ETCAMAH®
camizestrant
75 mg tablets

Under accelerated approval, in combination with a CDK4/6i for HR+/HER2- mBC upon detection of *ESR1*m during 1L AI + CDK4/6i[1]

A guide to ETCAMAH for advanced practice providers and nurses

Empowering your next-generation care of patients on 1L AI + CDK4/6i upon detection of *ESR1*m[1]

Learn more about ETCAMAH at etcamahHCP.com/S6NB

1L=first line; AI=aromatase inhibitor; CDK4/6i=cyclin-dependent kinase 4/6 inhibitor; *ESR1*m=estrogen receptor 1 gene mutation.

INDICATION

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.

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).

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING

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 (TdP), other ventricular arrhythmias, and sudden death.

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

Obtain electrocardiogram (ECG) prior to initiation and monitor heart rate (HR) 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.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING, and Patient Information for ETCAMAH.

Emergence of *ESR1*m during 1L ET starts the countdown to disease progression in HR+/HER2- mBC[2-4]

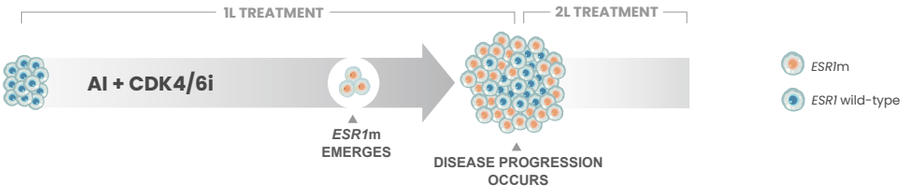
Upon progression to 2L, progression-free survival declines and quality of life **worsens**. PFS can decline by more than 60% after progression on 1L[5-12]

Up to 40% of patients on 1L AI + CDK4/6i will develop *ESR1*m[3]

After *ESR1*m emerges, risk of progression is **3x greater** within 6 months[2]

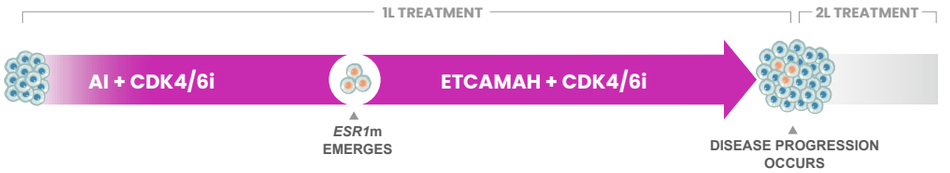
Current 1L approach

Unaddressed endocrine resistance **increases tumor genomic complexity**, which may be harder to treat in 2L[2-4,13,14]



Next-generation 1L approach

SERENA-6: Designed to proactively **address emerging endocrine resistance** to extend time on 1L CDK4/6i[3,13-16]



For illustrative purposes

2L=second line; *ESR1*=estrogen receptor 1; ET=endocrine therapy; HER2-=human epidermal growth factor receptor 2-negative; HR+=hormone receptor-positive; mBC=metastatic breast cancer; PFS=progression-free survival.

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (cont'd)

WARNINGS AND PRECAUTIONS

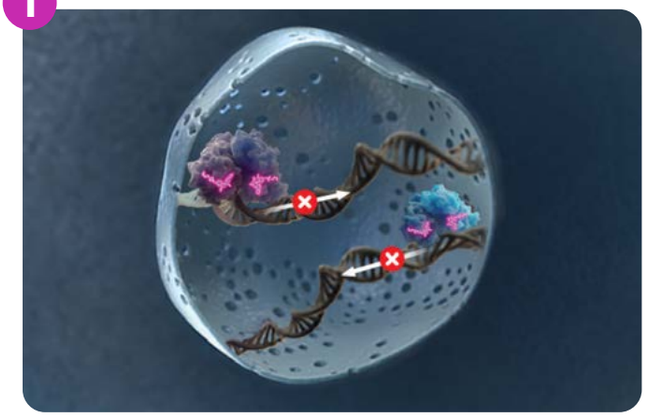
QTc Interval Prolongation: ETCAMAH in combination with a CDK4/6 inhibitor (CDK4/6i) is associated with QTc interval prolongation. When ETCAMAH is used in combination with ribociclib, a CDK4/6i, there is potential for increased risk of TdP, other ventricular arrhythmias, and sudden death. One Grade 4 case of TdP was observed in a dose-finding trial when ETCAMAH was used with ribociclib. In SERENA-6, QTc interval prolongation occurred in 2.6% of patients treated with ETCAMAH in combination with a CDK4/6i. QTc interval prolongation led to dose interruption in 0.6% of patients. No patients in SERENA-6 discontinued ETCAMAH due to QTc interval prolongation. ETCAMAH also causes bradycardia, which increases the risk of QTc interval prolongation.

Perform an ECG prior to initiating ETCAMAH, then every week for the first 2 weeks of treatment, and periodically during treatment as clinically indicated. Obtain serum electrolytes at baseline and during treatment as clinically indicated, and correct electrolyte abnormalities. Avoid concomitant use of ETCAMAH in combination with a CDK4/6i with products that cause QTc interval prolongation, are strong CYP3A inhibitors, and/or are drugs known to lower HR.

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ETCAMAH, a potent, next-generation oral SERD, **blocks and degrades both *ESR1*wt and *ESR1*m** receptors[3,17]

1

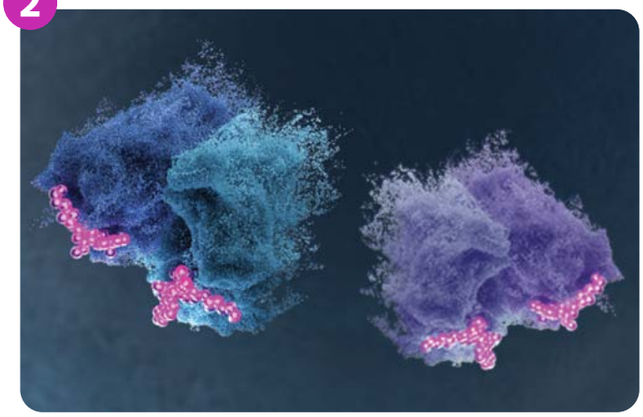


Complete ER antagonism

effectively blocks estrogen from binding to the receptor[17]

- Prevents ER-dependent changes in gene expression, reducing tumor growth

2



Potent ER degradation

reduces the pool of ERs available for downstream signaling[17]

The dual-action mechanism of ETCAMAH
can address or delay endocrine resistance[17,18]

Mechanism of action based on preclinical research.

ER=estrogen receptor; *ESR1*wt=estrogen receptor 1 wild-type; SERD=selective estrogen receptor degrader.

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

QTc Interval Prolongation (cont'd): For 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. Reassess 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: TdP, polymorphic ventricular tachycardia, syncope, or signs/symptoms of serious arrhythmia.

Bradycardia: ETCAMAH causes a decrease in HR. 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. In SERENA-6, bradycardia occurred in 8% of patients. The mean HR decrease from baseline was approximately 13 beats per minute (bpm) with the maximum decrease observed on day 15. Median time to onset was 17 days (range 13 to 283) after starting ETCAMAH. No patients discontinued ETCAMAH due to bradycardia. Dose interruption occurred in 3.9% of patients. The safety of ETCAMAH has not been established in patients with a baseline resting HR <55 bpm as these patients were excluded from SERENA-6. Monitor HR more frequently during the first 30 days of treatment in patients with bradycardia (HR <60 bpm) at baseline and those on concomitant medications known to lower HR (eg, beta-blockers).

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING, and Patient Information for ETCAMAH.

ETCAMAH + CDK4/6i: ctDNA-guided switch upon *ESR1*m detection during 1L ET may help to stay ahead of disease progression in HR+/HER2- mBC[1]

After 23.1 months median time on AI + CDK4/6i:

mPFS from time of ctDNA-guided switch[1]

16 months
ETCAMAH + CDK4/6i (95% CI: 12.7-18.2)[1]

vs

9.2 months
AI + CDK4/6i (95% CI: 7.2-9.5)[1]

(HR = 0.44, 95% CI: 0.31–0.60; *P*<0.00001)

Global health status/quality of life data[19]

Time to deterioration in QoL from time of ctDNA-guided switch measured patient-reported worsening in different aspects of quality of life, including role functioning, physical functioning, emotional functioning, pain, fatigue, and dyspnea.

Median time to deterioration in GHS/QoL[3]

21 months
ETCAMAH + CDK4/6i (95% CI: 13.8-NC)
n=107; Patients with event=37 (34.6%)

and

6.4 months
AI + CDK4/6i (95% CI: 2.8-14)
n=95; Patients with event=49 (51.6%)

The EORTC QLQ-C30 is not all inclusive and does not include adequate assessment of all expected treatment-related symptoms. TTD in GHS/QoL may be confounded by multiple factors not related to disease/treatment and may be affected by assessment schedule or patient censoring.

- Results are prespecified, exploratory in nature, and not tested for statistical significance. Data should be interpreted with caution[19]
- Clinically meaningful deterioration was defined as a decrease from baseline score ≥16.6 confirmed at a subsequent time point[19]

SERENA-6 Study Design

SERENA-6 is a ctDNA-guided phase 3 trial evaluating the efficacy and safety of ETCAMAH + CDK4/6i vs AI + CDK4/6i in patients with HR+/HER2- mBC. In this study, 315 patients who had received at least 6 months of first-line AI + CDK4/6i therapy and had no evidence of disease progression were enrolled. Patients underwent regular *ESR1*m monitoring every 2-3 months with ctDNA testing using the Guardant360® CDx assay. Upon central detection of *ESR1*m without clinical progression, patients were randomized 1:1 to either switch to ETCAMAH 75 mg daily (n=157) or continue on their AI therapy (n=158), both in combination with a CDK4/6i (ribociclib, abemaciclib, or palbociclib). Treatment continued until disease progression, unacceptable toxicity, patient withdrawal, or death occurred. The primary endpoint was PFS by investigator assessment according to RECIST v1.1, with key secondary and exploratory endpoints including OS, patient-reported outcomes, and chemotherapy/ADC-free survival.[1,3]

ADC=antibody-drug conjugate; CI=confidence interval; ctDNA=circulating tumor DNA; EORTC QLQ-C30=European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; GHS=global health status; HR=hazard ratio; mPFS=median progression-free survival; NC=not calculable; OS=overall survival; QoL=quality of life; RECIST=Response Evaluation Criteria in Solid Tumors; TTD=time to deterioration.

Support your patients through quarterly monitoring for *ESR1*m during 1L AI + CDK4/6i treatment[3]

Who to monitor

Patients with HR+/HER2- mBC on 1L AI + CDK4/6i for ≥6 months[3]

When to monitor



Add *ESR1*m testing to routine bloodwork

Repeat testing every 3 months[1]

How to monitor

Detect *ESR1*m with **ctDNA via liquid biopsy**, using an FDA-authorized test[1,20]

Alert the care team as soon as *ESR1*m is detected

If ctDNA ordering is not included in your office's EHR, fill out a lab requisition.
Specify "ctDNA testing for *ESR1* mutation (liquid biopsy, next-generation sequencing)"

EHR=electronic health record; FDA=Food and Drug Administration.

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Bradycardia (cont'd): For symptomatic (Grade 2 or above) bradycardia, withhold ETCAMAH until symptoms resolve. Obtain ECG to evaluate etiology. If a contributing concomitant medication is identified, modify the dosage or discontinue this medication, as appropriate, until bradycardia symptoms resolve, then resume ETCAMAH. Consider reassessing the HR after restart. Permanently discontinue for persistent symptomatic bradycardia.

Embryo-Fetal Toxicity: Based on findings in animals and its mechanism of action, ETCAMAH can cause fetal harm when administered to a pregnant woman. 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.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING, and Patient Information for ETCAMAH.

In SERENA-6,

Adverse reactions were mostly **grade 1 or 2**[1]

Adverse reactions in ≥10% of patients[1,*]	ETCAMAH + CDK4/6i (n=155)		AI + CDK4/6i (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

1.3%
discontinued due to ARs
with ETCAMAH + CDK4/6i[1,§]

~90%
of patients did not report diarrhea
9% had grade 1 or 2 diarrhea with ETCAMAH + CDK4/6i[3]

- Dose interruptions of ETCAMAH due to adverse reactions occurred in 22% of patients[1,‖]

*Graded according to National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 5.0.[1]
[†]Visual disturbances include: photopsia, blurred vision, visual field defect, decreased visual acuity, visual impairment, diplopia, photophobia, and visual perseveration.[1]
[‡]Fatigue includes: fatigue and asthenia.[1]
[§]Adverse reactions that resulted in permanent discontinuation of ETCAMAH included gastroesophageal reflux disease, cholestasis, and hepatic cytolysis (0.6% each).[1]
[‖]The adverse reactions (≥2%) leading to dose interruptions were bradycardia (3.9%) and visual disturbances (2.6%).[1]

AR=adverse reaction.

In SERENA-6,

Additional safety and tolerability data[1]

- The median duration of exposure was 10.1 months in the ETCAMAH + CDK4/6i arm[1]
- Serious adverse reactions occurred in 10% of patients in the ETCAMAH + CDK4/6i arm. 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 + CDK4/6i, including acute respiratory distress syndrome and sudden death (0.6% each)[1]

Laboratory abnormalities (≥10% of patients)[1,*,†]

	ETCAMAH + CDK4/6i (n=155)		AI + CDK4/6i (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
Lymphocytes 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
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 NCI CTCAE version 5.0.[1]
†Includes patients with at least one baseline and one post-baseline result.[1]

<1% of patients had a dose modification due to liver toxicity[1,‡]

‡0.6% permanently discontinued due to hepatic cytolysis.[1]

NCI=National Cancer Institute.

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (cont'd)

ADVERSE REACTIONS

The most common (≥20%) adverse reactions, including laboratory abnormalities, with ETCAMAH in combination with a CDK4/6i were decreased neutrophils (68%), decreased leukocytes (66%), decreased hemoglobin (47%), decreased lymphocytes (39%), decreased platelets (36%), visual disturbances (34%), and fatigue (23%).

Permanent discontinuation 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.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING, and Patient Information for ETCAMAH.

In SERENA-6,

Cardiac events associated with ETCAMAH were **generally low grade and reversible**[1]

Bradycardia

Low incidence – 8%[1]

No grade 3 or above events reported[3] (Grade 1–5.2%; Grade 2–2.6%)

No medical interventions were required beyond dose interruption[1]

Median time to onset was 17 days (range: 13-283)[1] Maximum decrease in heart rate observed on day 15[1]

Patients with bpm <55 were excluded in SERENA-6.[1]

QTc interval prolongation when combined with ribociclib or other known QTc interval prolonging drugs

Low incidence – 2.6%[1]

Generally low grade[21,22] (Grade 1–1.3%; Grade 2–0.6%; Grade 3–0.6%)

In a dose-finding trial, a Grade 4 Torsades de Pointes was observed in one patient with confounding factors receiving ETCAMAH + ribociclib

No clinically meaningful **arrhythmia reported**[26]

Reversible with dose interruption[22]

Please see full Prescribing Information for additional information on cardiac monitoring, dose modifications, and drug interactions.

No patients discontinued ETCAMAH due to a cardiac event[1]

3.9% of patients had a dose interruption due to bradycardia and 0.6% due to QTc prolongation[1]

bpm=beats per minute.

SAFETY

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (cont'd)

ADVERSE REACTIONS (cont'd)

Visual disturbances: For visual disturbances limiting instrumental ADLs (activities of daily living) (Grade 2) or above, withhold ETCAMAH until symptoms resolve to Grade 1 or below. Refer to an eye professional for an ophthalmic examination and treatment and reassess at the next visit.

For other Grade 3 or higher adverse reactions: Withhold ETCAMAH until resolution to Grade 2 or below, then resume. Permanently discontinue for recurrence of Grade 3 or higher adverse reactions.

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In SERENA-6,

Visual disturbances were reported to have **no or generally minimal effect on patients' daily activities**[1,3]

In patients who reported visual disturbances[1,3,23,*]:

The vast majority were grade 1

and not impacting activities of daily living

- **Rates:** ~90% grade 1, ~8% grade 2, and ~2% grade 3[†]
- **Median time to onset:** 8 days
- **Duration:** <1 minute/episode
- **Frequency:** ≤3 days a week

*34% of patients in the ETCAMAH + CDK4/6i arm (n=155) and 16% of patients in the AI + CDK4/6i arm (n=155).[23]
[†]Grade 2: Limiting instrumental ADL; Grade 3: Limiting self-care ADL.[1]



No increased risk of clinically meaningful changes in visual acuity[1,3,23]

- No or negligible impact on ability to drive or use machines



No baseline eye exam required[1]

- No increased severity over time[23,‡]
- Nonstructural and reversible effect on the eye[23,24,§]

Additional information

- The most common visual disturbance was photopsia (20%), which is the perception of flashing or flickering lights without an external stimulus[3]
  - Photopsia was typically observed in the periphery and was not associated with structural eye abnormalities[3]
- Other disturbances included vision blurred (7.1%), visual impairment (3.9%), diplopia (1.9%), photophobia (1.9%), and visual perseveration (1.3%)[23]

Dose interruptions

- Dose interruptions of ETCAMAH due to visual disturbances occurred in 2.6% of patients[1]

No patients discontinued ETCAMAH due to visual disturbances[1]

[‡]The NEI-VFQ-25 assesses how visual function affects daily activities and overall vision-related QoL. This questionnaire comprises 11 subscales. Adherence was calculated for each timepoint and was defined as the number of patients with an evaluable questionnaire (≥1 subscale completed) divided by the total number of patients expected to complete the questionnaire at that timepoint. At baseline, 69% of patients in the ETCAMAH + CDK4/6i arm and 59% of patients in the AI + CDK4/6i arm completed ≥1 subscale of the NEI-VFQ-25.[23]
[§]Based on ophthalmological review of patients reporting visual disturbances.[1]

Findings from the NEI-VFQ-25 are exploratory and descriptive, intended to characterize patient-reported visual symptoms and function and may be subject to inherent limitations of PRO measures. Clinicians should apply their own judgment. These questionnaires were not designed to evaluate early visual disability; results may underrepresent such impairments.

ADL=activities of daily living; NEI-VFQ-25=National Eye Institute-Visual Function Questionnaire-25; PRO=patient-reported outcome.

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (cont'd)

DRUG INTERACTIONS

• **Strong CYP3A Inhibitors:** Monitor for increased adverse reactions to ETCAMAH and modify the dosage as recommended

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING, and Patient Information for ETCAMAH.

In combination with CDK4/6i,

Cardiac assessments when switching to ETCAMAH **should be completed in the first 2 weeks of therapy**[1]

Assessment	Baseline	Week 1	Week 2	Week 3	Week 4
ECG	✓	✓	✓	*As clinically indicated*	
Electrolytes	✓	*As clinically indicated*			
AND	If patient has bradycardia at baseline (<60 bpm) or on a concomitant medication known to lower heart rate (eg, beta blockers):				
Heart Rate	✓	*As clinically indicated*			

- 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
- Obtain serum electrolytes at baseline and during treatment as clinically indicated, and correct electrolyte abnormalities
- 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 (eg, beta-blockers) if concomitant use cannot be avoided

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (cont'd)

DRUG INTERACTIONS (cont'd)

- **Strong and Moderate CYP3A Inducers:** Avoid the use of strong CYP3A inducers. Use caution with the co-administration of a moderate CYP3A inducer
  - 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. 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
- **CYP2C9 and/or CYP2C19 Substrates:** Avoid concomitant use of ETCAMAH with CYP2C9 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 or CYP2C19 substrate
- **Certain CYP3A Substrates:** Refer to the Prescribing Information for CYP3A substrates where minimal increases in the concentration may lead to serious adverse reactions

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Upon *ESR1*m detection,

Switch to ETCAMAH—a **convenient, once-daily tablet** taken in combination with any FDA-approved CDK4/6i[1]



*For patients with severe hepatic impairment receiving ETCAMAH in combination with ribociclib, dose 75 mg once every other day.[1]

Avoid concomitant use of strong and moderate CYP3A inducers when combining ETCAMAH with abemaciclib or palbociclib. If concomitant use of a moderate CYP3A inducer cannot be avoided, dose modifications will differ based on the CDK4/6i used.[1]

Advise patients when taking ETCAMAH[1,†]:



Take one tablet at the same time each day
If a dose of ETCAMAH is missed, instruct the patient to take the missed dose if it's within 6 hours or skip the missed dose if more than 6 hours have passed. The next dose should be taken at the usual time the following day. If the patient vomits a dose of ETCAMAH, instruct the patient not to take an additional dose and to take the next dose at the usual time.



Swallow the tablet whole
Do not cut, crush, or chew tablets prior to swallowing. Do not take any ETCAMAH tablets that are broken, cracked, or otherwise not intact.

Please see full Prescribing Information for drug interactions, dosing, and administration. Refer to the full Prescribing Information of the CDK4/6i or other concomitant medications for dosing.

The recommended dose of a CDK4/6 inhibitor is continued at the same dose at the time of initiation of ETCAMAH as when the *ESR1*m was detected.[1]

[†]Until disease progression or unacceptable toxicity.[1]

CDK4/6=cyclin-dependent kinase 4/6.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING, and Patient Information for ETCAMAH.

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Recommended dosage modifications of ETCAMAH for ARs[1,25]

- Dose interruption of ETCAMAH due to adverse reactions occurred in 22% of patients. The adverse reactions (≥2%) leading to dose interruptions were bradycardia (3.9%) and visual disturbances (2.6%)[1]

QTc Interval Prolongation **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† **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‡ **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 **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.

Refer to the full Prescribing Information for the coadministered CDK4/6 inhibitor for dose modification guidelines in the event of toxicity and other relevant safety information.[1]

*Severity as defined by NCI CTCAE version 5.0.[1]

†Bradycardia includes bradycardia and sinus bradycardia.[1]

‡Visual disturbances include: photopsia, blurred vision, visual field defect, decreased visual acuity, visual impairment, diplopia, photophobia, and visual perseveration.[1]

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (cont'd)
DRUG INTERACTIONS (cont'd)

- **Drugs that Prolong the QTc Interval:** ETCAMAH is indicated in combination with a CDK4/6i and there is increased risk of QTc interval prolongation with ribociclib, a strong CYP3A inhibitor that can prolong the QTc interval. 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 TdP. If concomitant use with other products cannot be avoided, monitor the QTc interval more frequently. ETCAMAH in combination with a CDK4/6i is associated with QTc interval prolongation
- **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. ETCAMAH causes decreases in HR that are dose and baseline HR dependent

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

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Discussing monitoring and ETCAMAH + CDK4/6i treatment with your patients

Patient needs	Why this matters	Tips for practice
Understand the potential benefits of early intervention	Patients may question why treatment changes are made before visible disease progression. Early intervention may delay disease progression.[1]	◆ Use simple analogies (“this is a proactive step to help you stay on hormone therapy for longer”) ◆ Reassure patients that changes are based on evidence and may help delay disease progression
Explanation of ctDNA monitoring	ctDNA liquid biopsy helps detect *ESR1* mutations early, before progression. This proactive approach may allow for appropriate changes in treatment.[3]	◆ Explain what ctDNA testing is and why it’s being done (“a blood test performed quarterly to look for changes in the cancer before the cancer grows or spreads”) ◆ Inform patients that identifying *ESR1*m provides the opportunity to adjust treatment and may help extend their time without progression on 1L CDK4/6i
Support for medication adherence	Taking ETCAMAH as prescribed is important.[1]	◆ Encourage use of phone alarms or medication diaries ◆ Review the dosing schedule with patients and caregivers
Support for side effects	Early identification and management of side effects may be helpful for your patients so they can seek appropriate care guidance. You can support treatment management by asking patients to report side effects.[1]	◆ Review possible adverse reactions at each visit ◆ Discuss visual disturbances associated with ETCAMAH + CDK4/6 inhibitors with patients ◆ Advise patients about the risk of QT prolongation. Tell them to seek immediate medical attention if they experience any related symptoms ◆ Encourage patients to report any new side effects or symptoms promptly ◆ Collaborate with the healthcare team for dose interruptions or permanent discontinuation, if necessary ◆ Screen for new drug-drug interactions at every appointment, including concomitant medications that may heighten the risk of QT prolongation

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (cont’d)

SPECIAL POPULATIONS

Pregnancy: Based on findings in animals and mechanism of action, ETCAMAH can cause fetal harm when administered to a pregnant woman. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

Lactation: 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.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING, and Patient Information for ETCAMAH.

ETCAMAH®
camizestrant
75 mg tablets

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IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING (cont'd)

SPECIAL POPULATIONS (cont'd)

Females and Males of Reproductive Potential: ETCAMAH can cause fetal harm when administered to pregnant women. Verify pregnancy status of female patients of reproductive potential prior to initiating ETCAMAH. Advise female patients 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. Refer to the Prescribing Information of the CDK4/6i palbociclib, if used in combination with ETCAMAH, for contraception information and use for the longest recommended post-treatment duration. ETCAMAH may impair fertility in female and male patients.

Pediatric Use: Safety and effectiveness have not been established in pediatric patients.

Hepatic Impairment: In patients with severe (Child-Pugh C) hepatic impairment, when ETCAMAH is combined with ribociclib, reduce the dosing frequency to every other day.

No dosage modifications are required in other patients with hepatic impairment of any level, or when ETCAMAH is combined with abemaciclib or palbociclib, although patients with moderate or severe hepatic impairment (Child-Pugh B or C) should be monitored for increased adverse reactions and dosage modified as recommended.

Please see additional Important Safety Information throughout and full Prescribing Information, including Boxed WARNING, and Patient Information for ETCAMAH.

You may report side effects related to AstraZeneca products.

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This product information is intended for US healthcare professionals

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