ETCAMAH®
camizestrant
75 mg tablets

ETCAMAH Oracle Health® EHR System Guide

Tipsheet for Patient Lists, Order Sets, and Incorporating *ESR1*m Testing Into Treatment Calendars

ETCAMAH introduces a new treatment paradigm in combination with a CDK4/6 inhibitor for HR-positive, HER2-negative locally advanced or metastatic breast cancer upon detection of *ESR1* mutation during aromatase inhibitor and CDK4/6 inhibitor therapy. It is important to update your Oracle Health EHR system today to stay up to date with the latest clinical advancements in locally advanced and metastatic breast cancer.

SELECT SAFETY INFORMATION INCLUDING BOXED WARNING ABOUT ETCAMAH® (camizestrant)

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.

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).

SELECT SAFETY INFORMATION ABOUT ETCAMAH® (CAMIZESTRANT)

WARNING AND PRECAUTIONS

QTc Interval Prolongation: ETCAMAH in combination with a CDK4/6 inhibitor (CDK4/6i) is associated with QTc interval prolongation.

CDK4/6i = cyclin-dependent kinase 4/6 inhibitor; EHR = electronic health record; *ESR1* = estrogen receptor 1 gene; *ESR1*m = estrogen receptor 1 mutation; FDA = US Food and Drug Administration; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor.

Please see additional Important Safety Information on pages 22 to 24 and full Prescribing Information, including Boxed WARNING, and Patient Information for ETCAMAH.

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Contents

Creating a Patient List 3

Suggested Instructions 3

To Identify Patients With HR-Positive, HER2-Negative, Locally Advanced or Metastatic Breast Cancer With an *ESR1* Mutation During AI and CDK4/6i Therapy, Based on an FDA-Authorized Test, or Those Eligible for *ESR1*m Testing 3

Creating Treatment Plans and Order Sets 8

Overview and Limitations 8

To Identify AI and CDK4/6i Treatment Plans for Locally Advanced or Metastatic Breast Cancer With an *ESR1* Mutation During 1L With ETCAMAH, for Oral Use 8

Suggested PowerPlan Instructions—ETCAMAH 14

To Update AI and CDK4/6i Treatment Plans for Locally Advanced or Metastatic Breast Cancer With an ESR1 Mutation During 1L With ETCAMAH, for Oral Use 14

Suggested PowerPlan Instructions—*ESR1*m 17

To Update Treatment Plans for Metastatic Breast Cancer That Use CDK4/6i With an AI to Include *ESR1*m Genomic Variant Testing Order Group 17

To Integrate Appropriate Timing for *ESR1*m Testing Into the Calendar 17

Notes 18

ETCAMAH Important Safety Information 22

1L = first line; AI = aromatase inhibitor.

Suggested Instructions to Identify Patients With HR-Positive, HER2-Negative, Locally Advanced or Metastatic Breast Cancer With an *ESR1* Mutation During AI and CDK4/6i Therapy, Based on an FDA-Authorized Test, or Those Eligible for *ESR1*m Testing

This document is intended to provide health systems with instructions to create a patient list in the Oracle Health® EHR system to identify certain adult patients with HR-positive, HER2-negative, locally advanced or metastatic breast cancer upon detection of *ESR1* mutation (*ESR1*m) during aromatase inhibitor and CDK4/6 inhibitor therapy, based on an FDA-authorized test, or those who may be eligible for *ESR1*m testing. This guide provides instructions for the following 3 scenarios:

- Adult patients with HR-positive/HER2-negative locally advanced or metastatic breast cancer AND aromatase inhibitor and CDK4/6 inhibitor therapy AND no *ESR1*m test ordered. For patients identified on this list, practitioners may consider ordering an *ESR1*m test
- Adult patients with HR-positive/HER2-negative locally advanced or metastatic breast cancer AND aromatase inhibitor and CDK4/6 inhibitor therapy AND *ESR1*m test ordered BUT no structured result for *ESR1*m test available in the EHR. For patients identified on this list, a manual chart view should be considered to determine *ESR1*m result and appropriateness for ETCAMAH or continued monitoring for *ESR1*m emergence
- Adult patients with HR-positive/HER2-negative locally advanced or metastatic breast cancer AND aromatase inhibitor and CDK4/6 inhibitor therapy AND *ESR1*m test ordered WITH result available in a structured field in the EHR. For patients identified on this list, practitioners may consider appropriateness for ETCAMAH or continued monitoring for *ESR1*m emergence

This guide is for the Oracle Health EHR system and is not appropriate for other conditions, treatments, or therapeutic areas or for other EHR systems.

The process outlined in this document is variable, and not all steps will apply to every organization. Any steps or settings that are not part of an organization's standard process should be excluded or modified accordingly. Any questions should be directed to the appropriate service provider. The organization is solely responsible for implementing, testing, monitoring, and the ongoing operation of any EHR tools.

Diagnoses:

HR-Positive/HER2-Negative Diagnoses[1]:

- The single code of Z17.411: Hormone Receptor (HR)-positive/Human Epidermal Growth Factor Receptor 2 (HER2)-negative status (this code represents a combination of the below 2 codes) OR
- Z17.0: HR-positive status AND Z17.32: HER2-negative status

Breast Cancer Diagnoses:

- Breast Cancer: See Appendix A
- Codes Indicating Metastases: See Appendix B

Suggested Instructions to Identify Patients With HR-Positive, HER2-Negative, Locally Advanced or Metastatic Breast Cancer With an *ESR1* Mutation During AI and CDK4/6i Therapy, Based on an FDA-Authorized Test, or Those Eligible for *ESR1*m Testing (cont'd)

Medications:

- Aromatase inhibitor and CDK4/6 inhibitor therapy, to be identified by each organization by medication grouper, therapeutic class, or individual medications

Procedure(s):

- FDA-authorized test for *ESR1*m detection, to be identified by organization-specific coding practices

Note: Consider running the report on a regular basis. Once the initial report has been created, it can be saved for future use and subsequent reports can be rerun. Running reports over time allows for the identification of new patients meeting the inclusion criteria.

Suggested Instructions to Identify Patients With HR-Positive, HER2-Negative, Locally Advanced or Metastatic Breast Cancer With an *ESR1* Mutation During AI and CDK4/6i Therapy, Based on an FDA-Authorized Test, or Those Eligible for *ESR1*m Testing (cont'd)

Consider Oracle Health's Discern Analytics 2 (DA2) to create the patient lists. Consult your organization if administrative user rights are required to access the reporting solutions. Review documentation practices in the EHR when considering creating the patient report.

1. Launch **Discern Analytics 2.0**. It may be found as DA2.exe in the Oracle Cerner applications folder
2. Click the **Domains** tab to access available domains
3. Select **File > New > Query** or select the desired domain by double-clicking it. The query wizard will display available categories
4. In the Qualifications window, select the **Diagnosis Code Filter** and click **Modify Filter List**
5. Enter the HR-positive/HER2-negative ICD-10 diagnosis codes Z17.411 (HR-positive/HER2-negative status) OR (Z17.0 AND Z17.32) in the search box and select them from the list. Click **Include**
6. In the Qualifications window, select the **Diagnosis Code Filter** and click **Modify Filter List**
7. Enter the diagnosis codes for breast cancer. Due to the number of codes used to designate these statuses, please refer to Appendix A for the list of recommended ICD-10 codes for identifying breast cancer and to Appendix B for the list of recommended ICD-10 codes for identifying metastases. Click **Include**
8. In the Qualifications window, select the **Orders > Orders Synonym ID Filter** and click **Modify Filter List**
9. Enter and select the 1L, endocrine-based therapy and select **Include** for all medications
10. In the Qualifications window, select the **Procedures Filter** and click **Modify Filter List**
11. Enter the billing CPT code or name of the FDA-authorized test for *ESR1*m detection, to be identified by organization-specific coding practices and select the appropriate test defining the logic: there are 3 different options presented for defining the logic. These 3 options align with the 3 scenarios presented in the Overview and Limitations section
    a. Set the logic to include patient living status AND age AND BOTH HR-positive/HER2-negative status AND at least one of the breast cancer diagnoses AND existence of aromatase inhibitor and CDK4/6 inhibitor therapy AND NOT existence of the FDA-authorized test for *ESR1*m
        i. This list identifies patients with HR-positive/HER2-negative locally advanced or metastatic breast cancer AND aromatase inhibitor and CDK4/6 inhibitor therapy AND no *ESR1*m test ordered. For patients identified on this list, practitioners may consider ordering an *ESR1*m test
    b. Set the logic to include patient living status AND age AND BOTH HR-positive/HER2-negative status AND at least one of the locally advanced OR metastatic breast cancer diagnoses AND existence of aromatase inhibitor and CDK4/6 inhibitor therapy AND existence of the FDA-authorized test for *ESR1*m

ICD-10 = International Classification of Diseases, 10th Revision.

Suggested Instructions to Identify Patients With HR-Positive, HER2-Negative, Locally Advanced or Metastatic Breast Cancer With an *ESR1* Mutation During AI and CDK4/6i Therapy, Based on an FDA-Authorized Test, or Those Eligible for *ESR1*m Testing (cont'd)

i. This list identifies patients with HR-positive/HER2-negative locally advanced or metastatic breast cancer AND aromatase inhibitor and CDK4/6 inhibitor therapy AND *ESR1*m test ordered BUT no structured result for *ESR1*m available in the EHR. For patients identified on this list, a manual chart view should be considered to determine *ESR1*m result and appropriateness for ETCAMAH

ii. If, upon review, an *ESR1* mutation is detected, these patients could be considered for ETCAMAH. In addition, for patients who are identified as having an *ESR1* mutation upon chart review, the HCP should also consider discontinuing any further *ESR1*m testing if any recurring orders remain active for testing. If, upon review, an *ESR1* mutation is not detected, these patients may be eligible for routine monitoring for *ESR1*m emergence ahead of disease progression. For organizations where *ESR1*m biomarker test results are stored as discrete fields in the EHR, proceed to the following additional steps

c. The following is only for organizations that store *ESR1*m results in discrete fields. If your organization stores *ESR1*m results in discrete fields, before setting the logic for this list, return to the **Qualifications** window, select the **Procedure Results Filter** and click **Modify Filter List**. Enter the billing CPT code or name of the FDA-authorized test for *ESR1*m detection, to be identified by organization-specific coding practices and select the appropriate test. Set the logic to include patient living status AND age AND BOTH HR-positive/HER2-negative status AND at least one of the locally advanced OR metastatic breast cancer diagnoses AND existence of aromatase inhibitor and CDK4/6 inhibitor therapy AND existence of the genomic variant result for *ESR1*m

i. This list identifies patients with HR-positive/HER2-negative locally advanced or metastatic breast cancer AND aromatase inhibitor and CDK4/6 inhibitor therapy AND *ESR1*m test ordered WITH result available in a structured field in the EHR. For patients identified on this list, practitioners may consider appropriateness for ETCAMAH. In addition, for patients who are identified as having an *ESR1* mutation upon chart review, the HCP should also consider discontinuing any further *ESR1*m testing if any recurring orders remain active for testing

ii. Note: While the above steps do consider genomic variant results stored in discrete fields, depending on workflow for incorporating external results at your organization, you may still consider a manual chart review to confirm results. The above list can be filtered to display patients with the targeted *ESR1* mutation(s) to consider for ETCAMAH. When no *ESR1* mutation is detected, these patients may be eligible for routine monitoring for *ESR1*m emergence ahead of disease progression

After completing Step 11 for each patient list you wish to create, continue with the below steps.

12. Select all the desired columns to include in the report by selecting the column and then clicking the right arrow to the **Selected Columns** window. Select and add the current diagnoses and current medications and any other desired display columns

HCP = healthcare professional.

Suggested Instructions to Identify Patients With HR-Positive, HER2-Negative, Locally Advanced or Metastatic Breast Cancer With an *ESR1* Mutation During AI and CDK4/6i Therapy, Based on an FDA-Authorized Test, or Those Eligible for *ESR1*m Testing (cont'd)

13. Save the query with a unique name (eg, "**Patients to Review for ETCAMAH Eligibility**" or "**Patients w/ HR-positive/HER2-negative mBC and *ESR1*m Results**")
14. Click **Query > Query review** or **Run Query in Viewer** in the Query tab to run and save the query
15. The results will display. The results may be further manipulated if desired or exported to Excel

Updating AI and CDK4/6i Treatment Plans for Locally Advanced or Metastatic Breast Cancer With an *ESR1* Mutation During 1L With ETCAMAH, for Oral Use

Overview and Limitations

This document is intended to provide health systems with instructions to update PowerPlans for the Oracle Health® EHR system with the following approved indication[2]:

- In combination with a CDK4/6i (palbociclib, ribociclib, or abemaciclib), ETCAMAH is indicated for the treatment of adult patients with HR-positive, HER2-negative, locally advanced or metastatic breast cancer upon detection of *ESR1* mutation during aromatase inhibitor and CDK4/6i 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).

This guide is for the Oracle Health EHR system and is not appropriate for other conditions, treatments, or therapeutic areas, or for other EHR systems. This guide is not endorsed, certified, or sponsored by Oracle Health. Oracle Health is not affiliated with AstraZeneca products and services.

The process outlined in this document is variable, and not all steps will apply to every organization. Any steps or settings that are not part of an organization's standard process should be excluded or modified accordingly. Any questions should be directed to the appropriate service provider. The organization is solely responsible for implementing, testing, monitoring, and the ongoing operation of any EHR tools.

Considerations

PowerPlans are commonly used in the management of oncology patients—your organization may refer to these as treatment regimens or protocols. After their initial release, PowerPlans may benefit from clinical updates to incorporate new products or new indications. The optimization of PowerPlans is a common process and provides an opportunity to incorporate treatment updates. PowerPlans are typically modified at the health system level to help reduce practice variation.

Typically, an organization will conduct a clinical review to confirm and approve the suggested optimization. Various stakeholders may participate in reviewing treatment plan optimization requests prior to implementation.

Suggested Instructions to Update AI and CDK4/6i Treatment Plans for Locally Advanced or Metastatic Breast Cancer With an *ESR1* Mutation During 1L With ETCAMAH, for Oral Use (cont'd)

Suggested PowerPlan

ETCAMAH is an oral next-generation selective estrogen receptor degrader (ngSERD) and complete estrogen receptor (ER) antagonist indicated under Accelerated Approval[2]:

- In combination with a CDK4/6i (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 *ESR1* mutation during aromatase inhibitor and CDK4/6i therapy, based on an FDA-authorized test

Key clinical details from the ETCAMAH Prescribing Information are included below and may be incorporated as part of the PowerPlan update based on steps in the instructions section that follows. The instructions are not fully inclusive of all details of the ETCAMAH Prescribing Information. The Prescribing Information in this section is only suggestive, and it is strongly recommended that clinical and operational leadership align the treatment plan contents with the expectations and goals of the organization. The organization may add or edit any details as desired to align with governing EHR policies and standards.

Please consult the most recent version of the ETCAMAH Prescribing Information for full medication details.

Suggested Instructions to Update AI and CDK4/6i Treatment Plans for Locally Advanced or Metastatic Breast Cancer With an *ESR1* Mutation During 1L With ETCAMAH, for Oral Use (cont'd)

Dosage and Administration[2]

Patient Selection

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

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

Recommended Cardiac Evaluation

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

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

Recommended Dosage and Administration

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

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

Take ETCAMAH at approximately the same time each day.

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

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

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

Suggested Instructions to Update AI and CDK4/6i Treatment Plans for Locally Advanced or Metastatic Breast Cancer With an *ESR1* Mutation During 1L With ETCAMAH, for Oral Use (cont'd)

Dosage Modifications for Adverse Reactions[2]

The recommended dosage modifications for ETCAMAH for adverse reactions are provided in Table 1.

Table 1. Recommended Dosage Modifications for ETCAMAH

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

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

*Severity as defined by NCI CTCAE version 5.0.

†Heart-rate corrected QTc using Fridericia's method.

‡Bradycardia includes bradycardia and sinus bradycardia.

§Visual disturbances include: photopsia, blurred vision, visual field defect, decreased visual acuity, visual impairment, diplopia, photophobia and visual perseveration.

ADL = Activities of daily living; CTCAE = Common Terminology Criteria for Adverse Events; ECG = electrocardiogram; NCI = National Cancer Institute.

Suggested Instructions to Update AI and CDK4/6i Treatment Plans for Locally Advanced or Metastatic Breast Cancer With an *ESR1* Mutation During 1L With ETCAMAH, for Oral Use (cont'd)

Drug Interactions[2]

Effect of Other Drugs on ETCAMAH

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

Table 5. Drug Interactions Involving ETCAMAH and Other Drug Products

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

CYP3A = cytochrome P450 family 3, subfamily A.

Suggested Instructions to Update AI and CDK4/6i Treatment Plans for Locally Advanced or Metastatic Breast Cancer With an *ESR1* Mutation During 1L With ETCAMAH, for Oral Use (cont'd)

Drug Interactions[2] (cont'd)

Effect of ETCAMAH on Other Drugs

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

Table 6. Drug Interactions Involving ETCAMAH and Other Drug Products

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

Drugs That Prolong the QTc Interval[2]

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

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

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

Drugs That Cause Bradycardia[2]

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

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

There are no contraindications for ETCAMAH.

CYP2C9 = cytochrome P450 family 2, subfamily C, member 9; CYP2C19 = cytochrome P450 family 2, subfamily C, member 19.

Please see additional Important Safety Information on pages 22 to 24 and full Prescribing Information, including Boxed WARNING, and Patient Information for ETCAMAH.

Suggested PowerPlan Instructions

An existing PowerPlan may be used as the foundation for a new one. For instance, an available clinical research PowerPlan for ETCAMAH may be available to use as a foundation in certain institutions. Consider modifying an existing PowerPlan that includes ETCAMAH or a CDK4/6i (palbociclib, ribociclib or abemaciclib) as a starting template, while saving the original PowerPlan. If an existing PowerPlan is unavailable, create a new one.

The steps below detail how to create the PowerPlan:

There are 3 main steps to create a PowerPlan in the Oracle Health® EHR system:

- **Step 1:** Find an existing PowerPlan to modify
- **Step 2:** Modify the PowerPlan to include ETCAMAH
- **Step 3:** Update PowerPlans for metastatic breast cancer containing CDK4/6i with AI to include *ESR1*m genetic testing order group

Step 1: Find an existing PowerPlan to modify

1. Open **DCP tools**
2. Select the **PowerPlan tool** in the Order Management section
3. Click **Task > Open Plan** to search for an existing PowerPlan
4. Enter search terms specific to each indication to find an existing PowerPlan that may serve as a template to optimize. Double-click on the plan to display its content
   Note: The existing PowerPlan will only serve as a template for the new ETCAMAH PowerPlan. If the original PowerPlan used to create the new ETCAMAH PowerPlan includes ETCAMAH, confirm it is retired or removed from the EHR production system according to the organization's EHR governing principles
   - When searching for existing search terms, consider searching for:
     – ETCAMAH for 1L HR-positive, HER2-negative, locally advanced or metastatic breast cancer with *ESR1* mutation, CDK4/6i (palbociclib, ribociclib or abemaciclib), SERENA-6
   - If no relevant PowerPlans exist, create a new one: Click **Tasks > New Plan**, define all clinical subcategories, and select orderable items as desired

Step 2: Modify the PowerPlan to include ETCAMAH

1. Update the **PowerPlan name**. A suggestion is listed below or select another name to align with internal naming conventions:
   - ETCAMAH in combination with a CDK4/6i (palbociclib, ribociclib, or abemaciclib) for the treatment of adult patients with HR-positive, HER2-negative, locally advanced or metastatic breast cancer upon detection of *ESR1* mutation during aromatase inhibitor and CDK4/6 inhibitor therapy
2. Update the **PowerPlan description**. A suggestion is listed below or select another name to align with internal naming conventions:
   - ETCAMAH in combination with a CDK4/6i (palbociclib, ribociclib or abemaciclib) is indicated for the treatment of adult patients with HR-positive, 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

Suggested PowerPlan Instructions (cont'd)

Step 2: Modify the PowerPlan to include ETCAMAH (cont'd)

3. In the **reference text** field, enter the following text:
   - ETCAMAH Prescribing Information: https://www.azpicentral.com/pi.html?product=etcamah
   - Patient Information https://www.azpicentral.com/pi.html?product=etcamah&medguide=y
   - Provider Support and Resources: www.ETCAMAHhcp.com/access-and-resources
   - Additional Resources for Patients and Caregivers: www.etcamah.com/educational-resources
   - Dosage and administration details for ETCAMAH. See the Dosage and Administration section starting on Page 2 of the Prescribing Information: https://www.azpicentral.com/pi.html?product=etcamah
4. Click **OK**
5. In the evidence text field, consider adding a Clinical Study References for ETCAMAH for SERENA-6: Advanced breast cancer upon detection of *ESR1* mutation during aromatase inhibitor and CDK4/6 inhibitor therapy:
   - See Section 14 of the Prescribing Information, Clinical Study of the ETCAMAH Prescribing Information for the SERENA-6 clinical study: https://www.azpicentral.com/pi.html?product=etcamah
6. Click the **Treatment Regimen** section to update the treatment regimen
   - ETCAMAH for 1L treatment with HR-positive, HER2-negative, locally advanced or metastatic breast cancer whose tumors have a detectable *ESR1* mutation: once daily, until disease progression or unacceptable toxicity
7. Select the **Medications** category. Enter "ETCAMAH" in the Start Search field in the lower right-hand panel. Click the right arrow to move ETCAMAH to the **Current List** box and click **Add**. Edit the **product details** and enter the desired dosage and administration details for ETCAMAH. Details may include Sig, dose, route, frequency, offset time, admin over, and any free-form special admin instructions for the nurse:
   - The recommended dosage of ETCAMAH is 75 mg orally once daily, with or without food, until disease progression or unacceptable toxicity
   - Administer ETCAMAH in combination with a CDK4/6 inhibitor (abemaciclib, palbociclib, or ribociclib). Continue the CDK4/6 inhibitor at the same dosage as when the *ESR1* mutation was detected. Refer to the Prescribing Information of the CDK4/6 inhibitor for additional dosing information
   - Take ETCAMAH at approximately the same time each day
   - Swallow tablets whole. Do not cut, crush, or chew tablets prior to swallowing. Do not take broken, cracked, or otherwise not intact tablets

Suggested PowerPlan Instructions (cont'd)

Step 2: Modify the PowerPlan to include ETCAMAH (cont'd)

- If a dose is missed within 6 hours, take the missed dose. If a dose of ETCAMAH is missed for more than 6 hours, skip the dose for the day and take the next dose at the usual time
- If a dose is vomited, do not take an additional dose and take the next dose at the usual time

8. Add orderable items specific to QTc interval prolongation monitoring and intervention as appropriate
   Note: QTc Interval Prolongation is defined as QTc > 500 msec or QTc > 480 msec and prolongation from baseline > 60 msec
   Consider adding orders for the following items, specific to QTc interval prolongation monitoring and intervention:
   - Lab Orders: Chem 10 (or equivalent) AND Calcium ionized (whole blood)
   - ECG/Cardiorespiratory Monitoring
     – Recommended Frequency: Before starting treatment, every week for the first 2 weeks of treatment, and periodically during treatment as clinically indicated
   - Cardiology Consult
9. Add any other desired orderable items and information to the PowerPlan and treatment schedule. This may include information for ETCAMAH treatment conditions, monitoring and hold parameters, Warnings and Precautions, supportive care, schedulable orders, HCP communications, hydration, and other sections as desired. Consider the Prescribing Information below:
   - There are dosage modifications for Adverse Reactions. (See the Dosage Modifications section starting on Page 2 or Section 2.4 Dosage Modifications of the Prescribing Information). Consider adding a referral to an eye care professional
   - For Dosage in Patients with Hepatic Impairment, see Section 2.5 of the Prescribing Information:
     – Dosage in Patients with Hepatic Impairment (2.5):
       - The recommended dosage for patients with hepatic impairment differs depending on the CDK4/6 inhibitor used in combination with ETCAMAH
       - For patients with severe (Child-Pugh C) hepatic impairment who are receiving ETCAMAH in combination with ribociclib, the recommended dosage of ETCAMAH is 75 mg once every other day
       - For patients with severe (Child-Pugh C) hepatic impairment who are receiving ETCAMAH in combination with abemaciclib or palbociclib, no dosage modification of ETCAMAH is recommended
       - Monitor patients with moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment receiving ETCAMAH in combination with any CDK4/6 inhibitor for increased adverse reactions and modify the dosage as recommended *[see Dosage and Administration (2.4)]*
   - For adverse reactions, see Section 6 of the Prescribing Information
10. Click **Task > Save Plan**
11. Validate the newly optimized PowerPlan
12. Release the PowerPlan to the production environment after completing testing

Suggested PowerPlan Instructions to Update Treatment Regimens for Metastatic Breast Cancer That Use CDK4/6i With an AI to Include *ESR1*m Genomic Variant Testing Order Group

Step 3: Updating PowerPlans for metastatic breast cancer containing CDK4/6i with an AI to include *ESR1*m genomic variant testing Order Group and PowerPlan Calendar

1. Open **DCP tools**
2. Select the **PowerPlan tool** in the Order Management section
3. Click **Task > Open Plan** to search for an existing PowerPlan. Enter search terms specific to plans designed for metastatic breast cancer that contain CDK4/6 with AI therapy
4. Determine which PowerPlans should be updated to include *ESR1*m genomic variant testing
5. While in the desired PowerPlan(s) to which you wish to add *ESR1*m testing, select the **Laboratory** category (or whichever category your organization uses for genomic/biomarker testing). Enter "*ESR1*" in the **Start Search** field in the lower right-hand panel. Find the appropriate *ESR1*m test, and click the right arrow to move it to the **Current List** box and click **Add**
   - The *ESR1*m test chosen should be blood-based (such as a circulating tumor DNA [ctDNA] blood test)
6. To ensure *ESR1*m monitoring occurs at the appropriate intervals after treatment initiation, configure the settings below for the *ESR1*m test added to the PowerPlan in the previous step:
   - **Order Activity** > **Start Offset** > **Relevant to Plan Initiation** > enter "6 months" or "180 days"
   - Recurrence: enter "every 3 months" or "every 90 days"
   - End condition: configure to stop when *ESR1* mutation is detected

<u>Integrating Appropriate Timing for *ESR1*m Testing Into the Calendar</u>

7. Preview the **Calendar** within the PowerPlan to ensure the *ESR1*m testing appears on the calendar as intended, to start at 6 months after plan initiation and to continue every 3 months thereafter or until *ESR1* mutation is detected

   While *ESR1*m testing is recommended at least every 3 months until detection of a mutation, if your organization performs routine blood work (ie, CBC, CMP) more frequently (ie, every 2 months) and chooses to include *ESR1*m ctDNA testing with that more frequent blood work, you may choose to do so at your organization's discretion. Whichever frequency is chosen, verify the *ESR1*m testing frequency is accurately reflected on the calendar.
8. Click **Task > Save Plan**
9. Consider updating the PowerPlan name to indicate *ESR1*m testing is now included
10. Consider updating the PowerPlan description to indicate *ESR1*m testing is now included

CBC = complete blood count; CMP = comprehensive metabolic panel.

Administer ETCAMAH prior to chemotherapy on the same day. Refer to the Prescribing Information for the agent administered in combination with ETCAMAH for recommended dosage information, as appropriate.

Notes

- The customer (eg, physician, medical group, integrated delivery network) shall be solely responsible for the implementation, testing, and monitoring of the instructions to ensure proper orientation in each customer's EHR system
- Capabilities, functionality, and setup (customization) for each EHR system may vary. AstraZeneca shall not be responsible for revising the implementation instructions it provides to any customer if the customer modifies or changes its software, or the configuration of its EHR system, after such time as the implementation instructions have been initially provided by AstraZeneca
- While AstraZeneca tests its implementation instructions on multiple EHR systems, the instructions are not guaranteed to work for all available EHR systems, and AstraZeneca shall have no liability thereto
- While EHRs may assist practitioners in identifying appropriate patients for consideration of assessment, treatment, and referral, the decision and action should ultimately be decided by a practitioner in consultation with the patient, after a review of the patient's records to determine eligibility, and AstraZeneca shall have no liability thereto
- The instructions have not been designed for, and are not tools and/or solutions for, meeting Advancing Care Information and/or any other quality/accreditation requirement
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Notes (cont'd)

Appendix A:
ICD-10 Codes for Breast Cancer[1]
Additional criteria are needed to properly stage, and a manual chart review may be needed to confirm presence of locally advanced disease

- C50.011 Malignant neoplasm of nipple and areola, right female breast
- C50.012 Malignant neoplasm of nipple and areola, left female breast
- C50.019 Malignant neoplasm of nipple and areola, unspecified female breast
- C50.021 Malignant neoplasm of nipple and areola, right male breast
- C50.022 Malignant neoplasm of nipple and areola, left male breast
- C50.029 Malignant neoplasm of nipple and areola, unspecified male breast
- C50.111 Malignant neoplasm of central portion of right female breast
- C50.112 Malignant neoplasm of central portion of left female breast
- C50.119 Malignant neoplasm of central portion of unspecified female breast
- C50.121 Malignant neoplasm of central portion of right male breast
- C50.122 Malignant neoplasm of central portion of left male breast
- C50.129 Malignant neoplasm of central portion of unspecified male breast
- C50.211 Malignant neoplasm of upper-inner quadrant of right female breast
- C50.212 Malignant neoplasm of upper-inner quadrant of left female breast
- C50.219 Malignant neoplasm of upper-inner quadrant of unspecified female breast
- C50.221 Malignant neoplasm of upper-inner quadrant of right male breast
- C50.222 Malignant neoplasm of upper-inner quadrant of left male breast
- C50.229 Malignant neoplasm of upper-inner quadrant of unspecified male breast
- C50.311 Malignant neoplasm of lower-inner quadrant of right female breast
- C50.312 Malignant neoplasm of lower-inner quadrant of left female breast
- C50.319 Malignant neoplasm of lower-inner quadrant of unspecified female breast
- C50.321 Malignant neoplasm of lower-inner quadrant of right male breast
- C50.322 Malignant neoplasm of lower-inner quadrant of left male breast
- C50.329 Malignant neoplasm of lower-inner quadrant of unspecified male breast

Notes (cont'd)

Appendix A:
ICD-10 Codes for Breast Cancer[1]
Additional criteria are needed to properly stage, and a manual chart review may be needed to confirm presence of locally advanced disease (cont'd)

- C50.411 Malignant neoplasm of upper-outer quadrant of right female breast
- C50.412 Malignant neoplasm of upper-outer quadrant of left female breast
- C50.419 Malignant neoplasm of upper-outer quadrant of unspecified female breast
- C50.421 Malignant neoplasm of upper-outer quadrant of right male breast
- C50.422 Malignant neoplasm of upper-outer quadrant of left male breast
- C50.429 Malignant neoplasm of upper-outer quadrant of unspecified male breast
- C50.511 Malignant neoplasm of lower-outer quadrant of right female breast
- C50.512 Malignant neoplasm of lower-outer quadrant of left female breast
- C50.519 Malignant neoplasm of lower-outer quadrant of unspecified female breast
- C50.521 Malignant neoplasm of lower-outer quadrant of right male breast
- C50.522 Malignant neoplasm of lower-outer quadrant of left male breast
- C50.529 Malignant neoplasm of lower-outer quadrant of unspecified male breast
- C50.611 Malignant neoplasm of axillary tail of right female breast
- C50.612 Malignant neoplasm of axillary tail of left female breast
- C50.619 Malignant neoplasm of axillary tail of unspecified female breast
- C50.621 Malignant neoplasm of axillary tail of right male breast
- C50.622 Malignant neoplasm of axillary tail of left male breast
- C50.629 Malignant neoplasm of axillary tail of unspecified male breast
- C50.811 Malignant neoplasm of overlapping sites of right female breast
- C50.812 Malignant neoplasm of overlapping sites of left female breast
- C50.819 Malignant neoplasm of overlapping sites of unspecified female breast
- C50.821 Malignant neoplasm of overlapping sites of right male breast
- C50.822 Malignant neoplasm of overlapping sites of left male breast
- C50.829 Malignant neoplasm of overlapping sites of unspecified male breast

Please see additional Important Safety Information on pages 22 to 24 and full Prescribing Information, including Boxed WARNING, and Patient Information for ETCAMAH.

Notes (cont'd)

Appendix A:
ICD-10 Codes for Breast Cancer[1]
Additional criteria are needed to properly stage, and a manual chart review may be needed to confirm presence of locally advanced disease (cont'd)

- C50.911 Malignant neoplasm of unspecified site of right female breast
- C50.912 Malignant neoplasm of unspecified site of left female breast
- C50.919 Malignant neoplasm of unspecified site of unspecified female breast
- C50.921 Malignant neoplasm of unspecified site of right male breast
- C50.922 Malignant neoplasm of unspecified site of left male breast
- C50.929 Malignant neoplasm of unspecified site of unspecified male breast

Appendix B:
ICD-10 Codes Indicating Metastases

- C79.51 Secondary malignant neoplasm of bone
- C79.52 Secondary malignant neoplasm of bone marrow
- C78.00 Secondary malignant neoplasm of unspecified lung
- C78.01 Secondary malignant neoplasm of right lung
- C78.02 Secondary malignant neoplasm of left lung
- C78.1 Secondary malignant neoplasm of mediastinum
- C78.2 Secondary malignant neoplasm of pleura
- C78.30 Secondary malignant neoplasm of unspecified respiratory organ
- C78.39 Secondary malignant neoplasm of other respiratory organs
- C79.31 Secondary malignant neoplasm of brain
- C79.32 Secondary malignant neoplasm of cerebral meninges
- C78.7 Secondary malignant neoplasm of liver and intrahepatic bile duct

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING ABOUT ETCAMAH® (camizestrant)

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.

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.

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 on pages 22 to 24 and full Prescribing Information, including Boxed WARNING, and Patient Information for ETCAMAH.

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING ABOUT ETCAMAH® (camizestrant) (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.

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.

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.

DRUG INTERACTIONS

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

Please see additional Important Safety Information on pages 22 to 24 and full Prescribing Information, including Boxed WARNING, and Patient Information for ETCAMAH.

IMPORTANT SAFETY INFORMATION INCLUDING BOXED WARNING ABOUT ETCAMAH® (camizestrant) (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.

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.

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 full Prescribing Information, including Boxed WARNING, and Patient Information for ETCAMAH.

You may report side effects related to AstraZeneca products (Opens new window).

References: 1. Centers for Medicare & Medicaid Services. ICD-10. Accessed July 17, 2026. https://www.cms.gov/medicare/coding-billing/icd-10-codes **2.** ETCAMAH® (camizestrant) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2026.

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