Your healthcare provider will check your heart rate frequently during the first 30 days of treatment with ETCAMAH if you have bradycardia (heart rate less than 60 beats per minute) before starting treatment and if you take medicines that lower heart rate.

Get medical help right away if you get the following signs or symptoms of QTc interval prolongation and bradycardia including:

- dizziness
- lightheadedness
- fainting
- feeling that your heart is pounding or racing (palpitations)
- shortness of breath
- chest pain

Your healthcare provider may delay treatment or completely stop treatment with ETCAMAH if you have severe side effects.

See **"What are the possible side effects of ETCAMAH?"** for more information about side effects.

What is ETCAMAH?

ETCAMAH is a prescription medicine used in combination with a CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib) to treat adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer that:

- has worsened or spread to other parts of the body (advanced or metastatic breast cancer)**, and**
- has an estrogen receptor-1 (*ESR1)* mutation detected during treatment with an aromatase inhibitor and a CDK4/6 inhibitor.

Your healthcare provider will perform a test to make sure that ETCAMAH is right for you.

It is not known if ETCAMAH is safe and effective in children.

Before you take ETCAMAH, tell your healthcare provider if you:

- have any liver-related problems.
- have a slow heartbeat (bradycardia).
- have heart problems including irregular heartbeats and QTc prolongation.
- are pregnant or plan to become pregnant. ETCAMAH can harm your unborn baby.
  Females who are able to become pregnant
  - Your healthcare provider will check that you are not pregnant before you start treatment with ETCAMAH.
  - Use effective non-hormonal birth control (contraception) during treatment with ETCAMAH and for 1 month after the last dose. Talk to your healthcare provider about birth control methods that may be right for you during this time.
  - Tell your healthcare provider if you become pregnant or think you may be pregnant.

  Males with female partners who can become pregnant
  - Use effective birth control during treatment with ETCAMAH and for 1 week after your last dose.
- are breast-feeding or plan to breast-feed. It is not known if ETCAMAH passes into your breast milk. Do not breast feed during treatment with ETCAMAH and for 1 week after the last dose. Talk to your healthcare provider about the best way to feed your baby during treatment with ETCAMAH.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Especially, tell your healthcare provider if you take any heart and blood pressure medicines.

ETCAMAH may affect the way other medicines work, and other medicines may affect how ETCAMAH works.

Know the medicines you take. Keep a list of them to show your healthcare provider or pharmacist when you get a new medicine.

How should I take ETCAMAH?

- Take ETCAMAH exactly as your healthcare provider tells you.
- Do not change your dose or stop taking ETCAMAH without talking to your healthcare provider.
- Take ETCAMAH 1 time a day, at about the same time each day.
- Take ETCAMAH with or without food.
- Swallow ETCAMAH whole. Do not cut, crush, or chew tablets before swallowing.
- Do not take ETCAMAH tablets that are broken, cracked or look damaged.
- Follow your healthcare providers' instructions for taking abemaciclib, palbociclib, or ribociclib (CDK4/6 inhibitors).
- If you miss a dose of ETCAMAH, take it within 6 hours from the time you usually take it. If it is more than 6 hours from the time you usually take your dose, skip the dose for the day. The next day, take the dose at your usual time. Do not take two doses to make up a missed dose.
- If you vomit after taking a dose of ETCAMAH, do not take another dose. Take your next dose of ETCAMAH at your usual time.

What are the possible side effects of ETCAMAH?

ETCAMAH can cause serious side effects, including:

- See **"What is the most important information I should know about ETCAMAH?"**

The most common side effects of ETCAMAH in combination with a CDK4/6 inhibitor include:

- decreased white blood cell counts
- decreased red blood cell counts
- decreased platelet counts
- vision problems such as seeing flashes of light, double or blurry vision, light sensitivity, new or increased floaters. Tell your healthcare provider if you have vision problems, you may need to see an eye care specialist
- tiredness

ETCAMAH may cause fertility problems in females and males, which may affect your ability to have children. Talk to your healthcare provider if you have concerns about fertility.

These are not all the possible side effects of ETCAMAH.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store ETCAMAH?

- Store ETCAMAH at room temperature between 68°F to 77°F (20°C to 25°C).
- Store ETCAMAH in the original bottle.
- The bottle contains a desiccant to keep tablets dry. **Do not** remove the desiccant from the bottle.
- Keep the bottle tightly closed to protect from moisture.
- Throw ETCAMAH away after 30 days if it has been stored in a bottle without a desiccant.

Keep ETCAMAH and all medicines out of the reach of children.

General information about the safe and effective use of ETCAMAH.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use ETCAMAH for a condition for which it was not prescribed. Do not give ETCAMAH to other people, even if they have the same symptoms you have. It may harm them. You can ask your pharmacist or healthcare provider for information about ETCAMAH that is written for health professionals.

What are the ingredients in ETCAMAH?

Active ingredient: camizestrant
Inactive ingredients: anhydrous dibasic calcium phosphate, magnesium stearate, microcrystalline cellulose, and sodium starch glycolate.
The tablet film-coating contains ferric oxide red, ferric oxide yellow, ferrosoferric oxide, polyethylene glycol 3350, polyvinyl alcohol, talc and titanium dioxide.

Distributed by: AstraZeneca Pharmaceuticals LP, Wilmington, DE 19850

For more information, go to https://www.ETCAMAH.com or call 1-800-236-9933. If you still have questions, contact your healthcare provider.

This Patient Information has been approved by the U.S. Food and Drug Administration Issued: 09/2026