Drug Monograph

A - Drug Name

capivasertib

COMMON TRADE NAME(S): Truqap™

back to top

B - Mechanism of Action and Pharmacokinetics

Capivasertib is an inhibitor of all 3 isoforms of serine/threonine kinase AKT (AKT1, AKT2 and AKT3) and blocks the AKT signaling pathway. This inhibits phosphorylation of downstream AKT substrates involved in cellular processes, such as cell division, apoptosis, and glucose and fatty acid metabolism. Capivasertib reduced the growth of various cancer cell lines in vitro and inhibited tumour growth in vivo for ER+ breast cancer models with or without PIK3CA, AKT1, or PTEN alterations.

Absorption	Bioavailability	29%
	Peak plasma levels	~1-2 hours after administration
	Effects with food	No clinically significant effect on exposure when given with food. AUC_T and C_{max} increased by up to 33% and 23%, respectively, depending on the fat and calorie content of the meal. A delay in T_{max} of 1 hour was also observed under fed conditions.
	Time to reach steady state	Every 3rd and 4th dosing day of each week, starting from week 2
Distribution	PPB	78%

Metabolism	Capivasertib is mainly metabolized by CYP3A4 and UGT2B7 enzymes.	
Elimination	Urine	45%
	Feces	50%
	Half-life	~8 hours
	Clearance	21%

back to top

C - Indications and Status

Health Canada Approvals:

- Breast cancer

Refer to the product monograph for a full list and details of approved indications

back to top

D - Adverse Effects

Emetogenic Potential: Low – No routine prophylaxis; PRN recommended

The following table lists adverse effects that occurred in ≥ 2% of patients with HR positive, HER2-negative advanced or metastatic breast cancer treated with capivasertib and fulvestrant versus placebo and fulvestrant in a phase 3 study. It also includes severe, life-threatening and post-marketing adverse effects from other sources.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Dermatological	Erythema multiforme (2%)	E
	Hand-foot syndrome	E
	Rash (47%) (17% severe)	E D L
Gastrointestinal	Anorexia (11%)	E

	Diarrhea (67%) (9% severe)	E
	Dry mouth (4%)	E
	Dyspepsia (3%)	E
	Mucositis (16%) (2% severe)	E
	Nausea, vomiting (27%) (1% severe)	E
General	Fatigue (22%)	E
	Fever (6%)	E
Hematological	Anemia (4%)	E
Hypersensitivity	DRESS syndrome (<1%)	E
	Hypersensitivity (<1%)	I E
Metabolic / Endocrine	Glucose intolerance (<1%)	E
	Hyperglycemia (14%) (2% severe)	E D
	↓ K (2%)	E
	Other (<1%) Diabetic ketoacidosis	E
Nervous System	Dysgeusia (6%)	E
	Headache (5%)	E
Renal	Creatinine increased (3%)	E
	Other (1%) Acute kidney injury	E

* "*Incidence*" may refer to an absolute value or the higher value from a reported range.
"*Rare*" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
D = *delayed* (weeks to months) L = *late* (months to years)

The most common side effects for capivasertib include diarrhea, rash, nausea/vomiting, fatigue, mucositis, hyperglycemia, and anorexia.

Severe **hyperglycemia**, including diabetic ketoacidosis (fatal in some cases), has been observed in patients treated with capivasertib. Comorbidities and concurrent treatments (e.g., dehydration, malnourishment, chemotherapy/steroids, sepsis) may increase the risk of progression from hyperglycemia to diabetic ketoacidosis, which can occur at any time during treatment with capivasertib. Among patients who experienced hyperglycemia, 12% were treated with insulin and 32% with metformin.

Severe **diarrhea** associated with dehydration and/or acute kidney injury was observed in patients treated with capivasertib. Coadministration with metformin may increase the frequency of diarrhea. Among patients who experienced diarrhea, 58% required antidiarrheal medications to manage symptoms.

Cutaneous adverse reactions were reported in patients treated with capivasertib, including severe reactions such as erythema multiforme (EM), palmar-plantar erythrodyesthesia and drug reaction with eosinophilia and systemic symptoms (DRESS). Among patients who experienced cutaneous adverse reactions, 39% were treated with topical corticosteroids and 22% with systemic steroids. Early consultation with a dermatologist is recommended.

back to top

E - Dosing

Refer to protocol by which the patient is being treated.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Presence of one or more PIK3CA/AKT1/PTEN genetic alterations in patients with hormone receptor (HR) positive, HER2-negative advanced breast cancer should be confirmed by a validated test prior to starting treatment with capivasertib.

Control and correct abnormal glucose levels before starting treatment.

Patients should be advised to increase oral fluids and start antidiarrheal treatment at the first sign of diarrhea while on treatment.

Adults:

Oral: 400 mg BID for 4 days, followed by 3 days off each week.

- Capivasertib should be co-administered with fulvestrant, refer to the fulvestrant Product Monograph for more information.
- Pre/perimenopausal women, or men, should also be treated with luteinizing hormone-releasing hormone (LHRH) agonists according to local clinical practice.

Refer to Interactions section for dosing recommendations when co-administered with **strong or moderate CYP3A4 inhibitors**.

Dosage with Toxicity:

Dose level	Capivasertib dose (mg, twice daily)*
0	400
-1	320
-2	200
-3	Discontinue

*Administered for 4 days, followed by 3 days off each week.

Toxicity	Severity/Grade	Action
Hyperglycemia§†	Grade 1 Fasting Glucose (FG) >ULN - 8.9 mmol/L or HbA1C >7%	No dose adjustment required. Consider initiating or intensifying oral anti-diabetic treatment.
	Grade 2 FG >8.9 - 13.9 mmol/L	Continue capivasertib and initiate/increase oral anti-diabetic. If no improvement to Grade ≤1, hold*. • If improvement in ≤28 days: Restart at same dose. • If improvement in >28 days: Restart at 1 dose level ↓.
	Grade 3 FG >13.9 - 27.8 mmol/L	Hold.* Consult with an expert. Start or optimize anti-diabetic treatment as clinically indicated, according to local guidelines. • If improvement in ≤28 days: Restart at 1 dose level ↓. • If improvement in >28 days: Discontinue.
	Grade 4 FG >27.8 mmol/L	Hold. Consult with an expert. Start or optimize anti-diabetic treatment as clinically indicated,

			according to local guidelines. • If FG improved to ≤ grade 3 within 24 hours after management, follow guidance for relevant grade. • If grade 4 after 24 hours despite management, discontinue.
		Life-threatening sequelae	Discontinue.
		Diabetic Ketoacidosis	Hold and investigate for any symptoms; discontinue if confirmed.
	Diarrhea	Grade 2	Hold.* Initiate or intensify anti-diarrheal treatment and monitor as clinically indicated. • If improvement in ≤28 days: Restart at same dose or 1 dose level ↓. • If improvement in >28 days or recurrent: Restart at 1 dose level ↓.
		Grade 3	Hold.* Initiate or intensify anti-diarrheal treatment and monitor as clinically indicated. • If improvement in ≤28 days: Restart at 1 dose level ↓. • If improvement in >28 days: Discontinue.
		Grade 4	Discontinue.
	Cutaneous Adverse Reactions	Grade 2	Start or increase topical steroid treatment. Optimize non-sedating antihistamine treatment. If no improvement, hold capivasertib. Resume at same dose once rash is clinically tolerable.
		Grade 3	Hold.* Manage appropriately (e.g. topical steroid of moderate/higher strength, non-sedating oral antihistamines, and/or systemic steroids). • If improvement in ≤28 days: Restart at 1 dose level ↓. • If improvement in >28 days or recurrence:

		Discontinue.
	Grade 4	Discontinue.
Other Adverse Reactions	Grade 2	Hold.* Restart at same dose.
	Grade 3	Hold.* Restart at same dose or at 1 dose level ↓, as clinically appropriate.
	Grade 4	Discontinue.

§ Dose adjustments and management are based on pre-dose fasting glucose (FG) and/or HbA1c levels.

†If hyperglycemia develops, monitor at least twice weekly (on days on and off capivasertib) until FG decreases to baseline. During treatment with anti-diabetic medication(s), monitor FG at least once a week for 2 months, followed by once q2 weeks or as clinically indicated.

* Hold until recovery to ≤Grade 1.

Dosage with Hepatic Impairment:

Bilirubin		AST	Capivasertib Dose
≤ULN	and	>ULN	No dose adjustment required.
>1 to 1.5 ULN	and	Any	
>1.5 to 3 ULN	and	Any	Limited data available. Administer only if benefit outweighs risk; monitor closely for signs of toxicity.
>3 ULN	and	Any	No data. Use not recommended.

Dosage with Renal Impairment:

Creatinine Clearance (mL/min)	Capivasertib Dose
≥30	No dose adjustment required.
<30 or ESRD	No data. Use not recommended.

Dosage in the elderly:

No dose adjustment is required for elderly patients aged ≥65 years. No clinically significant difference in efficacy was observed between patients ≥65 years of age and younger patients. Higher incidence of Grade ≥3 adverse reactions may be observed in patients ≥65 years old compared to younger patients.

Dosage based on gender:

No clinically significant differences in pharmacokinetics based on gender.

Dosage based on ethnicity:

No clinically significant differences in pharmacokinetics between White and Asian patients. There is limited information available about other race/ethnicities.

Children:

The safety and efficacy of capivasertib have not been established in patients under 18 years of age.

back to top

F - Administration Guidelines

- Administer capivasertib tablets with or without food.
- Swallow tablets whole with water. Do not chew, crush, dissolve, or divide tablets.
- If a dose is missed, it can be administered within 4 hours of the missed dose. If more than 4 hours, the dose should be skipped and the next dose should be given at the next planned time.
- Ensure at least 8 hours between doses.
- Do not administer a replacement dose if a dose is vomited. The next scheduled dose should be given on the next day.
- Store at room temperature between 15°C to 30°C in original package.

back to top

G - Special Precautions

Contraindications:

- Patients who have a hypersensitivity to this drug or any of its components

Other Warnings/Precautions:

- The safety of capivasertib has not been established in patients with certain medical conditions, including with Type 1 diabetes, diabetes requiring insulin and/or those with a HbA1C of ≥8%, history of clinically significant cardiac disease, or symptomatic visceral disease, as these patients were excluded from the CAPItello-291 trial.
- Diabetic ketoacidosis (fatal in some cases), severe cutaneous reactions, and severe diarrhea associated with dehydration and/or acute kidney injury have been observed in patients treated with capivasertib.

Other Drug Properties:

- Carcinogenicity: No information available

Pregnancy and Lactation:

- Genotoxicity: No
- Mutagenicity: No
- Embryotoxicity: Documented in animals
- Fetotoxicity: Documented in animals
- Pregnancy:
  Capivasertib is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners during treatment, and for at least **4 weeks** after the last dose.
- Breastfeeding:
  Breastfeeding is not recommended during treatment.
- Excretion into breast milk: Documented in animals
- Fertility effects: Unknown

back to top

H - Interactions

Capivasertib is mainly metabolized by CYP3A4 and UGT2B7 enzymes; however, UGT2B7 inhibitors (i.e. probenecid) are not predicted to have a clinically meaningful effect on capivasertib pharmacokinetics.

Capivasertib inhibits CYP2C9 (clinical significance not established), CYP2D6, CYP3A4 and UGT1A1. In vitro, capivasertib inhibited BCRP, OATP1B1, OATP1B3, OAT3, OCT2, MATE1 and MATE2K drug transporters.

Capivasertib is a substrate of P-glycoprotein (P-gp) transporter.

Sensitive substrates are substrates where minimal concentration changes due to enzyme/transporter inhibition may lead to serious adverse effects. Capivasertib can inhibit certain enzymes or transporters and increase sensitive substrate exposure. Generally, applicable inhibitors can increase sensitive substrate exposure (e.g. by 1.25 to <2-fold with weak inhibitors, 2 to <5-fold with moderate inhibitors, and ≥5-fold with strong inhibitors).

AGENT	EFFECT	MECHANISM	MANAGEMENT
Strong CYP3A4 inhibitors (e.g. clarithromycin, itraconazole, ritonavir, etc.)	↑ capivasertib concentration and/or toxicity (e.g. itraconazole ↑ capivasertib exposure by 1.6-fold)	↓ metabolism of capivasertib	Avoid concomitant use. If must co-administer, give capivasertib at 320 mg BID for 4 days, then 3 days off each week . Monitor for signs of toxicity. After discontinuation of the inhibitor wait for 3 half-lives (of the inhibitor), then resume the dose that was used prior to starting the inhibitor.
Moderate CYP3A4 inhibitors (e.g. aprepitant, erythromycin, verapamil, etc.)	↑ capivasertib concentration and/or toxicity	↓ metabolism of capivasertib	If given concomitantly, give capivasertib at 320 mg BID for 4 days, then 3 days off each week. Monitor for signs of toxicity. After discontinuation of the inhibitor wait for 3 half-lives (of the inhibitor), then resume the dose that was used prior to starting the inhibitor.

Strong or moderate CYP3A4 inducers (e.g. phenytoin, rifampin, dexamethasone, carbamazepine, St. John's Wort, etc.)	↓ capivasertib concentration and/or efficacy (e.g. enzalutamide ↓ capivasertib exposure by 40-50%)	↑ metabolism of capivasertib	Avoid concomitant use.
CYP3A4 substrates (e.g. midazolam)	↑ CYP3A4 substrates concentration and/or toxicity (e.g. ↑ midazolam AUC by 1.8-fold on day 4)	Capivasertib is a weak inhibitor of CYP3A4.	Avoid concomitant use with CYP3A4 sensitive substrates. If must co-administer, adjust dosage of these substrates based on their product monographs
OATP1B1 and/or OATP1B3 substrates, that are metabolized by CYP3A4	↑ OATP1B1, OATP1B3 substrate concentration and/or toxicity (theoretical; no clinically relevant effects on exposure of atorvastatin or rosuvastatin)	Capivasertib inhibits OATP1B1 and OATP1B3 in vitro; it may ↓ metabolism of OATP1B1, OATP1B3 substrates that are metabolized by CYP3A4.	Avoid concomitant use of sensitive substrates or adjust dosage for these substrates based on their product monographs.
MATE1, MATE2K, OCT2 substrates (e.g. procainamide)	↑ MATE1, MATE2K, OCT2 substrates concentration and/or toxicity (theoretical; no meaningful interaction with metformin); transient ↑ in serum creatinine	Capivasertib inhibits MATE1, MATE2K, OCT2 transporters in vitro.	Caution when used concomitantly with sensitive substrates; adjust dosage of these substrates based on their product monographs.

back to top

I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

Recommended Clinical Monitoring

Monitor Type	Monitor Frequency
CBC	Baseline, and at each visit
Liver function tests	Baseline, and at each visit
Renal function tests	Baseline, and at each visit
Fasting glucose* (patients without diabetes)	Baseline and at weeks 1, 2, 4, 6 and 8 after treatment start, then at least once a month thereafter. (Additional monitoring may be required within the first 2 weeks of treatment, as clinically indicated.)
Fasting glucose (patients with diabetes)	Baseline and daily for the first 2 weeks of treatment, then as frequently as needed to manage hyperglycemia.
HbA1c	Baseline, at week 4 (for patients with diabetes, pre-diabetes or hyperglycemia at baseline) and every 3 months
Clinical toxicity assessment for diarrhea, rash, fatigue, and other GI effects.	Baseline and at each visit

*It is recommended to test fasting glucose pre-dose on Day 3 or 4 of the dosing week.

Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

Monitor Type	Monitor Frequency
Blood ketones	As clinically indicated for diabetic ketoacidosis

back to top

J - Supplementary Public Funding

Exceptional Access Program (EAP Website)

- capivasertib - For the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer, based on criteria

back to top

K - References

NCI drug dictionary: capivasertib. Accessed February 24, 2025.

Prescribing Information: Truqap™ (capivasertib). AstraZeneca Pharmaceuticals LP. September 2024.

Product Information: Truqap™ (capivasertib). AstraZeneca AB. July 11, 2024.

Product Information: Truqap™ (capivasertib). AstraZeneca Pty Ltd. November 6, 2024.

Product Monograph: Truqap™ (capivasertib). AstraZeneca Canada Inc. January 3, 2025.

Turner NC, Oliveira M, Howell SJ, et al. Capivasertib in Hormone Receptor-Positive Advanced Breast Cancer. N Engl J Med. 2023 Jun 1;388(22):2058-2070. doi: 10.1056/NEJMoa2214131.

October 2025 New drug monograph

back to top

L - Disclaimer

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

While care has been taken in the preparation of the information contained in the Formulary, such information is provided on an “as-is” basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information’s quality, accuracy, currency, completeness, or reliability.

CCO and the Formulary’s content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person’s use of the information in the Formulary.

back to top