Product Monograph
Including Patient Medication Information

Pr **ETCAMAH™**

Camizestrant tablets

For oral use

75 mg of camizestrant

Anti-estrogen

AstraZeneca Canada Inc.
1004 Middlegate Road
Mississauga, Ontario
L4Y 1M4
www.astrazeneca.ca

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Certain sections or subsections that are not applicable at the time of the preparation of the most recent authorized product monograph are not listed.

Part 1: Healthcare Professional Information

1. Indications

ETCAMAH (camizestrant) is indicated in combination with a CDK4/6 inhibitor (palbociclib, ribociclib, or abemaciclib) 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 Estrogen Receptor 1 mutation (*ESR1*m) during first-line aromatase inhibitor (AI)-based endocrine therapy.

1.1. Pediatrics

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use (see 7.1.3 Pediatrics).

1.2. Geriatrics

Geriatrics (≥65 years of age): Evidence from clinical studies suggests no overall differences in safety and efficacy between patients (≥65 years of age) and patients (<65 years of age) who received ETCAMAH (see 7.1.4 Geriatrics).

2. Contraindications

ETCAMAH (camizestrant) is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 Dosage Forms, Strengths, Composition, and Packaging.

4. Dosage and Administration

4.1. Dosing Considerations

- Patients should be selected for treatment with ETCAMAH based on the presence of an *ESR1*m in plasma specimens, as determined by a validated circulating tumor DNA (ctDNA) test (see 14 Clinical Trials).
- In pre- or peri-menopausal women and in men, ETCAMAH plus a CDK4/6 inhibitor should be combined with a Luteinizing Hormone-Releasing Hormone (LHRH) agonist, in accordance with current clinical practice standards.
- A pregnancy test should be performed and confirmed as negative prior to initiating treatment. Females of reproductive potential should use effective non-hormonal contraception during treatment with ETCAMAH (see 7 Warnings and Precautions).
- Patients with moderate and severe (Child-Pugh B, C) hepatic impairment should be monitored closely for adverse reactions due to an increased systemic exposure to ETCAMAH, especially when indicated in combination with ribociclib (see 10.3 Pharmacokinetics). Consider reducing the dosing frequency of ETCAMAH 75 mg to every other day in patients with severe hepatic impairment and in patients with moderate and severe hepatic impairments when ETCAMAH is used in combination with ribociclib (see 4.2 Recommended Dose and Dosage Adjustment).
- Patients receiving concomitant treatment with ribociclib should be monitored closely for adverse reactions, as ribociclib may increase ETCAMAH systemic exposure (see 9.2 Drug Interactions Overview).
- Camizestrant is a strong inhibitor of CYP2C9 and CYP2C19. Avoid concomitant use of ETCAMAH with sensitive substrates or substrates with narrow therapeutic range of CYP2C9 and/or CYP2C19 during treatment with ETCAMAH and for 2 weeks after the last dose. If an

alternative drug product cannot be used or concomitant use cannot be avoided, reduce the dose of the CYP2C9 or CYP2C19 substrate in accordance with the respective Product Monograph, as appropriate. (See 9.2 Drug Interactions Overview and 9.4 Drug-Drug Interactions).
- Avoid concomitant use of ETCAMAH with strong CYP3A inducers. Moderate CYP3A inducers may be used with caution (See 9.2 Drug Interactions Overview and 9.4 Drug-Drug Interactions).

4.2. Recommended Dose and Dosage Adjustment

- The recommended dose of ETCAMAH in combination with a CDK4/6 inhibitor is 75 mg once daily.
- The CDK4/6 inhibitor should be continued at the same dose as was used before the detection of the *ESR1*m. For full dosing instructions of the selected CDK4/6 inhibitor, consult the corresponding Product Monograph.
- Treatment with ETCAMAH should continue as long as clinical benefit is observed or until unacceptable toxicity occurs.

Health Canada has not authorized an indication for pediatric use.

Dosage Adjustment
Treatment with ETCAMAH may be temporarily interrupted and/or discontinued to manage adverse reactions per dose modification guideline provided in Table 1.

Table 1 – Recommended dose modification for ETCAMAH

NCI CTCAE (v5.0) Toxicity	Details	Action
Bradycardia[a]	Symptomatic, CTCAE Grade ≥2	Suspend ETCAMAH dosing until bradycardia resolves to ≤ Grade 1. If a concomitant medication contributing to bradycardia is identified, discontinue or modify its dose until bradycardia resolves to ≤ Grade 1. Monitor the heart rate 7 and 14 days after restarting ETCAMAH. Permanently discontinue ETCAMAH if symptomatic bradycardia persists, or if heart rate is persistently low (below 45 bpm).
QT interval prolongation	QTcF > 480 ms or > 500 ms and prolongation from baseline > 60 ms	Suspend ETCAMAH until QTcF returns to ≤ 480 ms and stabilizes. Monitor with ECGs 7 and 14 days after restarting ETCAMAH. Permanently discontinue ETCAMAH if QTcF interval is > 500 ms or if prolongation from baseline is > 60 ms

NCI CTCAE (v5.0) Toxicity	Details	Action
		and is associated with Torsade de Pointes or polymorphic ventricular tachycardia, unexplained syncope or signs/symptoms of serious arrhythmia.
Visual effects[b]	CTCAE Grade ≥ 2/limiting instrumental ADLs	If visual symptoms are progressive, persistent, or interfere with instrumental ADLs suspend ETCAMAH treatment until symptoms resolve and refer the patient for an ophthalmological evaluation. Monitor visual effects at the next visit.
Other ≥ Grade 3 adverse events assessed as causally related to ETCAMAH	Severe AEs considered to be causally related to ETCAMAH after consideration of possible alternative contributing factors and concomitant medications	Suspend ETCAMAH dosing until resolution of AEs to ≤ Grade 2. Permanently discontinue ETCAMAH if ≥ Grade 3 AEs recur.

ADL = Activities of daily living; AE = Adverse Event; CTCAE = Common Terminology Criteria for Adverse Events; NCI = National Cancer Institute.
[a.] Bradycardia: (heart rate < 60 bpm) includes bradycardia and sinus bradycardia.
[b.] Visual effects include photopsia, vision blurred, visual impairment, diplopia, and photophobia of eye disorders MedDRA SOC, and visual perseveration of nervous system disorders MedDRA SOC.

Refer to the Product Monograph for the co-administered CDK4/6 inhibitor or LHRH agonist for dose modification guidelines in the event of toxicity, and other relevant safety information.

Special populations

Renal impairment
No dose adjustment of ETCAMAH is required for patients with mild or moderate renal impairment. ETCAMAH is not recommended for patients with severe renal impairment (see 10 Clinical Pharmacology).

Hepatic impairment
Consider reducing the dosing frequency of ETCAMAH 75 mg to every other day in patients with severe hepatic impairment (Child-Pugh C) and in patients with moderate and severe hepatic impairment when ETCAMAH is indicated in combination with ribociclib. These patients should be monitored closely (see 10.3 Pharmacokinetics).

The efficacy and safety of ETCAMAH have not been studied in advanced breast cancer patients with moderate and severe hepatic impairment; initiate ETCAMAH treatment in these patients only when the potential benefit outweighs potential risk.

4.4. Administration

ETCAMAH is for oral use.

The tablet should be swallowed whole with water and may be taken with or without food, at

approximately the same time each day. ETCAMAH should not be ingested if it is broken, cracked, or otherwise not intact. The tablet should not be chewed, crushed, dissolved, or divided.

4.5. Missed Dose

If a dose of ETCAMAH is missed, it can be taken immediately within 6 hours after the time it is usually taken. After more than 6 hours, the dose should be skipped for that day. If the patient vomits, an additional dose should not be taken. The next dose of ETCAMAH should be taken at the usual time.

5. Overdose

There is limited experience with reported cases of ETCAMAH overdose. In case of suspected overdose, patients should be closely monitored and treated with general symptomatic and supportive measures if necessary.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6. Dosage Forms, Strengths, Composition, and Packaging

Table 2 – Dosage Forms, Strengths, and Composition

Route of Administration	Dosage Form/ Strength/Composition	Non-Medicinal Ingredients
Oral	Tablet 75 mg camizestrant	Calcium hydrogen phosphate, iron oxide black, iron oxide red, iron oxide yellow, macrogol 3350, magnesium stearate, microcrystalline cellulose, polyvinyl alcohol, sodium starch glycolate (type A), talc, and titanium dioxide.

Description
ETCAMAH (camizestrant) is a beige, round, bi-convex, film-coated tablet, debossed with 'CM' above '75' on one side and plain on the reverse. Approximate diameter: 9 mm.

Packaging
ETCAMAH (camizestrant) is supplied in aluminum blisters containing 28 film-coated tablets: 2 blisters with 14 tablets each.

7. Warnings and Precautions

Cardiovascular

Bradycardia
ETCAMAH causes dose-dependent decrease in heart rate with a maximum decrease observed on day 15 (mean heart rate decrease from baseline of around 14 bpm), which remains stable thereafter. Bradycardia events (including sinus bradycardia) were reported in 10.3% of patients in the ETCAMAH plus a CDK4/6 inhibitor group vs no patients in the AI plus a CDK4/6 inhibitor group. No Grade ≥ 3 events reported. Monitor for bradycardia, particularly in patients receiving

concomitant ribociclib, other medications known to cause bradycardia, or those with additional risk factors for bradycardia.

QT interval prolongation

ETCAMAH carries a potential for QT-prolonging effects. AEs of electrocardiogram QT prolonged were reported in 3.9% of patients in the ETCAMAH plus a CDK4/6 inhibitor group and in 1.3% of patients in the AI plus a CDK4/6 inhibitor group. No patients in either treatment group had a QTcF value above 500 ms during treatment. There were 2 patients in the ETCAMAH plus a CDK4/6 inhibitor group with an increase from baseline > 60 ms during the study. One patient (0.6%) in the ETCAMAH plus a CDK4/6 inhibitor group had a non-serious CTCAE Grade 3 AE. This event resolved after the dose of ETCAMAH was interrupted and the dose of the CDK4/6 inhibitor (ribociclib) was reduced. Close monitoring is recommended when ETCAMAH is used in combination with ribociclib or other drugs known to cause QT prolongation (see 9.2 Drug Interactions Overview).

Driving and Operating Machinery

No studies on the effects of ETCAMAH on the ability to drive or operate machinery have been conducted. However, since visual effects have been reported, patients should exercise caution when driving or operating machinery while taking ETCAMAH.

Monitoring and Laboratory Tests

- Conduct periodic, routine heart rate evaluation during standard oncology clinic visit, especially on **Day 15 to Day 28** of Cycle 1, when a maximum heart rate decrease is observed.
- Electrocardiogram (ECG) assessment should be performed prior to initiating treatment, during Cycle 1 at approximately Day 15, at the start of new treatment cycle (e.g., Cycle 2) and then periodically every 2 months. Patients with bradycardia (HR <60 bpm) at baseline or who are receiving drugs that prolong the QT interval and/or have a known risk of TdP require close monitoring.

Ophthalmologic

- ETCAMAH causes visual side effects including photopsia, vision blurred, visual impairment, diplopia, photophobia and visual perseveration, which tend to appear within a few weeks after start of treatment. Visual effects were reported in 32.9% patients in the ETCAMAH plus a CDK4/6 inhibitor group and 16.8% in the AI plus a CDK4/6 inhibitor group. Structural ocular disorder AEs were reported at low frequency and at comparable rates across both treatment groups. Patients should be advised to report new or worsening visual symptoms.

Reproductive Health

- Contraception: Women of childbearing potential should be advised to avoid becoming pregnant while receiving ETCAMAH. A pregnancy test should be performed and verified as negative on women of childbearing potential prior to initiating treatment and re-testing should be considered throughout treatment.
  Advise females of reproductive potential to use effective non-hormonal contraception during treatment with ETCAMAH and for 4 weeks after last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ETCAMAH and for 1 week after last dose.

- Fertility: Based on findings in animals, 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 16 Non-Clinical Toxicology). The effects of ETCAMAH on fertility were not assessed in humans.

7.1. Special Populations

7.1.1. Pregnancy

Advise pregnant women of the potential risk to a fetus. There are no data from the use of ETCAMAH in pregnant women to inform drug-associated risk. Studies in animals have shown reproductive toxicity (see 16 Non-Clinical Toxicology). Based on its mechanism of action and preclinical data, ETCAMAH may cause fetal harm when administered to a pregnant woman. Embryofetal lethality, dystocia, pup mortality and impaired offspring growth was observed in a rat study where animals were dosed from implantation throughout gestation, parturition and lactation at exposures below the human AUC at the recommended dose (see 16 Non-Clinical Toxicology). ETCAMAH is not recommended during pregnancy and for women of childbearing potential not using contraception.

7.1.2. Breastfeeding

It is unknown whether camizestrant and its metabolites are excreted in human milk. Since a risk to the breastfed child cannot be excluded, patients should be advised to avoid breastfeeding during treatment with ETCAMAH, and for at least one week after the last dose.

7.1.3. Pediatrics

Pediatrics (<18 years of age): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.

7.1.4. Geriatrics

Of the 155 patients who received ETCAMAH in combination with a CDK4/6 inhibitor (palbociclib, ribociclib, or abemaciclib) in the phase III study SERENA-6, 62 patients (39.4%) were ≥65 years of age (see 14 Clinical Trials). No overall differences in efficacy or safety were observed between patients ≥65 years of age and patients <65 years of age who received ETCAMAH plus a CDK4/6 inhibitor.

8. Adverse Reactions

8.1. Adverse Reaction Overview

The safety profile of ETCAMAH in combination with a CDK4/6 inhibitor (palbociclib, ribociclib, or abemaciclib) was evaluated in 155 patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer upon detection of *ESR1*m during first-line AI-based endocrine therapy in the SERENA-6 study (see 14 Clinical Trials). The safety profile of camizestrant in combination with palbociclib, ribociclib, or abemaciclib was consistent with the known safety profile of each drug.

The most commonly reported adverse reactions regardless of causality (in ≥20% of patients) in the ETCAMAH plus a CDK4/6 inhibitor group were neutropenia, neutrophil count decreased, anemia and photopsia.

Adverse reactions with a ≥5% difference between both treatment groups (ETCAMAH plus a

CDK4/6 inhibitor vs AI plus a CDK4/6 inhibitor) were neutropenia (36% vs 26%), neutrophil count decreased (28% vs 23%), photopsia (21% vs 8%), dry eye (13% vs 7%), leukopenia (8% vs 2%), and bradycardia (7% vs 0%).

The most common CTCAE Grade ≥ 3 adverse reactions were hematologic (primarily neutropenia, neutrophil count decreased, white blood cell count decreased, and anaemia). When adjusted for duration of exposure, the incidence rates of haematological toxicities were comparable between treatment groups and consistent with the known safety profiles associated with CDK4/6 inhibitors.

Serious adverse reactions were reported in 1.9% of patients in the ETCAMAH plus a CDK4/6 inhibitor group and 7.7% of patients in the AI plus a CDK4/6 inhibitor group.

The most common adverse reactions leading to dose modifications in the ETCAMAH plus a CDK4/6 inhibitor group compared with the AI plus CDK4/6 inhibitor group included: bradycardia /sinus bradycardia, (6 % vs 0%), neutropenia (3% vs 2%). Other adverse reactions leading to dose modifications (approximately 1 - 2%), included anaemia, pneumonia, photopsia, electrocardiogram QT prolonged, neutrophil count decreased, vision blurred, leukopenia and thrombocytopenia.

The incidence of adverse reactions leading to discontinuation was very low (<3%) and balanced across treatment groups.

8.2. Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. Therefore, the frequencies of adverse reactions observed in the clinical trials may not reflect frequencies observed in clinical practice and should not be compared to frequencies reported in clinical trials of another drug.

Table 3 lists the incidence of adverse drug reactions from the SERENA-6 study reported in at least ≥5% of patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer upon detection of *ESR1*m during first-line AI-based endocrine therapy. The median duration of exposure to ETCAMAH in combination with a CDK4/6 inhibitor was 15.9 months and to AI in combination with a CDK4/6 inhibitor was 7.36 months.

Table 3 – Adverse Reactions (≥ 5%) in patients treated with ETCAMAH plus a CDK4/6 inhibitor versus AI plus a CDK4/6 inhibitor in SERENA-6 study

System Organ Class / Preferred Term	ETCAMAH + CDK4/6 inhibitor		AI + CDK4/6 inhibitor	
	All grades (%)	Grade ≥3 (%)	All grades (%)	Grade ≥3 (%)
Blood and lymphatic system disorders				
Neutropenia	33	27	26	17
Anaemia	23	6	22	8
Leukopenia	8	5	2	1
Thrombocytopenia	7	2	5	0
Cardiac disorders				

Bradycardia / Sinus bradycardia	11	0	0	0
Eye disorders				
Photopsia	21	1	8	0
Dry eye	13	0	7	0
Vision Blurred	8	0	8	0
Vitreous floaters	9	0	3	0
Gastrointestinal disorders				
Nausea	11	0	16	1
Diarrhoea	10	0	14	1
General disorders and administration site conditions				
Fatigue	16	1	17	1
Asthenia	8	0	7	0
Investigations				
Neutrophil count decreased	28	23	23	19
White blood cell count decreased	10	8	7	1
Aspartate aminotransferase increased	6	0	8	1
Alanine aminotransferase increased	5	1	8	0
Musculoskeletal and connective tissue disorders				
Arthralgia	19	0	19	1
Skin and subcutaneous tissue disorders				
Pruritus	6	0	4	0
Vascular disorders				
Hot flush	8	0	5	0

Graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.
The table includes adverse events with an onset date or that worsened on or after the date of first dose of study treatment up to and including 28 days following the date of last dose of study treatment and prior to the start of any subsequent cancer therapy.
Patients with multiple occurrences were counted once per SOC and PT regardless of the number of occurrences.
MedDRA Version 28.1

8.3. Less Common Clinical Trial Adverse Reactions

Other clinically relevant adverse reactions reported in less than 5% of patients treated with ETCAMAH in combination with a CDK4/6 inhibitor in the SERENA-6 study were:

Blood and lymphatic system disorders: febrile neutropenia (0.6%)

General disorders and administration site conditions: sudden death (0.6%)

Infections and infestations: pneumonia (3.9%)

Vascular disorders: deep vein thrombosis (2.6%)

8.4. Abnormal Laboratory Findings: Hematologic, Clinical Chemistry, and Other Quantitative Data

Clinical Trial Findings

Table 4 – Laboratory Abnormalities Occurring in ≥10% of Patients Treated with ETCAMAH in SERENA-6

Laboratory Abnormality	Camizestrant + CDK4/6 inhibitor N=155		Aromatase inhibitor + CDK4/6 inhibitor N=155	
	Any grade (%)	Grade 3 or 4 (%)	Any grade (%)	Grade 3 or 4 (%)
Hematology				
Leukocytes decreased	94	28	89	23
Neutrophils decreased	88	48	83	46
Hemoglobin decreased	77	6	79	10
Lymphocyte decreased	68	12	61	12
Platelets decreased	48	3	39	3
Chemistry				
Creatinine increased	31	1	40	1
Triglycerides increased	26	2	20	1
Aspartate aminotransferase increased	29	3	43	1
Corrected calcium decreased	26	0	16	1
Gamma glutamyl transferase increased	22	3	32	10
Alanine aminotransferase increased	19	2	27	0
Albumin decreased	15	0	17	0
Sodium decreased	15	1	13	3
Alkaline phosphatase increased	12	1	30	2

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

9. Drug Interactions

9.2. Drug Interactions Overview

Clinical Studies and modelling approaches

Strong CYP3A inhibitors
Camizestrant is a CYP3A substrate. Co-administration of ETCAMAH with a strong CYP3A inhibitor, e.g. itraconazole and ribociclib (see 9.4 Drug-Drug Interactions), increases ETCAMAH plasma concentrations, which may increase the incidence and severity of adverse reactions of ETCAMAH.

ETCAMAH is indicated for use in combination with CDK4/6 inhibitors, including ribociclib, which

is a strong CYP3A inhibitor and QT prolonging drug. Monitor for increased adverse reactions to ETCAMAH.

Strong and moderate CYP3A4 inducers
Co-administration of ETCAMAH with CYP3A inducers decreases camizestrant plasma concentrations, which may decrease the efficacy of ETCAMAH. Avoid concomitant use with strong CYP3A4 inducers. Use of moderate CYP3A4 inducers in combination with ETCAMAH and abemaciclib or palbociclib may be used with caution.

CYP3A substrates
ETCAMAH is a CYP3A inhibitor. Exercise caution with co-administration of ETCAMAH with sensitive CYP3A substrates as the plasma concentrations of these substrates may be increased, which may increase the severity of adverse reactions related to these substrates. The co-administration of CYP3A substrates with a narrow therapeutic index may require dose adjustment of the substrate and should be closely monitored for adverse reactions.

CYP2C9 and CYP2C19 substrates
ETCAMAH is a strong inhibitor of CYP2C9 and CYP2C19. Avoid co-administration of ETCAMAH with sensitive substrates or substrates with narrow therapeutic range of CYP2C9 and/or CYP2C19, which may increase the risk of adverse reactions related to these substrates.

Drug products known to prolong the QT interval
ETCAMAH in combination with ribociclib has been studied clinically. Clinical monitoring and dose modifications with reference to the ribociclib Product Monograph are recommended. Avoid the use of drug products known to prolong the QT interval. Monitor ECGs as clinically indicated if concomitant use cannot be avoided (see 7 Warnings and Precautions).

***In vitro* studies**

CYP 450 Enzymes: Camizestrant is a reversible inhibitor of CYP2B6, and CYP2D6 but does not inhibit CYP1A2, CYP2A6, CYP2C8, and CYP2E1. Camizestrant has a low potential to induce CYP1A2, and CYP2B6.

UGT Enzymes: Camizestrant inhibits UGT1A1 and UGT2B7.

Transporters: 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, MATE1, MATE-2K, OAT1, OAT3, and OCT2.

9.4. Drug-Drug Interactions

No clinically meaningful drug-drug interactions for palbociclib or abemaciclib in combination with camizestrant were observed. Ribociclib increases 75 mg camizestrant exposure to a similar level to that observed following 150 mg camizestrant exposure.

The drugs listed below are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction.

Table 5 – Established or Potential Drug-Drug Interactions (Victim DDI)

Effect of other drugs on ETCAMAH			
Name of the drug product	**Source of evidence**	**Effect**	**Clinical comment**
Strong CYP3A inducers[a]	PBPK modelling	Camizestrant C_{max} and AUC are predicted to decrease by 0.4-fold and 0.2-fold, respectively, following concomitant administration of rifampicin (strong CYP3A inducer; 600 mg once daily for 17 days).	Avoid co-administration of strong CYP3A inducers, which decreases camizestrant plasma concentrations and may decrease the efficacy of ETCAMAH.
Moderate CYP3A inducers[b]	PBPK modelling	Camizestrant C_{max} and AUC are predicted to decrease by 0.5-fold and 0.4-fold, respectively, following concomitant administration of phenobarbital (moderate CYP3A inducer) 100 mg once daily for 17 days.	Camizestrant is a CYP3A substrate. Use caution when moderate CYP3A inducers are administered in combination with ETCAMAH and abemaciclib or palbociclib.
Strong CYP3A inhibitors[c]	Clinical Trial	Itraconazole (strong CYP3A inhibitor, 200 mg); increased single 75 mg camizestrant dose C_{max} and AUC by 1.37-fold and 1.90-fold respectively.	Camizestrant is a CYP3A substrate. Concomitant use with strong CYP3A inhibitors increases camizestrant plasma concentration, which may increase the risk of adverse reactions related to ETCAMAH.
	PopPK	Camizestrant C_{max} and AUC increased approximately 2-fold when administered concomitantly with ribociclib (strong CYP3A inhibitor; 400 or 600 mg once daily).	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. Monitor for increased adverse reactions.

Effect of other drugs on ETCAMAH			
Name of the drug product	**Source of evidence**	**Effect**	**Clinical comment**
Drug Products Known to Prolong the QT Interval	Theoretical	QT interval prolongation may occur when ETCAMAH is co-administered with drug products known to prolong the QT interval.	ETCAMAH in combination with ribociclib has been studied clinically. Clinical monitoring and dose modifications with reference to the approved ribociclib label are recommended. Co-administration of other medicinal products known to prolong the QT interval and/or have a known risk of Torsades de Pointes (e.g., ciprofloxacin and ondansetron) should be avoided. If concomitant use cannot be avoided, monitor ECGs as clinically indicated.

C=Case Study; CT = Clinical Trial; T = Theoretical; PBPK = Physiologically based pharmacokinetic modeling; PopPK = population-based pharmacokinetic modeling.
[a] Strong inducers decrease the AUC of sensitive substrates by ≥80%.
[b] Moderate inducers decrease the AUC of sensitive substrates by ≥50% to <80%.
[c] Strong inhibitor increases the AUC of sensitive substrates (e.g. midazolam) by ≥5-fold

Table 6 - Established or Potential Drug-Drug Interactions (Perpetrator DDI)

Effect of ETCAMAH on other drugs			
Name of the drug product	**Source of evidence**	**Effect**	**Clinical comment**
CYP2C9 and/or CYP2C19 substrates	PBPK modelling	**CYP2C9 substrates**: S-warfarin (sensitive[a] CYP2C9 substrate: 10 mg dose oral on Day 8) C_{max} and AUC are predicted to increase by 1.1-fold and 9.7-fold, respectively, following co-administration with camizestrant. Siponimod (moderately[b] sensitive CYP2C9 substrate; single 0.25 mg dose) C_{max} and AUC are predicted to increase by 1.1-fold and 4.7-fold, respectively, following co-administration with camizestrant. **CYP2C19 substrates:** Omeprazole (sensitive CYP2C19 substrate; single 20 mg dose) C_{max} and AUC are predicted to increase by 3.3-fold and 8.5-fold, respectively, following co-administration with camizestrant. Lansoprazole (moderately sensitive CYP2C19 substrate) C_{max} and AUC are predicted to increase by 1.5-fold and 4.3-fold, respectively, following co-administration with camizestrant.	Camizestrant is a strong CYP2C9 and CYP2C19 inhibitor. Avoid concomitant use of ETCAMAH with sensitive substrates or substrates with narrow therapeutic range of CYP2C9 or CYP2C19 substrates during treatment with ETCAMAH and for 2 weeks after the last dose. If an alternative drug product cannot be used or concomitant use cannot be avoided, reduce the dose of the CYP2C9 or CYP2C19 substrate in accordance with the respective Product Monograph, as appropriate.

Effect of ETCAMAH on other drugs			
Name of the drug product	**Source of evidence**	**Effect**	**Clinical comment**
CYP3A substrates	Clinical Trial	Camizestrant is a CYP3A inhibitor. Midazolam (sensitive CYP3A substrate; single 1 mg dose) C_{max} and AUC increased by 1.52-fold and 1.99-fold, respectively, following co-administration with camizestrant.	ETCAMAH increases exposure of CYP3A substrates which may increase the risk of adverse reaction related to these substrates. Refer to the Product Monograph for CYP3A substrates where minimal increases in the concentration may lead to serious adverse reactions.

C=Case Study; CT = Clinical Trial; T = Theoretical; PBPK = Physiologically based pharmacokinetic modeling
[a] AUC of sensitive substrates increase by ≥5-fold.
[b] AUC of moderately sensitive substrates increase by ≥2 to <5-fold.

9.5. Drug-Food Interactions

ETCAMAH tablets may be administered with or without food (see 10.3 Pharmacokinetics).

9.6. Drug-Herb Interactions

St. John's Wort may decrease camizestrant plasma concentrations. Use of St. John's Wort with ETCAMAH is not recommended.

9.7. Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10. Clinical Pharmacology

10.1.Mechanism of Action

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

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

10.2.Pharmacodynamics

Exposure-Response Relationship
The exposure-response relationships for efficacy of ETCAMAH at 75 mg QD in combination with abemaciclib, palbociclib, and ribociclib has been characterized in SERENA-6 and showed

that there is no exposure-efficacy relationship between camizestrant exposure and PFS at the 75 mg dose level.

Cardiac electrophysiology
Exposure response analysis of potential QTcI prolongation of daily 75 mg to 300 mg of camizestrant monotherapy was assessed in 30 patients. The predicted drug related mean QTcI prolongation was 2.99 ms (90% CI: (-0.11, 6.09)) at the mean steady state C_{max} with an upper bound of 6.09 ms (90% CI) following 75 mg camizestrant daily. At the recommended 75 mg dose of camizestrant, a mean increase in QTcI >10 ms was not observed.

10.3.Pharmacokinetics

Camizestrant pharmacokinetic parameters have been characterized in healthy volunteers and breast cancer patients. The pharmacokinetics of camizestrant 75 mg QD have been characterized in patients by population pharmacokinetic analysis (Table 7). Camizestrant steady state is reached by day 5 following once daily dosing.

Camizestrant AUC and C_{max} showed greater than dose-proportional increase over the dose range of 25 mg to 450 mg.

Table 7 - Summary of Camizestrant Steady-State Pharmacokinetic Parameters

	C_{max} (ng/mL)	T_{max} (h)	$t_{½}$ (h)	AUC_{tau} (ng.h/mL)	CL/F (L/h)	Vss/F (L)
Median	73.51	2.9	23	1116	69.1	1888

Absorption
Following oral administration, camizestrant median time to maximum plasma concentration (T_{max}) is 2 hours to 4 hours after dosing. Camizestrant 75 mg dose oral bioavailability is 43%.

Effect of Food
Similar camizestrant plasma exposures were observed following administration with a high fat meal or fasted overnight. ETCAMAH can be taken either with or without food.

Distribution
Based on population pharmacokinetic analysis, camizestrant is distributed in the tissues with an apparent peripheral volume of distribution of 608 L.

Plasma protein binding of camizestrant was 75% and was not concentration-dependent *in vitro*. The blood-to-plasma concentration ratio was 0.99.

Metabolism
In vitro data studies suggest that camizestrant is primarily metabolized by CYP3A and UGT1A4. Human metabolites of camizestrant were detected and quantified in pharmacokinetic samples from healthy female volunteers receiving a single oral dose of 75 mg of [^{14}C]-camizestrant. The major drug-related circulating materials were the N-glucuronide conjugate of camizestrant, the N-glucuronide of the acid metabolite and camizestrant, which accounted for 20.1%, 11.2%, and 13.6% of the circulating radioactivity in plasma. No active metabolites have been identified.

Elimination
Following single oral administration of 75 mg [^{14}C]-camizestrant, mean total radioactivity was

recovered in feces (14.5% unchanged) indicating fecal excretion was the main route of elimination following oral dosing, with 16.8% of the total radioactivity being recovered from the urine (4.8% unchanged).

Special populations and conditions

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

- **Sex, Ethnic Origin and Weight**
  Based on population pharmacokinetic analysis (n=756), no clinically significant relationships were identified between model predicted steady state exposure, area under the curve at steady state (AUC_{ss}) and the following covariates: baseline age median 61 years (29-89 years), body weight median 69.9 kg (34.2-150 kg), and racial groups (86% White, 8.5% Asian, and 1.3% Black). Population pharmacokinetic analysis showed baseline body weight affected apparent volume of distribution (V2/F), but this was not clinically relevant; it did not significantly impact apparent total body clearance (CL/F) or AUC_{ss}. No dose adjustments for ETCAMAH are required based on gender, race, or body weight.

- **Hepatic Insufficiency**
  As hepatic elimination is a major route of excretion for camizestrant, hepatic impairment may result in increased plasma camizestrant concentrations.

  Based on a clinical pharmacokinetic study in patients following a single 75 mg dose, camizestrant C_{max} and $AUC_{0\text{-}INF}$ in patients with moderate (Child-Pugh B) hepatic impairment was 2.7-fold and 2.4-fold, respectively, compared to patients with normal hepatic function. Camizestrant C_{max} and $AUC_{0\text{-}INF}$ in patients with severe (Child-Pugh C) hepatic impairment was 3.1-fold and 3.8-fold, respectively, compared to patients with normal hepatic function.

  Physiological based pharmacokinetic (PBPK) modelling of camizestrant at 75 mg as monotherapy predicts that for patients with mild hepatic impairment (Child-Pugh A), the steady state C_{max} and AUC is predicted to increase by 1.4-fold and 1.3-fold, respectively, compared to patients with normal hepatic function. For moderate hepatic impairment (Child-Pugh B), C_{max} and AUC are predicted to increase by 2.1-fold and 2.0-fold, respectively. In these patients, combination with ribociclib 400 mg increased camizestrant C_{max} and AUC by 2.7-fold and 2.8-fold, respectively, compared to patients with normal hepatic function. For severe hepatic impairment (Child-Pugh C), C_{max} and AUC are predicted to increase 2.7-fold and 3.2-fold respectively. In these patients, combination with ribociclib 400 mg increased camizestrant C_{max} and AUC by 3.4-fold and 4.0-fold, respectively, compared to patients with normal hepatic function.

- **Renal Insufficiency**
  There were no clinically significant differences in the pharmacokinetics of camizestrant based on baseline creatinine clearance (CrCl) 30 mL/min to <90 mL/min (mild to moderate; calculated using the Cockcroft-Gault equation).

  The effect of CrCl in patients with severe renal impairment (baseline CrCl≥15 mL/min and <30 mL/min) and end-stage renal disease (baseline CrCl <15 mL/min) on camizestrant pharmacokinetics has not been established.

11. Storage, Stability, and Disposal

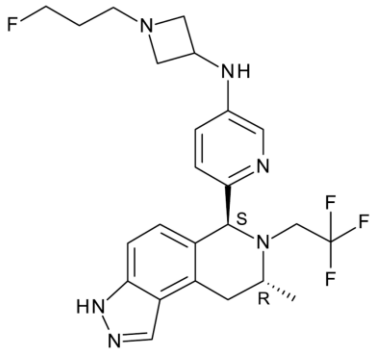
Store between 2°C to 30°C in original package.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Keep out of reach and sight of children

Part 2: Scientific Information

13. Pharmaceutical Information

Drug Substance

Non-proprietary name of the drug substance(s):	Camizestrant
Chemical name:	N-[1-(3-Fluoropropyl)-3-azetidinyl]-6-[(6S,8R)- 8-methyl-7-(2,2,2-trifluoroethyl)-6,7,8,9-tetrahydro-3H-pyrazolo[4,3-f]isoquinolin-6-yl]-3-pyridinamine
Molecular formula and molecular mass:	$C_{24}H_{28}F_4N_6$; 476.51 g/mol
Structural formula:	
Physicochemical properties:	Camizestrant is a crystalline powder with a melting point, defined as the onset temperature (differential scanning calorimetry) of approximately 132°C. Camizestrant has a high aqueous solubility across the physiological pH range. It is an anhydrous and non-hygroscopic substance with a distribution coefficient (logD) of 2.3 (at pH 7.4) and two measured pKa values of 4.8 and 8.4.

14. Clinical Trials

14.1.Clinical Trials by Indication

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

Table 8 - Summary of Patient Demographics for Clinical Trials in HR-positive, HER2-negative Locally Advanced or Metastatic Breast Cancer in SERENA-6

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (range)	Sex
NCT04964934 (SERENA-6)	Phase III, randomized, double-blind, placebo controlled multi-center, international study	Route of administration: Oral Camizestrant 75 mg oral tablet, once daily consecutively for 28 days per cycle. Aromatase Inhibitors: Anastrozole 1 mg oral tablet or letrozole 2.5 mg oral over-encapsulated tablet, once daily, consecutively for 28 days per cycle. CDK4/6 inhibitors (palbociclib, abemaciclib or ribociclib oral tablets) administered at the same dose as was used prior to the detection of *ESR1*m. Duration: continue as long as clinical benefit is observed or until unacceptable toxicity occurs.	Camizestrant + CDK4/6 inhibitor: 157 patients AI + CDK4/6 inhibitor: 158 patients	Camizestrant + CDK4/6 inhibitor: 59 years (29-81) AI + CDK4/6 inhibitor: 60 years (35-89)	Camizestrant + CDK4/6 inhibitor: Males: 0 Females: 157 (100%) AI + CDK4/6 inhibitor: Males: 3 (1.9%) Females: 155 (98.1%)

SERENA-6 was a randomized, double-blind, placebo controlled study conducted in adult pre/peri/post-menopausal females and males with ER-positive, HER2-negative, locally advanced or metastatic breast cancer without evident disease progression. The study was designed to assess the efficacy and safety of switching to ETCAMAH plus a CDK4/6 inhibitor versus continuing with AI (letrozole or anastrozole) plus a CDK4/6 inhibitor once an *ESR1*m was detected by ctDNA testing. All patients had to have received ≥6 months of AI plus a CDK4/6 inhibitor and could have received one prior line of chemotherapy.

In SERENA-6 patients entered a surveillance period where serial Guardant360 CDx ctDNA tests were conducted (every 2-3 months) to monitor for the emergence of an *ESR1*m. Upon detection of an *ESR1*m confirmation of eligibility, patients were randomized 1:1 to receive either ETCAMAH (75 mg once daily) plus a CDK4/6 inhibitor and a placebo of AI (n=157), or AI plus a CDK4/6 inhibitor and placebo of ETCAMAH (n=158). Of all randomized patients, 75.6% received palbociclib, 14.9% received ribociclib, and 9.5% received abemaciclib. CDK4/6 inhibitors were administered at the same dose as was used prior to the detection of *ESR1*m. Randomization was stratified by disease site (visceral disease versus non-visceral disease), *ESR1*m detection timing (first test versus subsequent ctDNA tests), time for prior AI plus CDK4/6 inhibitor to randomization (<18 months versus ≥18 months), and type of CDK4/6 inhibitor (palbociclib versus ribociclib versus abemaciclib). Pre/perimenopausal female patients and male patients taking an LHRH agonist continued to receive it as before randomization. Treatment with ETCAMAH continued as long as clinical benefit was observed or until unacceptable toxicity occurred.

The primary endpoint was progression free survival (PFS) assessed by investigator, defined as the time from the date of randomization (*ESR1*m detection) until the date of objective disease progression according to the Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 or death. The key secondary endpoints were PFS2, defined as the time from randomization to second progression or death (PFS2) and overall survival (OS) defined as the time from randomization until death due to any cause.

Demographic and baseline characteristics were well balanced between groups. The median age was 61.0 years (range 29.0 to 89.0 years). The majority of patients were female (99.0%). Patients were white (63.2%), Asian (23.2%), black (1.9%), or of other races (1.0%), and had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 (65.1%) or 1 (33.0%). In total, 79.4% were postmenopausal women and 20.6% were premenopausal/perimenopausal women or men.

Study Results

At the PFS interim analysis, SERENA-6 study met its primary endpoint with a median treatment exposure of approximately 10 months in the ETCAMAH plus a CDK4/6 inhibitor group and approximately 6 months in the AI plus a CDK4/6 inhibitor group. This primary analysis demonstrated a statistically significant and clinically meaningful 56% reduction in the risk of disease progression in patients treated with ETCAMAH plus a CDK4/6 inhibitor compared to those treated with AI plus a CDK4/6 inhibitor (see Table 9 and Figure 1). Consistent results in PFS were observed across patient subgroups defined by study stratification factors including the disease site (visceral or non-visceral), *ESR1*m detection (first or subsequent ctDNA testing), time from initiation of AI plus CDK4/6 inhibitor to randomisation (<18 months or ≥18 months), and the choice of CDK4/6 inhibitor (palbociclib, ribociclib or abemaciclib).

At the final PFS2 analysis, with a median treatment exposure of approximately 16 months in the ETCAMAH plus a CDK4/6 inhibitor group versus approximately 7 months in the AI plus a CDK4/6 inhibitor group, it was demonstrated there was a statistically significant and clinically meaningful 37% reduction in the risk of second disease progression or death following subsequent therapy in patients treated with ETCAMAH plus a CDK4/6 inhibitor compared with those treated with AI plus a CDK4/6 inhibitor (see Table 9).

At the PFS2 analysis, overall survival data were not mature (HR 0.87; 95% CI: 0.57, 1.30; p=0.48777).

Table 9 - Efficacy Results in SERENA-6

	Camizestrant + CDK4/6 inhibitor N=155	**AI + CDK4/6 inhibitor N=158**
Primary Endpoint: Progression Free Survival (PFS)[d]		
Number of events[a] (%)	71 (45.2%)	100 (63.3%)
Median months[b] (95% CI)	16.0 (12.7, 18.2)	9.2 (7.23, 9.53)
Hazard ratio[c] (95% CI)	0.44 (0.31, 0.60)	
p-value	<0.00001	
Key secondary endpoint: Second Progression or Death (PFS2)[d]		
Number of events (%)	80 (51%)	90 (57%)
Median months[b] (95% CI)	25.7 (20.4, 30.3)	19.6 (16.8, 21.0)
Hazard ratio[c] (95% CI)	0.63 (0.46, 0.86)	
p-value	0.00373	

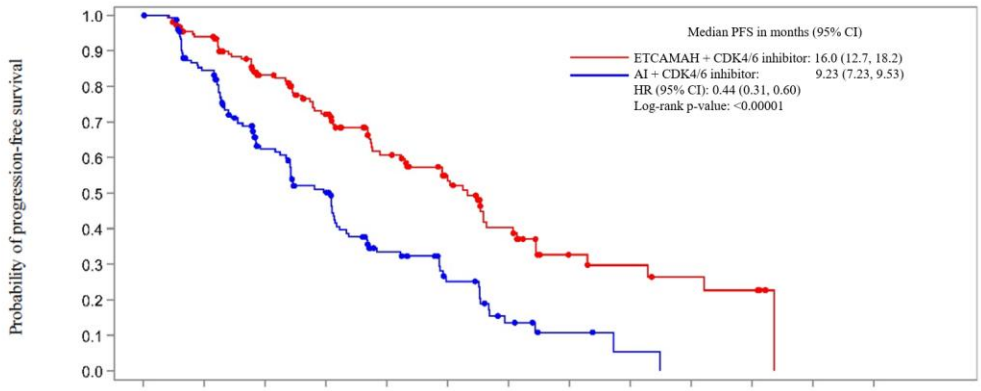
[a] Includes progression events that occur within 2 visits of last evaluable assessment.

[b] The calculation is based on the Kaplan-Meier method.

[c] A hazard ratio < 1 favours ETCAMAH plus CDK4/6 inhibitor treatment arm.

[d] Results are based on PFS interim analysis (data-cutoff [DCO]: 28 November 2024) and PFS2 final analysis (DCO: 2 January 2026).

Figure 1 Kaplan Meier Plot of Progression Free Survival by Investigator Assessment in SERENA-6



Number of subjects at risk													Number of randomised subjects/number of events
Month	**000**	**003**	**006**	**009**	**012**	**015**	**018**	**021**	**024**	**027**	**030**	**033**	
ETCAMAH + CDK4/6 inhibitor	157	138	105	82	55	41	26	11	9	7	6	0	157/71
AI + CDK4/6 inhibitor	158	124	73	55	29	17	7	3	1	0	0	0	158/100

16. Non-Clinical Toxicology

General toxicology

In repeat-dose toxicology studies in rats up to 6 months duration, camizestrant-related findings in male rats included lower spermatid/sperm counts, atrophy of prostate and seminal vesicle glands, decreased sperm cellularity in the epididymis and tubular dilatation and degeneration/atrophy of the testis at ≥10 mg/kg/day (approximately 2-fold the human exposure at the recommended dose based on AUC), increased sperm abnormalities and lower mating rate at ≥25 mg/kg/day (approximately 6.7-fold the human exposure at the recommended dose based on AUC). These findings indicate an effect on male fertility in rats. Reversibility of male reproductive findings was not assessed. Camizestrant-related findings in female rats included cyst and granulosa cell hyperplasia in the ovaries, hypertrophy/hyperplasia in the mammary glands, and atrophy in oviduct, cervix, uterus, and vagina at doses ≥10 mg/kg/day (approximately 2.3-fold the human exposure at the recommended dose based on AUC), and atrophy of the ovaries at ≥25 mg/kg/day (approximately 11-fold the human exposure at the recommended dose based on AUC). Reversibility was not assessed in the 6-month study.

In repeat-dose toxicology studies in dogs of up to 9 months duration, camizestrant-related findings in female dogs included increased luteal cellularity, luteal and follicular cysts and benign granulosa cell tumours in the ovaries, and atrophy in cervix, uterus, and vagina at doses ≥5 mg/kg/day (approximately 3.5-fold the human exposure at the recommended dose based on AUC). Camizestrant-related findings in the reproductive organs of male dogs included interstitial (Leydig) cell hypertrophy/hyperplasia, seminiferous tubule degeneration/atrophy of the testis, cellular debris in the epididymis at doses ≥5 mg/kg/day (approximately 3.5-fold the human exposure at the recommended dose based on AUC) and interstitial (Leydig) cell adenoma at 10 mg/kg/day in the testis (approximately 13.4-fold the human exposure at the recommended dose based on AUC). Reversibility was not assessed in the 9-month study.

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

Carcinogenicity
No long-term animal studies have been performed to evaluate the carcinogenic potential of camizestrant.

Reproductive and developmental toxicology
In a fertility and early embryofetal development study, female rats orally administered camizestrant daily for 2 weeks prior to and during mating and up to gestation day 6 showed camizestrant-related reproductive effects, including estrous cycle disruption, changes in mating behaviour and decreased number of pregnancies at doses ≥0.075 mg/kg/day, and decreased number of corpora lutea, implants and live embryos, increased pre- and post-implantation loss at doses ≥0.001 mg/kg/day. In a recovery phase, female rats administered camizestrant daily at 0.75 mg/kg/day for 3 weeks followed by a 4-week treatment-free period prior to mating, showed reversibility of fertility-related effects. In this study, the maternal exposure in rats was below the human exposure at the recommended clinical dose.

Administration of camizestrant in a modified embryofoetal development study including assessment when dosing from implantation through parturition and into lactation resulted in increased length of gestation, dystocia, impaired offspring survival and growth at doses of ≥0.075 mg/kg/day with maternal exposures lower than those observed at the recommended clinical dose.

Special toxicity - Cardiotoxicity
Functional cardiovascular effects were observed in dogs and demonstrated a dose-related pattern. In the 1-month dog toxicity study, cardiovascular changes showed a delayed onset and returned to pre-study baseline values following a 4-week recovery period.

In the 9-month dog toxicity study, a time and dose-dependent decrease in heart rate and prolongation of QTc interval (QTca) were observed at all dose levels.

These findings indicate that the drug has the potential to affect cardiac electrophysiology and heart rate, supporting the need for appropriate clinical monitoring of cardiovascular parameters, including heart rate and QT interval.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr **ETCAMAH™**
camizestrant tablets

This Patient Medication Information is written for the person who will be taking **ETCAMAH**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **ETCAMAH**, talk to a healthcare professional.

What ETCAMAH is used for:
ETCAMAH is used with other cancer drugs to treat adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, breast cancer. The breast cancer:

- is outside the breast or has spread to other parts of the body, and
- has changes in a gene called '*ESR1*', and
- is found during estrogen lowering-based therapy.

How ETCAMAH works:
ETCAMAH works by directly blocking and destroying proteins that help breast cancer grow and multiply. This cuts down on the growth and spread of the cancer.

The ingredients in ETCAMAH are:
Medicinal ingredient(s): camizestrant
Non-medicinal ingredients: calcium hydrogen phosphate, iron oxide black, iron oxide red, iron oxide yellow, macrogol 3350, magnesium stearate, microcrystalline cellulose, polyvinyl alcohol, sodium starch glycolate (type A), talc, titanium dioxide.

ETCAMAH comes in the following dosage form(s):
Tablets; 75 mg camizestrant

Do not use ETCAMAH if:
You are allergic to camizestrant or to any ingredients in ETCAMAH or the container.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ETCAMAH. Talk about any health conditions or problems you may have, including if you:

- Have severe liver problems.
- Have eye problems.
- Have heart or heart rhythm problems.

Other warnings you should know about:

Female Patients: pregnancy, breastfeeding, birth control

- Do not become pregnant while taking ETCAMAH. ETCAMAH can harm your unborn baby if you become pregnant.

- If you are pregnant, think you may be pregnant or able to get pregnant, there are risks you should discuss with your healthcare professional.
- If you do become pregnant during treatment, tell your healthcare professional right away. They will decide if you should still take ETCAMAH.
- If you are able to become pregnant:
    - Your healthcare professional will do a pregnancy test before you start taking ETCAMAH. This test must show that you are not pregnant. You will do more pregnancy tests during the course of your treatment.
    - Avoid becoming pregnant while you are taking ETCAMAH. Use effective birth control during your treatment and for 4 weeks after your last dose. The birth control must not contain hormones. Ask your healthcare professional about methods of birth control available to you.
- Do not breastfeed while you are taking ETCAMAH and for at least 1 week after your last dose.

Male Patients: birth control
- During treatment with ETCAMAH, use birth control each time you have sex with a woman who is able to get pregnant. Continue using birth control for 1 week after your last dose. The birth control must not contain hormones.
- Your female partner must also use a suitable method of contraception. You must tell your healthcare professional if your female partner becomes pregnant.

Fertility
- Treatment with ETCAMAH may affect your ability to have or father a child. If you have questions about this, talk to your healthcare professional.

Effects on vision:
- ETCAMAH can cause vision side effects like:
    - brief trailing or floating lights in your vision, blurry vision, dry eyes, increased sensitivity of the eyes to light.
- These vision side effects can happen within a few weeks after starting ETCAMAH treatment. Talk to your healthcare professional right away if you notice new or worsening vision symptoms.

Children and adolescents (under 18 years old)
- Do not give ETCAMAH to children or adolescents aged less than 18 years old.

Driving and using machines
- ETCAMAH can cause vision problems. You should be careful when driving or using machines during treatment with ETCAMAH.

Check-ups and testing:
- You will have regular visits with your healthcare professional, before, during and at the end of your treatment. They will:
    - Check your heart rate and rhythm during treatment. An Electrocardiogram (ECG) assessment should be done.
    - Check your eye health before and during treatment.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with ETCAMAH:

- Medicines used to treat seizures such as carbamazepine, phenobarbital, phenytoin.
- An herbal treatment for depression called St. John's Wort.
- Medicines used to treat excess stomach acid such as omeprazole, lansoprazole.
- A medicine used as a blood thinner called warfarin.
- A medicine used to lower cholesterol called simvastatin.
- A medicine used to produce sleepiness or drowsiness called midazolam.
- A medicine used to treat multiple sclerosis called siponimod.
- A medicine used to treat nausea and vomiting called ondansetron.
- A medicine used to treat bacterial infections such as ciprofloxacin.
- A medicine used to treat cancer called ribociclib. Taking ETCAMAH with ribociclib may increase the risk of heart problems.

The medicines listed here may not be the only ones that could interact with ETCAMAH.

How to take ETCAMAH:

- Always take ETCAMAH exactly as your healthcare professional has told you. Check with your healthcare professional if you are not sure.
- Swallow tablet whole with water. Do not chew, crush, dissolve or divide the tablets.
- Take ETCAMAH with or without food.
- For women who have not reached menopause and for some men, your healthcare professional might tell you to take a medicine that lowers sex hormone levels. Your healthcare professional will tell you how much of this medicine you will take and how to take it.

Usual dose:

Adults: Take one 75 mg tablet once per day by mouth at about the same time each day.
You will also receive treatment with another medicine (palbociclib, ribociclib or abemaciclib). Your healthcare professional will tell you how much of this medicine you will take and how to take it.

Overdose:

If you think you, or a person you are caring for, have taken too much ETCAMAH, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed dose:

- If you miss a dose, you may take it right away 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, then skip that dose.
- Do not take a double dose to make up for a forgotten dose. Take the next dose of ETCAMAH at the usual time.
- If you vomit after taking your dose, do not take another dose. Take the next dose of ETCAMAH at the usual time.

Possible side effects from using ETCAMAH:
These are not all the possible side effects you may have when taking ETCAMAH in combination with other cancer drugs. If you experience any side effects not listed here, tell your healthcare professional.

- tiredness
- feeling unwell
- dry eyes
- cough
- dizziness
- nausea, vomiting
- itchy skin
- joint pain
- hot flushes

ETCAMAH can cause abnormal blood test results. Your healthcare professional will do blood tests during your treatment. These will tell your healthcare professional how ETCAMAH is affecting your blood and heart.

Serious side effects and what to do about them

Frequency/Side Effect/Symptom	**Talk to your healthcare professional**		**Stop taking this drug** and get immediate medical help
	Only if severe	**In all cases**	
Very Common			
Anemia (decreased number of red blood cells): fatigue, loss of energy, looking pale, shortness of breath, weakness.		✓	
Bradycardia (abnormally slow heartbeat).		✓	
Effects on vision: brief trailing or floating lights in your vision, blurry vision, dry eyes, increased sensitivity of the eyes to light.		✓	
Neutropenia, Leukopenia (decreased white blood cells): infections, fatigue, fever, aches, pains and flu-like symptoms.		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting side effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Keep out of the reach and sight of children.
- Store between 2°C to 30°C in original package.
- Do not use:
  - after the expiry date on the package or container. The expiry date refers to the last day of that month
  - if you notice the package or container has signs of damage or tampering
  - if the tablets are broken, cracked.

Return any unused medication to your healthcare professional. Ask your healthcare professional how to throw away medicines you no longer use. Do not throw away any medicines in wastewater or household waste. These measures will help protect the environment.

If you want more information about ETCAMAH:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes the Patient Medication Information by visiting the Health Canada Drug Product Database website (Drug Product Database: Access the database); the manufacturer's website www.astrazeneca.ca; or by calling 1-800-668-6000.
- This Patient Medication Information is current at the time of printing. The most up-to-date version can be found at www.astrazeneca.ca.

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AstraZeneca