

TRUQAP- capivasertib tablet, film coated

AstraZeneca Pharmaceuticals LP

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TRUQAP safely and effectively. See full prescribing information for TRUQAP.

TRUQAP® (capivasertib) tablets, for oral use
Initial U.S. Approval: 2023

-----RECENT MAJOR CHANGES-----

Warnings and Precautions, Hyperglycemia (5.1) 02/2025

-----INDICATIONS AND USAGE-----

TRUQAP is a kinase inhibitor indicated, in combination with fulvestrant 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 with one or more *PIK3CA/AKT1/PTEN*-alterations as detected by an FDA-approved test following progression on at least one endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy. (1)

-----DOSAGE AND ADMINISTRATION-----

- Select patients for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer with TRUQAP based on the presence of one or more of the following genetic alterations in tumor tissue: *PIK3CA/AKT1/PTEN*. (2.1)
- Recommended Dosage: 400 mg orally twice daily, with or without food, for 4 days followed by 3 days off. (2.3)

-----DOSAGE FORMS AND STRENGTHS-----

Tablets: 160 mg and 200 mg (3)

-----CONTRAINDICATIONS-----

Severe hypersensitivity to TRUQAP or any of its components. (4)

-----WARNINGS AND PRECAUTIONS-----

- Hyperglycemia: TRUQAP can cause hyperglycemia. Evaluate blood glucose levels prior to starting and at regular intervals during treatment. Withhold, reduce dose, or permanently discontinue TRUQAP based on severity. (2.2, 2.4, 5.1)
- Diarrhea: TRUQAP caused diarrhea in most patients. Advise patients to increase oral fluids, start antidiarrheal treatment, and consult with a healthcare provider if diarrhea occurs while taking TRUQAP. Withhold, reduce dose, or permanently discontinue TRUQAP based on severity. (2.4, 5.2)
- Cutaneous Adverse Reactions: Monitor for signs and symptoms of cutaneous adverse reactions. Withhold, reduce dose, or permanently discontinue TRUQAP based on severity. (2.4, 5.3)
- Embryo-Fetal Toxicity: TRUQAP can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception. Refer to the Full Prescribing Information of fulvestrant for pregnancy and contraception information. (5.4, 8.1, 8.3)

-----ADVERSE REACTIONS-----

Most common adverse reactions (incidence $\geq 20\%$), including laboratory abnormalities, were diarrhea, cutaneous adverse reactions, increased random glucose, decreased lymphocytes, decreased hemoglobin, increased fasting glucose, nausea, fatigue, decreased leukocytes, increased triglycerides, decreased neutrophils, increased creatinine, vomiting and stomatitis. (6.1)

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

-----DRUG INTERACTIONS-----

- Strong CYP3A Inhibitors: Avoid concomitant use. If concomitant use cannot be avoided, reduce TRUQAP dose. (2.5, 7.1)
- Moderate CYP3A Inhibitors: Reduce TRUQAP dose. (2.5, 7.1)
- Strong and Moderate CYP3A Inducers: Avoid concomitant use. (7.1)

-----USE IN SPECIFIC POPULATIONS-----

Lactation: Advise not to breastfeed. (8.2)

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

TRUQAP, in combination with fulvestrant, 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 with one or more *PIK3CA/AKT1/PTEN*-alteration as detected by an FDA-approved test following progression on at least one endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy.

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Select patients for the treatment of HR-positive, HER2-negative advanced or metastatic breast cancer with TRUQAP, based on the presence of one or more of the following genetic alterations in tumor tissue: *PIK3CA/AKT1/PTEN* [see *Clinical Studies (14)*].

Information on FDA-approved tests for the detection of *PIK3CA*, *AKT1*, and *PTEN* alterations is available at: <http://www.fda.gov/CompanionDiagnostics>.

2.2 Recommended Evaluation Before Initiating TRUQAP

Evaluate fasting blood glucose (FG) and hemoglobin A1C (HbA1C) prior to starting TRUQAP and at regular intervals during treatment [see *Warnings and Precautions (5.1)*].

2.3 Recommended Dosage and Administration

The recommended dosage of TRUQAP, in combination with fulvestrant, is 400 mg orally twice daily (approximately 12 hours apart) with or without food, for 4 days followed by 3 days off. Continue TRUQAP until disease progression or unacceptable toxicity.

TRUQAP dosing schedule for each week is provided in Table 1.

Table 1: TRUQAP Dosing Schedule for Each Week

Day	1	2	3	4	5*	6*	7*
Morning	2 x 200 mg	2 x 200 mg	2 x 200 mg	2 x 200 mg			
Evening	2 x 200 mg	2 x 200 mg	2 x 200 mg	2 x 200 mg			

* No dosing on day 5, 6 and 7.

Swallow TRUQAP tablets whole. Do not chew, crush, or split tablets prior to swallowing. Do not take tablets that are broken, cracked, or otherwise not intact.

If a patient misses a dose within 4 hours of the scheduled time, instruct the patient to take the missed dose. If a patient misses a dose more than 4 hours of the scheduled time, instruct the patient to skip the dose and take the next dose at its usual scheduled time.

If a patient vomits a dose, instruct the patient not to take an additional dose and take the next dose at its usual scheduled time.

Refer to the fulvestrant Full Prescribing Information for recommended fulvestrant dosing information.

For premenopausal and perimenopausal women, administer a luteinizing hormone-releasing hormone (LHRH) agonist according to current clinical practice standards.

For men, consider administering a LHRH agonist according to current clinical practice standards.

2.4 Dosage Modifications for Adverse Reactions

The recommended dose reductions for adverse reactions are listed in Table 2. Permanently discontinue TRUQAP if unable to tolerate the second dose reduction.

Table 2: Recommended Dose Reductions of TRUQAP for Adverse Reactions

TRUQAP	Dose and Schedule
First dose reduction	320 mg twice daily for 4 days followed by 3 days off
Second dose reduction	200 mg twice daily for 4 days followed by 3 days off

The recommended dosage modifications for adverse reactions are provided in Table 3.

Table 3: Recommended Dosage Modifications of TRUQAP for Adverse Reactions

Adverse Reaction	Severity*	TRUQAP Dosage Modification
Hyperglycemia [†] (Fasting Glucose [FG]) [see Warnings and Precautions (5.1)]	FG > ULN-160 mg/dL or FG > ULN-8.9 mmol/L or HbA1C > 7%	Consider initiation or intensification of oral anti-diabetic treatment.
	FG 161-250 mg/dL or FG 9-13.9 mmol/L	Withhold TRUQAP until FG decrease ≤ 160 mg/dL (or ≤ 8.9 mmol/L). If recovery occurs in ≤ 28 days, resume TRUQAP at same dose. If recovery occurs in > 28 days, resume TRUQAP at one lower dose.
	FG 251-500 mg/dL or FG 14-27.8 mmol/L	Withhold TRUQAP until FG decrease ≤ 160 mg/dL (or ≤ 8.9 mmol/L). If recovery occurs in ≤ 28 days, resume TRUQAP at one lower dose. If recovery occurs in > 28 days, permanently discontinue TRUQAP.
	FG > 500 mg/dL or FG > 27.8 mmol/L	Withhold TRUQAP. For life-threatening sequelae of hyperglycemia or if FG persists at ≥ 500 mg/dL after 24

	or life-threatening sequelae of hyperglycemia at any FG level	hours, permanently discontinue TRUQAP. If FG \leq 500 mg/dL (or \leq 27.8 mmol/L) within 24 hours, then follow the guidance in the table for the relevant grade
Diarrhea [see Warnings and Precautions (5.2)]	Grade 2	Withhold TRUQAP until recovery to \leq Grade 1. If recovery occurs in \leq 28 days, resume TRUQAP at same dose or one lower dose as clinically indicated. If recovery occurs in $>$ 28 days, resume at one lower dose as clinically indicated. For recurrence, reduce TRUQAP by one lower dose.
	Grade 3	Withhold TRUQAP until recovery to \leq Grade 1. If recovery occurs in \leq 28 days, resume TRUQAP at same dose or one lower dose as clinically indicated. If recovery occurs in $>$ 28 days, permanently discontinue TRUQAP.
	Grade 4	Permanently discontinue TRUQAP.
Cutaneous Adverse Reactions [see Warnings and Precautions (5.3)]	Grade 2	Withhold TRUQAP until recovery to \leq Grade 1. Resume TRUQAP at the same dose. Persistent or recurrent: reduce TRUQAP by one lower dose.
	Grade 3	Withhold TRUQAP until recovery to \leq Grade 1. If recovery occurs in \leq 28 days, resume TRUQAP at same dose. If recovery occurs in $>$ 28 days, resume TRUQAP at one lower dose. For recurrent Grade 3, permanently discontinue TRUQAP.
	Grade 4	Permanently discontinue TRUQAP.
Other Adverse Reactions [see Adverse Reactions (6.1)]	Grade 2	Withhold TRUQAP until recovery to \leq Grade 1. Resume TRUQAP at the same dose.
	Grade 3	Withhold TRUQAP until recovery to \leq Grade 1. If recovery occurs in \leq 28 days, resume TRUQAP at same dose. If recovery occurs in $>$ 28 days, resume TRUQAP at one lower dose.
	Grade 4	Permanently discontinue TRUQAP.

* Severity grading according to Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0.

† For the management of suspected or confirmed diabetic ketoacidosis (DKA) refer to section *Warnings and Precautions (5.1)*.

2.5 Dosage Modifications for Strong and Moderate CYP3A Inhibitors

Avoid concomitant use with strong CYP3A inhibitors. If concomitant use with a strong CYP3A inhibitor cannot be avoided, reduce the dosage of TRUQAP to 320 mg orally twice daily for 4 days followed by 3 days off [see *Drug Interactions (7.1)*].

When concomitantly used with a moderate CYP3A inhibitor, reduce the dosage of TRUQAP to 320 mg orally twice daily for 4 days followed by 3 days off.

After discontinuation of a strong or moderate CYP3A inhibitor, resume the TRUQAP dosage (after 3 to 5 half-lives of the inhibitor) that was taken prior to initiating the strong or moderate CYP3A inhibitor.

3 DOSAGE FORMS AND STRENGTHS

Tablets:

- 160 mg: beige film-coated, round, biconvex tablets debossed with 'CAV' above '160' on one side and plain on the reverse.
- 200 mg: beige film-coated, capsule-shaped, biconvex tablets debossed with 'CAV 200' on one side and plain on the reverse.

4 CONTRAINDICATIONS

TRUQAP is contraindicated in patients with severe hypersensitivity to TRUQAP or any of its components.

5 WARNINGS AND PRECAUTIONS

5.1 Hyperglycemia

Severe hyperglycemia, including diabetic ketoacidosis and fatal outcomes, can occur in patients treated with TRUQAP.

Increased fasting glucose from baseline occurred in 37% of patients treated with TRUQAP, including 11% of patients with Grade 2 (FG > 160 to 250 mg/dL), 2% with Grade 3 (FG > 250 to 500 mg/dL), and 1.1% with Grade 4 (FG > 500 mg/dL) events.

The median time to first occurrence of hyperglycemia was 15 days (range: 1 to 367). Dose reduction for hyperglycemia was required in 0.6% of patients and permanent discontinuation was required in 0.6% of patients.

Diabetic ketoacidosis occurred in 0.3% of patients and diabetic metabolic decompensation in 0.6% of patients.

In CAPItello-291, 12% (43/355) of patients who received TRUQAP had an anti-hyperglycemic medication regimen either initiated or changed during the study, including treatment with insulin in 4.8% (17/355) of patients.

The safety of TRUQAP has not been established in patients with Type I diabetes or diabetes requiring insulin. Patients with insulin-dependent diabetes were excluded from CAPItello-291.

Before initiating treatment with TRUQAP, test fasting glucose levels (FPG or FBG), HbA1C levels, and optimize fasting glucose.

After initiating treatment with TRUQAP, monitor or self-monitor fasting glucose levels on Day 3 or 4 of the dosing week during weeks 1, 2, 4, 6 and 8; then monthly while on

treatment with TRUQAP; and as clinically indicated. Monitor HbA1C levels every 3 months during treatment with TRUQAP and as clinically indicated. Patients with a history of well-controlled Type 2 diabetes mellitus may require intensified anti-hyperglycemic treatment and close monitoring of fasting glucose levels.

For patients who experience hyperglycemia during treatment with TRUQAP, monitor fasting glucose at least twice weekly, on days on and off TRUQAP, until fasting glucose decreases to baseline levels. During treatment with anti-diabetic medications, monitor fasting glucose at least once a week for 2 months, followed by once every 2 weeks, or as clinically indicated.

Consider consultation with a healthcare practitioner with expertise in the treatment of hyperglycemia and initiation of fasting glucose monitoring at home for patients who have risk factors for hyperglycemia or who experience hyperglycemia. Advise patients of the signs and symptoms of hyperglycemia and counsel patients on lifestyle changes.

Withhold TRUQAP immediately when ketoacidosis is suspected. If ketoacidosis is confirmed, permanently discontinue TRUQAP.

Based on the severity of the hyperglycemia, withhold, reduce dose, or permanently discontinue TRUQAP [see *Dosage and Administration (2.4)*].

5.2 Diarrhea

Severe diarrhea associated with dehydration occurred in patients who received TRUQAP.

Diarrhea occurred in 72% of patients. Grade 3 or 4 diarrhea occurred in 9% of patients. The median time to first occurrence was 8 days (range 1 to 519). In the 257 patients with diarrhea, 59% required anti-diarrheal medications to manage symptoms. Dose reductions were required in 8% of patients, and 2% of patients permanently discontinued TRUQAP due to diarrhea. In patients with Grade ≥ 2 diarrhea (n=93) with at least 1 grade improvement (n=89), median time to improvement from the first event was 4 days (range: 1 to 154).

Monitor patients for signs and symptoms of diarrhea. Advise patients to increase oral fluids and start antidiarrheal treatment at the first sign of diarrhea while taking TRUQAP. Withhold, reduce dose, or permanently discontinue TRUQAP based on severity [see *Dosage and Administration (2.4)*].

5.3 Cutaneous Adverse Reactions

Cutaneous adverse reactions, which can be severe, including erythema multiforme (EM), palmar-plantar erythrodysesthesia, and drug reaction with eosinophilia and systemic symptoms (DRESS), occurred in patients who received TRUQAP.

Cutaneous adverse reactions occurred in 58% of patients. Grade 3 or 4 cutaneous adverse reactions occurred in 17% of patients receiving TRUQAP. EM occurred in 1.7% of patients and DRESS occurred in 0.3% of patients. Dose reduction was required in 7% of patients and 7% of patients permanently discontinued TRUQAP due to cutaneous adverse reactions.

The median time to onset of cutaneous adverse reactions was 13 days (range 1 to 575 days). Among the 204 patients with cutaneous adverse reactions, 44% (90/204) required corticosteroid treatment. Of these, 37% (76/204) were treated with topical corticosteroids and 19% (39/204) with systemic corticosteroids. In patients with Grade

≥ 2 cutaneous adverse reaction (n= 116) with at least 1 grade improvement (n=104), median time to improvement from the first event was 12 days (range 2 to 544).

Monitor patients for signs and symptoms of cutaneous adverse reactions. Early consultation with a dermatologist is recommended. Withhold, reduce dose, or permanently discontinue TRUQAP based on severity [see *Dosage and Administration (2.4)*].

5.4 Embryo-Fetal Toxicity

Based on findings from animals and mechanism of action, TRUQAP can cause fetal harm when administered to a pregnant woman [see *Clinical Pharmacology (12.1)*]. In an animal reproduction study, oral administration of capivasertib to pregnant rats during the period of organogenesis caused adverse developmental outcomes, including embryo-fetal mortality, and reduced fetal weights at maternal exposures 0.7 times the human exposure (AUC) at the recommended dosage of 400 mg twice daily.

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

TRUQAP is used in combination with fulvestrant. Refer to the Full Prescribing Information of fulvestrant for pregnancy and contraception information.

6 ADVERSE REACTIONS

The following adverse reactions are also discussed in greater details in other sections of the labeling:

- Hyperglycemia [see *Warnings and Precautions (5.1)*]
- Diarrhea [see *Warnings and Precautions (5.2)*]
- Cutaneous Adverse Reactions [see *Warnings and Precautions (5.3)*]

6.1 Clinical Trials Experience

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

The safety population described in WARNINGS and PRECAUTIONS reflects exposure to TRUQAP 400 mg orally, twice a day for 4 days followed by 3 days off, in combination with fulvestrant, in 355 patients in CAPitello-291 until disease progression or unacceptable toxicity. Among the 355 patients who received TRUQAP, 52% were exposed for 6 months or longer, and 27% were exposed for greater than one year. In this safety population, the most common (≥ 20%) adverse reactions including laboratory abnormalities were diarrhea (72%), cutaneous adverse reactions (58%), increased random glucose (57%), decreased lymphocytes (47%), decreased hemoglobin (45%), increased fasting glucose (37%), nausea and fatigue (35% each), decreased leukocytes (32%), increased triglycerides (27%), decreased neutrophils (23%), increased creatinine (22%), vomiting (21%), and stomatitis (20%).

CAPitello-291

The safety of TRUQAP was evaluated in CAPitello-291, a clinical trial including 288 adult patients (155 patients in TRUQAP with fulvestrant arm and 133 patients in placebo with fulvestrant arm) whose breast cancer had one or more *PIK3CA/AKT1/PTEN*-alterations [see *Clinical Studies (14)*]. Among patients who received TRUQAP, 61% were exposed for 6 months or longer and 30% were exposed for greater than one year.

Of the 155 patients who received TRUQAP with fulvestrant, the median age was 58 years (range 36 to 84); female (99%); White (48%), Asian (31%), Black (1.3%), American Indian/Alaska Native (0.6%), and other races (19%).

Serious adverse reactions occurred in 18% of patients receiving TRUQAP with fulvestrant. The most common serious adverse reactions ($\geq 1\%$) were cutaneous adverse reaction (3.9%), diarrhea and pneumonia (2.6% each), vomiting and pyrexia (1.9% each), hyperglycemia, hypersensitivity, fatigue, renal injury and second malignancy (1.3% each).

Fatal adverse reactions occurred in 1.3% of patients who received TRUQAP with fulvestrant, including sepsis (0.6%), and acute myocardial infarction (0.6%).

Permanent TRUQAP discontinuation due to an adverse reaction occurred in 10% of patients. The most common adverse reaction ($\geq 2\%$) leading to permanent discontinuation of TRUQAP was cutaneous adverse reactions (6%). Dosage interruptions of TRUQAP due to an adverse reaction occurred in 39% of patients. Adverse reactions leading to dosage interruption in $\geq 2\%$ of patients included cutaneous adverse reactions (14%), diarrhea (10%), pyrexia (4.5%), vomiting and nausea (3.2% each), and fatigue (2.6%).

Dose reductions of TRUQAP due to adverse reactions occurred in 21% of patients receiving TRUQAP with fulvestrant. Adverse reactions leading to TRUQAP dose reductions in $\geq 2\%$ of patients were diarrhea and cutaneous adverse reactions (8% each).

The most common ($\geq 20\%$) adverse reactions including laboratory abnormalities were diarrhea (77%), increased random glucose (58%), cutaneous adverse reaction (56%), decreased lymphocytes (49%), decreased hemoglobin (47%), fatigue (38%), increased fasting glucose (37%), nausea and decreased leukocytes (35% each), increased triglycerides (30%), stomatitis (25%), decreased neutrophils (25%), and vomiting (21%). Adverse reactions and laboratory abnormalities are listed in Table 4 and Table 5, respectively.

Table 4: Adverse Reactions $\geq 10\%$ in Patients who Received TRUQAP with Fulvestrant [with a Difference Between Arms of $\geq 3\%$] in CAPitello-291

Adverse Reaction	TRUQAP with Fulvestrant N=155		Placebo with Fulvestrant N=133	
	All Grades %	Grade 3 or 4 %	All Grades %	Grade 3 or 4 %
Gastrointestinal Disorders				
Diarrhea	77	12	19	0.8
Nausea	35	1.3	14	0.8
Stomatitis*	25	1.9	5	0

Vomiting	21	1.9	7	0.8
Skin and Subcutaneous Tissue Disorders				
Cutaneous adverse reactions [†]	56	15	16	0.8
General Disorders and Administration Site Conditions				
Fatigue [*]	38	1.9	27	1.5
Metabolism and Nutrition Disorders				
Decreased appetite	17	0	8	0.8
Nervous System Disorders				
Headache [*]	17	0	13	0.8
Infections and Infestations				
Urinary tract infection [*]	14	0.6	5	0
Renal and Urinary disorders				
Renal injury [‡]	11	2.6	1.5	0.8

* Includes other related terms.

† Cutaneous adverse reaction includes butterfly rash, dermatitis, allergic dermatitis, dry skin, eczema, erythema multiforme, hand dermatitis, palmar-plantar erythrodysesthesia syndrome, pruritus, rash, erythematous rash, maculo-papular rash, papular rash, skin discoloration, skin fissures, skin reaction, skin ulcer, urticaria, purpura, erythema and drug eruption.

‡ Renal injury includes acute kidney injury, renal failure, renal impairment, glomerular filtration rate decreased, increased creatinine and proteinuria.

Clinically relevant adverse reactions occurring in < 10% of patients treated with TRUQAP included anemia, pyrexia, dysgeusia, dyspepsia, pneumonia, weight decreased, and hypersensitivity (including anaphylactic reaction).

Table 5: Laboratory Abnormalities (≥ 10%) That Worsened from Baseline in Patients who Received TRUQAP with Fulvestrant [With a Difference Between Arms ≥3%] in CAPItello-291

Laboratory Abnormality	TRUQAP with Fulvestrant [*]		Placebo with Fulvestrant [†]	
	All Grades (%)	Grade 3 or 4 (%)	All Grades (%)	Grade 3 or 4 (%)
Glucose Metabolism				
Increased random glucose	58	9	17	0
Increased fasting glucose	37	0.6	29	0
Hematology				
Decreased lymphocytes	49	11	14	2.3
Decreased hemoglobin	47	2	22	2.3
Decreased leukocytes	35	0.6	23	0
Decreased neutrophils	25	1.9	16	0.8
Decreased platelets	12	1.9	6	0.8

Other Categories				
Increased triglycerides	30	0.7	22	0.9
Increased alanine aminotransferase	23	2.6	13	0
Electrolytes/Renal				
Decreased corrected calcium	19	0.6	8	0
Increased creatinine	19	1.3	4.6	0.8
Decreased potassium	17	4.5	8	0

* The denominator used to calculate the rate varied from 129 to 155 based on the number of patients with a baseline value and at least one post-treatment value.

† The denominator used to calculate the rate varied from 109 to 131 based on the number of patients with a baseline value and at least one post-treatment value.

7 DRUG INTERACTIONS

7.1 Effects of Other Drugs on TRUQAP

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

Table 6: Drug Interactions with TRUQAP

Strong CYP3A Inhibitors	
Clinical Impact	<ul style="list-style-type: none"> • Capivasertib is a CYP3A substrate. Strong CYP3A inhibitors increase capivasertib exposure [see <i>Clinical Pharmacology (12.3)</i>], which may increase the risk of TRUQAP adverse reactions.
Prevention or Management	<ul style="list-style-type: none"> • Avoid concomitant use with a strong CYP3A inhibitor. If concomitant use cannot be avoided, reduce the dose of TRUQAP and monitor patients for adverse reactions [see <i>Dosage and Administration (2.5)</i>].
Moderate CYP3A Inhibitors	
Clinical Impact	<ul style="list-style-type: none"> • Capivasertib is a CYP3A substrate. Moderate CYP3A inhibitors increase capivasertib exposure [see <i>Clinical Pharmacology (12.3)</i>], which may increase the risk of TRUQAP adverse reactions.
Prevention or Management	<ul style="list-style-type: none"> • When concomitantly used with moderate CYP3A inhibitor, reduce the dose of TRUQAP and monitor patients for adverse reactions [see <i>Dosage and Administration (2.5)</i>].
Strong and Moderate CYP3A Inducers	
Clinical Impact	<ul style="list-style-type: none"> • Capivasertib is a CYP3A substrate. Strong and moderate CYP3A inducers decrease capivasertib exposure [see <i>Clinical Pharmacology</i>

	(12.3)], which may reduce the effectiveness of TRUQAP.
Prevention or Management	<ul style="list-style-type: none"> • Avoid concomitant use of TRUQAP with strong or moderate CYP3A inducers.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

TRUQAP is used in combination with fulvestrant. Refer to the Full Prescribing Information of fulvestrant for pregnancy information.

Based on findings in animals and mechanism of action, TRUQAP can cause fetal harm when administered to a pregnant woman [see *Clinical Pharmacology (12.1)*]. There are no available data on the use of TRUQAP in pregnant women. In an animal reproduction study, oral administration of capivasertib to pregnant rats during the period of organogenesis caused adverse developmental outcomes, including embryo-fetal mortality and reduced fetal weights at maternal exposures 0.7 times the human exposure (AUC) at the recommended dose of 400 mg twice daily (see *Data*). Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies in the U.S. general population.

Data

Animal Data

In an embryo-fetal development study, pregnant rats received oral doses of capivasertib up to 150 mg/kg/day during the period of organogenesis. Administration of capivasertib resulted in maternal toxicities (reduced body weight gain and food consumption, increased blood glucose) and adverse developmental outcomes, including embryo-fetal deaths (post-implantation loss), reduced fetal weights, and minor fetal visceral variations at a dose of 150 mg/kg/day (0.7 times the human exposure at the recommended dose of 400 mg twice daily based on AUC).

In a pre- and post-natal assessment, pregnant rats received oral doses of capivasertib up to 150 mg/kg/day from gestation day 6 through at least lactation day 6. Administration of 150 mg/kg/day resulted in reduced litter and pup weights.

8.2 Lactation

Risk Summary

TRUQAP is used in combination with fulvestrant. Refer to the Full Prescribing Information of fulvestrant for lactation information.

There are no data on the presence of capivasertib or its metabolites in human milk or their effects on milk production or the breastfed child. Capivasertib was detected in the

plasma of suckling rat pups (see *Data*). Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with TRUQAP.

Data

Animal Data

In a pre- and post-natal assessment, when capivasertib was administered to maternal rats during the lactation period, capivasertib was detected in plasma of suckling rat pups on lactation day 7 to 8 [see *Use in Specific Populations (8.1)*]. Plasma concentrations in pups were up to 0.6% of concentrations in maternal plasma in the 150 mg/kg/day group.

8.3 Females and Males of Reproductive Potential

TRUQAP is used in combination with fulvestrant. Refer to the Full Prescribing Information of fulvestrant for contraception and infertility information.

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

Pregnancy Testing

Verify pregnancy status of females of reproductive potential prior to initiating TRUQAP [see *Use in Specific Populations (8.1)*].

Contraception

Females

Advise females of reproductive potential to use effective contraception during treatment with TRUQAP and for 1 month after the last dose.

Males

Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TRUQAP and for 4 months after the last dose.

8.4 Pediatric Use

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

8.5 Geriatric Use

Of the 355 patients who received TRUQAP in CAPItello-291, 115 (32%) patients were \geq 65 years of age and 24 (7%) patients were \geq 75 years of age. No overall differences in the efficacy of TRUQAP were observed between patients \geq 65 years of age and younger patients. Analysis of the safety of TRUQAP comparing patients \geq 65 years of age to younger patients suggest a higher incidence of Grade 3 to 5 adverse reactions (57% versus 36%), dosage reductions (30% versus 15%), dose interruptions (57% versus 30%), and permanent discontinuations (23% versus 8%), respectively.

8.6 Renal Impairment

No dosage modification is recommended for patients with mild to moderate (creatinine clearance (CLcr) 30 to 89 mL/min) renal impairment [see *Clinical Pharmacology (12.3)*].

TRUQAP has not been studied in patients with severe (CLcr 15 to 29 mL/min) renal impairment.

8.7 Hepatic Impairment

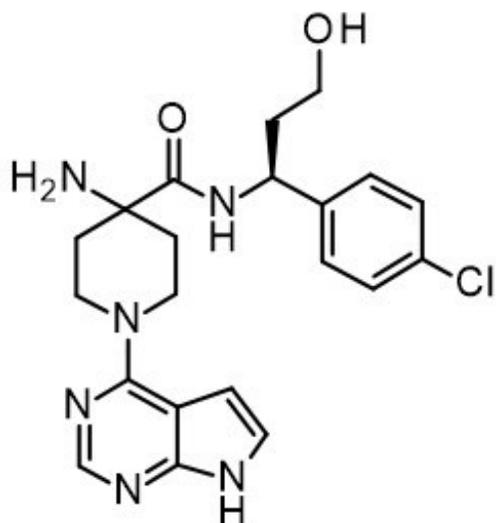
No dosage modification is recommended for patients with mild hepatic impairment (bilirubin \leq upper limit of normal (ULN) and AST $>$ ULN or bilirubin $>$ 1 to 1.5x ULN and any AST) [see *Clinical Pharmacology* (12.3)].

Monitor patients with moderate (bilirubin $>$ 1.5 to 3x ULN and any AST) hepatic impairment for adverse reactions due to potential increased capivasertib exposure [see *Warnings and Precautions* (5.1, 5.2, 5.3)].

TRUQAP has not been studied in patients with severe (bilirubin $>$ 3x ULN and any AST) hepatic impairment.

11 DESCRIPTION

TRUQAP (capivasertib) is a kinase inhibitor. The molecular formula for capivasertib is $C_{21}H_{25}ClN_6O_2$ and the molecular weight is 428.92 g/mol. The chemical name of capivasertib is 4-amino-*N*-[(1*S*)-1-(4-chlorophenyl)-3-hydroxypropyl]-1-(7*H*-pyrrolo[2,3-*d*]pyrimidin-4-yl)-4-piperidinecarboxamide. Capivasertib is a white to off-white powder with pH-dependent solubility. It is freely soluble in water at pH values below 1.2 and practically insoluble at pH values above 6.8. Capivasertib has the following structural formula:



TRUQAP film-coated tablets are supplied for oral administration with 160 mg or 200 mg capivasertib. The tablets also contain croscarmellose sodium, dibasic calcium phosphate, magnesium stearate, and microcrystalline cellulose. The film coat contains the following inactive ingredients: copovidone, hypromellose, iron oxide black, iron oxide red, iron oxide yellow, medium chain triglycerides, polydextrose, polyethylene glycol 3350, and titanium dioxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Capivasertib is an inhibitor of all 3 isoforms of serine/threonine kinase AKT (AKT1, AKT2 and AKT3) and inhibits phosphorylation of downstream AKT substrates. AKT activation in tumors is a result of activation of upstream signaling pathways, mutations in *AKT1*, loss of phosphatase and tensin homolog (PTEN) function and mutations in the catalytic subunit alpha of phosphatidylinositol 3-kinase (*PIK3CA*).

In vitro, capivasertib reduced growth of breast cancer cell lines including those with relevant *PIK3CA* or *AKT1* mutations or *PTEN* alteration. *In vivo*, capivasertib alone and in combination with fulvestrant inhibited tumor growth of mouse xenograft models including estrogen receptor positive breast cancer models with alterations in *PIK3CA*, *AKT1*, and *PTEN*.

12.2 Pharmacodynamics

Exposure-Response Relationships

The exposure-response relationship and time course of pharmacodynamic response for the effectiveness of capivasertib have not been fully characterized. Exposure-response relationships were observed for diarrhea (CTCAE Grade 2 to 4), rash (CTCAE Grade 2 to 4) and hyperglycemia (CTCAE Grades 3 or 4) at doses of 80 to 800 mg (0.2 to 2 times the approved recommended dosage).

Cardiac Electrophysiology

At the recommended TRUQAP dose, a mean increase in the QTc interval > 20 ms was not observed.

12.3 Pharmacokinetics

Capivasertib pharmacokinetic parameters are presented as the mean [%coefficient of variation (%CV)], unless otherwise specified. The capivasertib steady-state AUC is 8,069 h·ng/mL (37%) and C_{max} is 1,371 ng/mL (30%). Steady-state concentrations are predicted to be attained on the 3rd and 4th dosing day of each week, starting week 2.

Capivasertib plasma concentrations are approximately 0.5% to 15% of the steady state C_{max} during the off-dosing days.

Capivasertib AUC and C_{max} are proportional with dose over a range of 80 to 800 mg (0.2 to 2 times the approved recommended dosage).

Absorption

T_{max} is approximately 1-2 hours. The absolute bioavailability is 29%.

Effect of Food

No clinically meaningful differences in capivasertib pharmacokinetics were observed following administration of TRUQAP with a high-fat meal (approximately 1,000 kcal; fat 60%) or a low-fat meal (approximately 400 kcal; fat 26%).

Distribution

The steady state oral volume of distribution is 1,847 L (36%). Capivasertib plasma

protein binding is 78% and the plasma-to-blood ratio is 0.71.

Elimination

The half-life is 8.3 hours, and the steady-state oral clearance is 50 L/h (37% CV). Renal clearance was 21% of total clearance.

Metabolism

Capivasertib is primarily metabolized by CYP3A4 and UGT2B7.

Excretion

Following a single radiolabeled oral dose of 400 mg, the mean total recovery was 45% from urine and 50% from feces.

Specific Populations

No clinically significant differences in capivasertib pharmacokinetics were observed based on race/ethnicity (including White, Asian, Black, American Indian or Alaskan Native, and Native Hawaiian or Other Pacific Islander), sex (88% females), body weight (32 to 150 kg), age (26 to 87 years), mild hepatic impairment (bilirubin \leq ULN and AST $>$ ULN or bilirubin $>$ 1 to 1.5x ULN), or mild to moderate renal impairment (CLcr 30 to 89 mL/min).

The effect of moderate (bilirubin $>$ 1.5 to 3x ULN and any AST) hepatic impairment is not fully characterized.

TRUQAP has not been studied in patients with severe (bilirubin $>$ 3x ULN and any AST) hepatic impairment or severe renal impairment (CLcr 15 to 29 mL/min).

Drug Interaction Studies

Clinical Studies and Model-Informed Approaches

Effect of Strong and Moderate CYP3A Inhibitors on Capivasertib: Itraconazole (strong CYP3A4 inhibitor) is predicted to increase capivasertib AUC by up to 1.7-fold and C_{max} by up to 1.4-fold.

Erythromycin and verapamil (moderate CYP3A inhibitors) are predicted to increase capivasertib AUC by up to 1.5-fold and C_{max} by up to 1.3-fold.

Effect of Strong and Moderate CYP3A Inducers on Capivasertib: Rifampicin (strong CYP3A4 inducer) is predicted to decrease capivasertib AUC by 70% and C_{max} by 60%.

Efavirenz (moderate CYP3A4 inducer) is predicted to decrease capivasertib AUC by 60% and C_{max} by 50%.

Effect of UGT2B7 Inhibitors on Capivasertib: Probenecid (UGT2B7 inhibitor) is not predicted to have a clinically meaningful effect on capivasertib pharmacokinetics.

Effect of Acid Reducing Agents on Capivasertib: Rabeprazole (gastric acid reducing agent) did not have a clinically meaningful effect on capivasertib pharmacokinetics.

Effect of Capivasertib on CYP3A Substrates: Concomitant use of TRUQAP increased midazolam (CYP3A substrate) AUC by 1.8-fold on day 4 and by 1.2-fold on day 7.

Effect of Capivasertib on CYP2D6 Substrates: TRUQAP is predicted to increase desipramine (CYP2D6 substrate) AUC by up to 2.1-fold on day 4.

Effect of Capivasertib on CYP2C9 Substrates: Concomitant use of TRUQAP with warfarin (CYP2C9 substrate) is not predicted to have a clinically meaningful effect on warfarin pharmacokinetics.

Effect of Capivasertib on UGT1A1 Substrates: TRUQAP is predicted to increase raltegravir (UGT1A1 substrate) AUC by up to 1.7-fold on day 4.

In-Vitro Studies

Capivasertib inhibits BCRP, OATP1B1, OATP1B3, OAT3, MATE1, MATE2-K, and OCT2.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

In a 2-year rat carcinogenicity study, rats received oral doses up to 30 mg/kg/day in males and 75 mg/kg/day in females (approximately 0.2 times and 0.4 times the human exposure at the recommended dose based on AUC, respectively). While there were no statistically significant increases in tumors, there was an increase in malignant mesothelioma in the testis of male rats at 30 mg/kg/day, which is considered a rare tumor in the tested rat strain.

Capivasertib was genotoxic in the in vivo rat bone marrow micronucleus assay through an aneugenic mechanism. Capivasertib was not mutagenic in vitro in a bacterial reverse mutation (Ames) assay or mouse lymphoma gene mutation assay.

In repeat-dose toxicity studies up to 26 weeks duration in rats and 39 weeks duration in dogs, tubular degeneration in the testes and cellular debris in the epididymides were observed at oral capivasertib doses of 100 mg/kg/day in rats and 15 mg/kg/day in dogs (approximately 1 time the human exposure at the recommended dose of 400 mg twice daily based on AUC). In a male fertility study, capivasertib had no effect on fertility in male rats at oral doses up to 100 mg/kg/day following 10 weeks of treatment. Effects of capivasertib on female fertility have not been studied in animals.

13.2 Animal Toxicology and/or Pharmacology

Oral administration of capivasertib for up to 2 years resulted in islet of Langerhans hypertrophy/ hyperplasia in the pancreas and lens degeneration in rats at doses ≥ 15 mg/kg/day (≥ 0.1 times the human exposure at the recommended dose based on AUC).

14 CLINICAL STUDIES

The efficacy of TRUQAP with fulvestrant was evaluated in CAPItello-291 (NCT04305496), a randomized, double-blind, placebo-controlled, multicenter trial that enrolled 708 adult patients with locally advanced (inoperable) or metastatic HR-positive, HER2-negative (defined as IHC 0 or 1+, or IHC 2+/ISH-) breast cancer of which 289 patients had tumors with eligible *PIK3CA/AKT1/PTEN*-alterations. Eligible *PIK3CA/AKT1* activating mutations or *PTEN* loss of function alterations were identified in the majority of FFPE tumor specimens using FoundationOne®CDx next-generation sequencing (n=686). All patients were required to have progression on an aromatase inhibitor (AI) based treatment in the metastatic setting or recurrence on or within 12 months of completing (neo) adjuvant treatment with an AI. Patients could have received up to two prior lines of

endocrine therapy and up to 1 line of chemotherapy for locally advanced (inoperable) or metastatic disease. Patients were excluded if they had clinically significant abnormalities of glucose metabolism (defined as patients with diabetes mellitus Type 1, Type 2, requiring insulin treatment, or HbA1c $\geq 8\%$ (63.9 mmol/mol)).

Patients were randomized (1:1) to receive either 400 mg of TRUQAP (n=355) or placebo (n=353), given orally twice daily for 4 days followed by 3 days off treatment each week of 28-day treatment cycle. Fulvestrant 500 mg intramuscular injection was administered on cycle 1 days 1 and 15, and then at day 1 of each subsequent 28-day cycle. Patients were treated until disease progression, or unacceptable toxicity. Randomization was stratified by presence of liver metastases (yes vs. no), prior treatment with CDK4/6 inhibitors (yes vs. no) and geographical region (region 1: US, Canada, Western Europe, Australia, and Israel vs region 2: Latin America, Eastern Europe and Russia vs Region 3: Asia).

The major efficacy outcomes were investigator-assessed progression-free survival (PFS) in the overall population, and in the population of patients whose tumors have *PIK3CA/AKT1/PTEN*-alterations evaluated according to Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1. Additional efficacy outcome measures were overall survival (OS), investigator assessed objective response rate (ORR) and duration of response (DoR).

A statistically significant difference in PFS was observed in the overall population and the population of patients whose tumors have *PIK3CA/AKT1/PTEN*-alteration. An exploratory analysis of PFS in the 313 (44%) patients whose tumors did not have a *PIK3CA/AKT1/PTEN*-alteration showed a HR of 0.79 (95% CI: 0.61, 1.02), indicating that the difference in the overall population was primarily attributed to the results seen in the population of patients whose tumors have *PIK3CA/AKT1/PTEN*-alteration.

Of the 289 patients whose tumors were *PIK3CA/AKT1/PTEN*-altered, the median age was 59 years (range 34 to 90); female (99%); White (52%), Asian (29%), Black (1%), American Indian/Alaska Native (0.7%), other races (17%) and 9% were Hispanic/Latino. Eastern Cooperative Oncology Group (ECOG) performance status was 0 (66%) or 1 (34%), and 18% were premenopausal or perimenopausal. Seventy-six percent of patients had an alteration in *PIK3CA*, 13% had an alteration in *AKT1*, and 17% had an alteration in *PTEN*. All patients received prior endocrine-based therapy (100% AI based treatment and 44% received tamoxifen). Seventy-one percent of patients were previously treated with a CDK4/6 inhibitor and 18% received prior chemotherapy for locally advanced (inoperable) or metastatic disease.

Efficacy results for *PIK3CA/AKT1/PTEN*-altered subgroup are presented in Table 7 and Figure 1. Results from the blinded independent review committee (BICR) assessment were consistent with the investigator assessed PFS results. Overall survival results were immature at the time of the PFS analysis (30% of the patients died).

Table 7: Efficacy Results for CAPItello-291 (Patients with *PIK3CA/AKT1/PTEN*-Altered Tumors)

	TRUQAP with fulvestrant N=155	Placebo with fulvestrant N=134
Investigator-Assessed Progression-Free Survival (PFS)		
	121 (78%)	115 (86%)

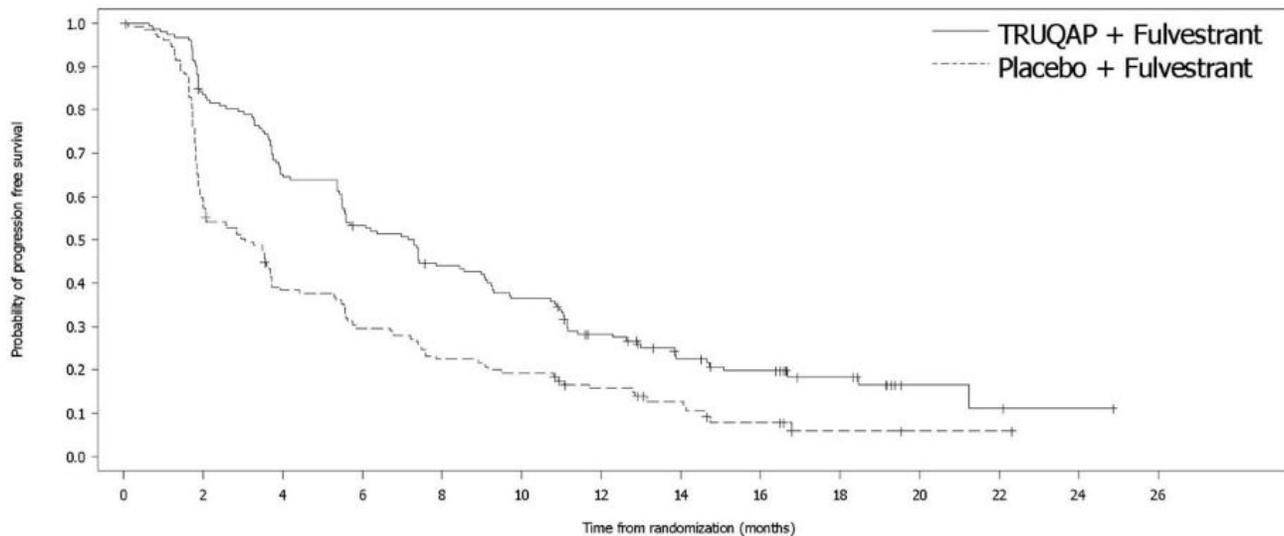
Number of events (%)		
Median, months (95%CI)	7.3 (5.5, 9.0)	3.1 (2.0, 3.7)
Hazard ratio (95% CI)*	0.50 (0.38, 0.65)	
p-value†	<0.0001	
Investigator-Assessed Confirmed Objective Response Rate (ORR)		
Patients with measurable disease	132	124
ORR (95% CI)	26% (19, 34)	8% (4, 14)
Complete response rate	2.3%	0
Partial response rate	23%	8%
Median DoR, months (95%CI)	10.2 (7.7, NC‡)	8.6 (3.8, 9.2)

* Stratified Cox proportional hazards model stratified by presence of liver metastases (yes vs no), and prior use of CDK4/6 inhibitors (yes vs no).

† Stratified log-rank test stratified by presence of liver metastases (yes vs no), and prior use of CDK4/6 inhibitors (yes vs no).

‡ NC = not calculable

Figure 1: Kaplan-Meier Plot of Progression-Free Survival in CAPItello-291 (Investigator Assessment, Patients with *PIK3CA*/*AKT1*/*PTEN*-Altered Tumors)



	Number of patients at risk													
TRUQAP + Fulvestrant	155	127	99	80	65	54	38	26	21	12	3	2	1	0
Placebo + Fulvestrant	134	77	48	37	28	24	17	11	6	2	1	1	0	0

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Table 8: TRUQAP 160 mg and 200 mg Tablets

Strength	Description	Package Size and Type	NDC Number
TRUQAP 160 mg	Beige film-coated, round, biconvex tablets debossed with 'CAV' above '160' on one side and plain on the reverse supplied in HDPE bottle with child-resistant closure.	Bottle of 64 tablets	0310-9500-01
TRUQAP 200 mg	Beige film-coated, capsule-shaped, biconvex tablets debossed with 'CAV 200' on one side and plain on the reverse supplied in HDPE bottle with child-resistant closure.	Bottle of 64 tablets	0310-9501-01
TRUQAP 160 mg	Beige film-coated, round, biconvex tablets debossed with 'CAV' above '160' on one side and plain on the reverse supplied in a blister with a child-resistant closure.	Each carton has 4 blister packs (64 tablets total)-each blister pack contains 16 tablets.	0310-9500-02

TRUQAP 200 mg	Beige film-coated, capsule-shaped, biconvex tablets debossed with 'CAV 200' on one side and plain on the reverse supplied in a blister with a child-resistant closure.	Each carton has 4 blister packs (64 tablets total)-each blister pack contains 16 tablets.	0310-9501-02
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Storage and Handling

Store TRUQAP in original packaging to maintain stability at 20°C to 25°C (68°F to 77°F). Excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

Dispense bottled TRUQAP tablets either in:

- The original bottle.
- A USP equivalent tight container. Instruct patients to keep the unused tablets in the container at 20°C to 25°C (68°F to 77°F) and discard after 45 days.

17 PATIENT COUNSELING INFORMATION

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

Hyperglycemia

Advise patients that TRUQAP can cause hyperglycemia and that they will need to monitor their fasting blood glucose periodically during therapy. Advise patients to contact their healthcare provider immediately for signs and symptoms of hyperglycemia (e.g., excessive thirst, urinating more often, blurred vision, mental confusion, difficulty breathing, or increased appetite with weight loss) or ketoacidosis [see *Warnings and Precautions (5.1)*].

Diarrhea

Advise patients that TRUQAP can cause diarrhea and to start antidiarrheal treatment, increase oral fluids, and notify their healthcare provider if diarrhea occurs while taking TRUQAP [see *Warnings and Precautions (5.2)*].

Cutaneous Adverse Reactions

Advise patients that TRUQAP can cause cutaneous adverse reactions and to contact their healthcare provider immediately to report new or worsening rash, erythematous and exfoliative skin reactions [see *Warnings and Precautions (5.3)*].

Embryo-Fetal Toxicity

- Advise females to inform their healthcare provider of a known or suspected pregnancy [see *Warnings and Precautions (5.4) and Use in Specific Populations (8.1)*]. Advise pregnant women and females of reproductive potential of the potential risk to a fetus.
- Advise females of reproductive potential to use effective contraception during treatment with TRUQAP and for 1 month after the last dose [see *Use in Specific Population (8.3)*].

- Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TRUQAP and for 4 months after the last dose [see *Use in Specific Populations (8.3)*].
- Refer to the Full Prescribing Information of fulvestrant for pregnancy and contraception information.

Lactation

Advise women to not breastfeed during treatment with TRUQAP [see *Use in Specific Populations (8.2)*]. Refer to the Full Prescribing Information of fulvestrant for lactation information.

Dosing Instructions

Instruct patients to take TRUQAP 2 times each day, at about the same times each day, for four days on and 3 days off, with or without food. Swallow the tablet(s) whole with water. Tablets should not be chewed, crushed, or split prior to swallowing. [see *Dosage and Administration (2.3)*].

Instruct patients that if the dose is missed, it can be taken within 4 hours after the time it is usually taken. If more than 4 hours has passed, skip the dose. Take the next dose at the usual time.

Instruct patients that if they vomit after taking the dose, an additional dose should not be taken. The next dose of TRUQAP should be taken at the usual time [see *Dosage and Administration (2.3)*].

Drug Interactions

Advise patients to inform their healthcare providers of all concomitant medications, including prescription medicines, over-the-counter medications, vitamins, and herbal products [see *Drug Interactions (7.1)*].

Grapefruit may interact with TRUQAP. Patients should not consume grapefruit products while taking TRUQAP.

Distributed by:

AstraZeneca Pharmaceuticals LP

Wilmington, DE 19850

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Patient Package Insert

<p style="text-align: center;">PATIENT INFORMATION TRUQAP® (TRUE-cap) (capiwasertib) tablets</p>
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What is TRUQAP?

TRUQAP is a prescription medicine used in combination with the medicine fulvestrant to treat adults who have hormone receptor (HR)-positive, human epidermal growth factor

receptor 2 (HER2)-negative breast cancer that is advanced or that has spread to other parts of the body (metastatic), with an abnormal “*PIK3CA*”, “*AKT1*”, or “*PTEN*” gene, and whose disease has progressed on or after endocrine therapy.

Your healthcare provider will test your cancer for an abnormal “*PIK3CA*”, “*AKT1*”, or “*PTEN*” gene to make sure that TRUQAP is right for you.

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

Do not take TRUQAP if you:

Have had a severe allergic reaction to TRUQAP or are allergic to any of the ingredients of TRUQAP. See the end of this leaflet for a list of the ingredients in TRUQAP.

Before you take TRUQAP, tell your healthcare provider about all of your medical conditions, including if you:

- have a history of high levels of sugar in your blood or diabetes.
- have a history of rash or other skin disorders.
- have liver problems.
- have any current infection.
- are pregnant or plan to become pregnant. TRUQAP can harm your unborn baby.

Females who are able to become pregnant:

- Your healthcare provider will check to see if you are pregnant before you start treatment with TRUQAP.
- You should use effective birth control during treatment with TRUQAP and for 1 month after the last dose. Talk to your healthcare provider about birth control methods that may be right for you during this time.
- If you become pregnant or think you are pregnant, tell your healthcare provider right away.

Males with female partners who are able to become pregnant should use effective birth control during your treatment with TRUQAP and for 4 months after the last dose. If your female partner becomes pregnant, tell your healthcare provider right away.

- are breastfeeding or plan to breastfeed. Do not breastfeed during treatment with TRUQAP. Talk to your healthcare provider about the best way to feed your baby during treatment with TRUQAP.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. TRUQAP may affect the way other medicines work, and other medicines may affect how TRUQAP works.

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

How should I take TRUQAP?

- Take TRUQAP exactly as your healthcare provider tells you.
- Do not change your dose or stop taking TRUQAP unless your healthcare provider tells you.
- Take TRUQAP 2 times each day (about 12 hours apart) in the morning and evening, at about the same times each day.
- Take TRUQAP for 4 days in a row, followed by 3 days not taking TRUQAP each week.
- Take TRUQAP with or without food.

- Swallow TRUQAP tablets whole with water. Do not chew, crush, or split the tablets.
- Do not take any tablets that are broken, cracked, or that look damaged.
- If you miss a dose of TRUQAP, you may still take it within 4 hours from the time you usually take it. If it has been more than 4 hours after you usually take your dose, skip that dose. Take the next dose at your usual time. Do not take 2 doses at the same time to make up for a missed dose.
- If you vomit after taking a dose of TRUQAP, do not take an additional dose. Take your next dose at your usual time.
- For women who have not reached menopause or are just starting menopause, your healthcare provider will prescribe a medicine called a luteinizing hormone-releasing hormone (LHRH) agonist to take with TRUQAP and fulvestrant. For men, your healthcare provider may prescribe a LHRH agonist to take with TRUQAP and fulvestrant.

What are the possible side effects of TRUQAP?

TRUQAP may cause severe side effects, including:

- **High blood sugar levels (hyperglycemia)** - Hyperglycemia is common with TRUQAP and may be severe. Untreated severe hyperglycemia can lead to a condition called diabetic ketoacidosis that can happen in people treated with TRUQAP. Diabetic ketoacidosis is a serious condition that requires treatment in a hospital and that can lead to death. Your healthcare provider will monitor your blood sugar levels before you start and during treatment with TRUQAP. It is not known if TRUQAP is safe in people with type 1 diabetes or people who use insulin to treat their diabetes. Your healthcare provider will monitor your blood sugar levels more often if you have a history of diabetes. Tell your healthcare provider right away if you develop symptoms of hyperglycemia,:
 - excessive thirst
 - dry mouth
 - more frequent urination than usual or a bigger amount of urine than normal
 - blurred vision
 - increased appetite with weight loss
 - stomach area (abdominal) pain
 - unusual tiredness
 - confusion
 - nausea
 - vomiting
 - fruity odor on breath
 - dry or flushed skin
 - difficulty breathing
 - sleepiness
- **Diarrhea.** Diarrhea is common during treatment with TRUQAP and may be severe. Severe diarrhea can lead to the loss of too much body water (dehydration). Tell your healthcare provider if you develop any signs of diarrhea, including loose or watery stool. Your healthcare provider will tell you to drink more fluids or take medicines to treat diarrhea.
- **Skin reactions.** Skin reactions are common with TRUQAP and can be severe. Tell your healthcare provider or get medical help right away if you get a new or worsening rash, reddening of the skin, fever, blistering of the lips, eyes or mouth, blisters on the skin, skin peeling, or dry skin.

Your healthcare provider may tell you to decrease your dose, temporarily stop your treatment, or completely stop your treatment with TRUQAP if you get certain serious

side effects.

The most common side effects of TRUQAP include:

- nausea
- tiredness
- vomiting
- mouth sores
- changes in certain blood tests

These are not all of the possible side effects of TRUQAP. Call your healthcare provider for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

What should I avoid while taking TRUQAP?

- You should not drink grapefruit juice or eat grapefruit during treatment with TRUQAP.

How should I store TRUQAP?

- Store TRUQAP in original packaging at room temperature between 68°F to 77°F (20°C to 25°C).
- Throw away (discard) TRUQAP after 45 days if the tablets are not kept in the original packaging.
- TRUQAP comes in child resistant packaging.

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

General information about the safe and effective use of TRUQAP.

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

What are the ingredients in TRUQAP?

Active ingredient: capivasertib.

Inactive ingredients: copovidone, croscarmellose sodium, dibasic calcium phosphate, hypromellose, iron oxide black, iron oxide red, iron oxide yellow, magnesium stearate, medium chain triglycerides, microcrystalline cellulose, polydextrose, polyethylene glycol 3350, and titanium dioxide

Distributed by:

AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850

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

PRINCIPAL DISPLAY PANEL - 160mg tablets

Rx Only NDC 03109500-01

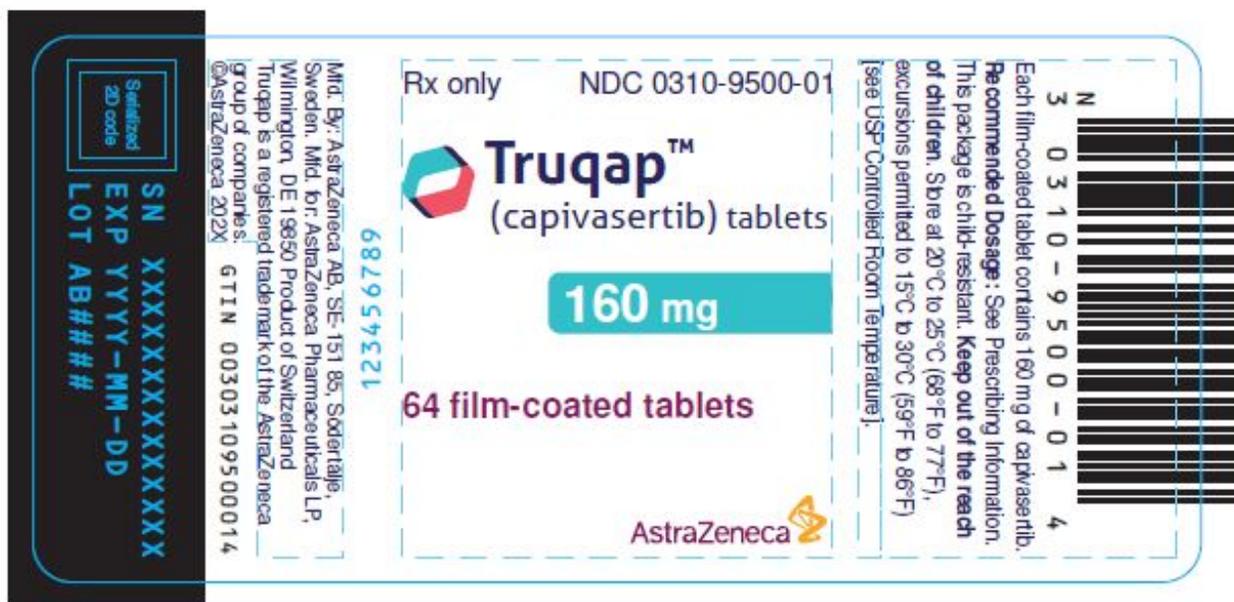
TRUQAP™

(capivasertib) tablets

160mg

64 film-coated tablets

AstraZeneca



PRINCIPAL DISPLAY PANEL - 200mg tablet

Rx only NDC 0310-9501-01

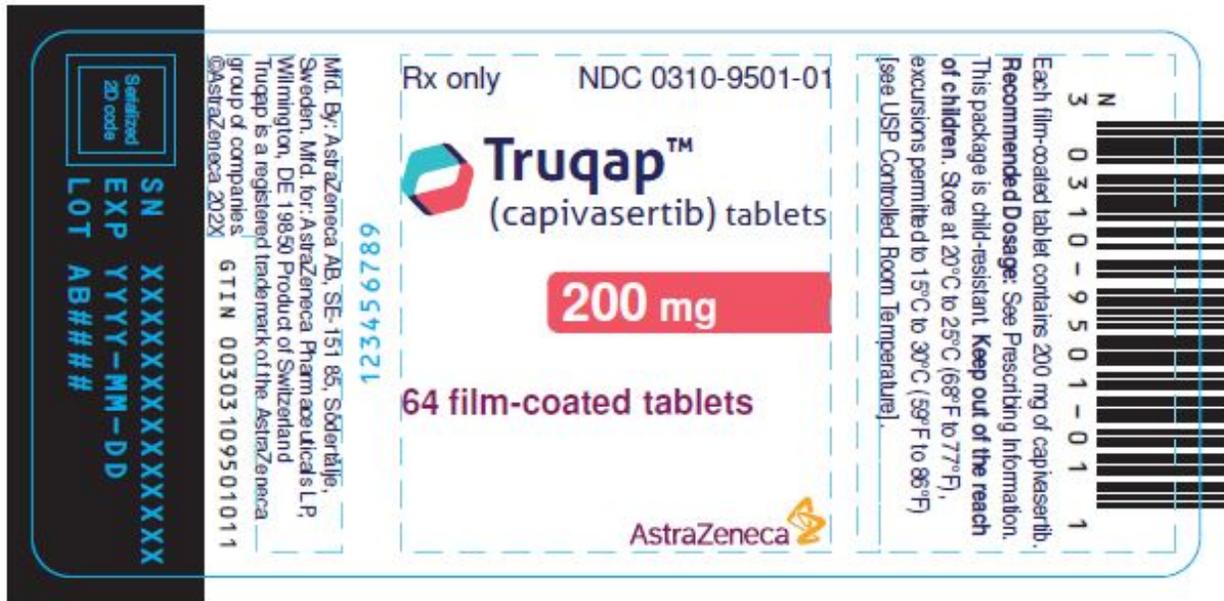
TRUQAP™

(capivasertib) tablets

200mg

64 film-coated tablets

AstraZeneca



TRUQAP

capiwasertib tablet, film coated

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:0310-9500
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CAPIVASERTIB (UNII: WFR23M21IE) (CAPIVASERTIB - UNII: WFR23M21IE)	CAPIVASERTIB	160 mg

Inactive Ingredients

Ingredient Name	Strength
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
ANHYDROUS DIBASIC CALCIUM PHOSPHATE (UNII: L11K75P92J)	
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
HYPROMELLOSE, UNSPECIFIED (UNII: 3NXW29V3WO)	
COPOVIDONE K25-31 (UNII: D9C330MD8B)	
POLYETHYLENE GLYCOL 3350 (UNII: G2M7P15E5P)	
POLYDEXTROSE (UNII: VH2XOU12IE)	
MEDIUM-CHAIN TRIGLYCERIDES (UNII: C9H2L21V7U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	
FERRIC OXIDE RED (UNII: 1K09F3G675)	
FERROSFERRIC OXIDE (UNII: XM0M87F357)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics

Color	BROWN (Beige)	Score	no score
Shape	ROUND (Biconvex)	Size	10mm
Flavor		Imprint Code	CAV;160
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0310-9500-01	64 in 1 BOTTLE; Type 0: Not a Combination Product	11/16/2023	
2	NDC:0310-9500-02	4 in 1 CARTON	10/18/2024	
2		16 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA218197	11/16/2023	

TRUQAP

capivasertib tablet, film coated

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:0310-9501
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
CAPIVASERTIB (UNII: WFR23M21IE) (CAPIVASERTIB - UNII:WFR23M21IE)	CAPIVASERTIB	200 mg

Inactive Ingredients

Ingredient Name	Strength
MICROCRYSTALLINE CELLULOSE (UNII: OP1R32D61U)	
ANHYDROUS DIBASIC CALCIUM PHOSPHATE (UNII: L11K75P92J)	
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
HYPROMELLOSE, UNSPECIFIED (UNII: 3NXW29V3WO)	
COPOVIDONE K25-31 (UNII: D9C330MD8B)	
POLYETHYLENE GLYCOL 3350 (UNII: G2M7P15E5P)	

POLYDEXTROSE (UNII: VH2XOU12IE)	
MEDIUM-CHAIN TRIGLYCERIDES (UNII: C9H2L21V7U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	
FERRIC OXIDE RED (UNII: 1K09F3G675)	
FERROSFERRIC OXIDE (UNII: XM0M87F357)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics

Color	BROWN (Beige)	Score	no score
Shape	CAPSULE (Biconvex)	Size	14mm
Flavor		Imprint Code	CAV200
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0310-9501-01	64 in 1 BOTTLE; Type 0: Not a Combination Product	11/16/2023	
2	NDC:0310-9501-95	64 in 1 BOTTLE; Type 0: Not a Combination Product	02/01/2024	10/28/2024
3	NDC:0310-9501-02	4 in 1 CARTON	10/18/2024	
3		16 in 1 BLISTER PACK; Type 0: Not a Combination Product		
4	NDC:0310-9501-96	4 in 1 CARTON	10/23/2024	
4		16 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA218197	11/16/2023	

Labeler - AstraZeneca Pharmaceuticals LP (054743190)

Revised: 11/2025

AstraZeneca Pharmaceuticals LP