

Capiwasertib (TRUQAP) in Breast Cancer National Drug Mini-Monograph November 2025

VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. Updates will be made if new clinical data warrant additional formulary discussion. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL INFORMATION	Description / MOA	Kinase inhibitor
	Indication Under Review¹	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
	Dosage Regimen	400 mg orally twice daily, with or without food, for 4 days followed by 3 days off
	Dosage Forms	Tablets: 160 mg and 200 mg
	Under Review	

EFFICACY CONSIDERATIONS	Trial	CAPItello-291 (NCT04305496)		
	Design	Multicenter, randomized, double-blind, placebo-controlled		
	Population	Adult patients (pre-, peri-, post-menopausal women or men) with locally advanced (inoperable) or metastatic HR-positive, HER2-negative (defined as IHC 0 or 1+, or IHC 2+/ISH-) breast cancer with activating mutations in PIK3CA and AKT1 and inactivating alterations in PTEN genes; also with progressive disease on AI with or w/o a CDK4/6 inhibitor in metastatic setting or within 12 months of neoadjuvant or adjuvant AI		
	Intervention	400 mg of capivasertib 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 day 1 of each subsequent 28-day cycle		
	Comparator	Placebo plus fulvestrant		
	Results	Efficacy results in CAPItello-291 (Patients with PIK3CA/AKT1/PTEN- altered tumors)		
			Capiwasertib with fulvestrant N=155	Placebo with fulvestrant N=134
		Investigator-Assessed Progression-Free Survival (PFS)		
		Number of events (%)	121 (78)	115 (86)
		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#	<0.001	
		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. DoR; duration of response			

SAFETY CONSIDERATIONS	Boxed Warnings	None
	Contraindications	Severe hypersensitivity to capivasertib or any of its components
	Other Warnings	Hyperglycemia (all grades 37%) in CAPitello-291, 12% initiated or changed anti-hyperglycemic med regimen; including insulin in 4.8% of patients; IDDM patients were excluded; safety has not been determined in Type I DM or IDDM; test FBG, HbA1C and optimize FG; monitor per prescribing info. Diarrhea (72%; gr 3-4: 9%) Manage with anti-diarrheal medication and dose-reductions; monitor for signs and symptoms, start anti-diarrheal medication at first indication Cutaneous adverse reactions (58%; gr 3-4: 17%) Corticosteroids (topical or systemic) may be required; monitor for signs and symptoms of cutaneous reactions; consider dermatology consultation Embryo-fetal toxicity
	Top 5 AEs	Diarrhea, increased random glucose, cutaneous adverse reactions, decreased lymphocytes, decreased hemoglobin
	Drug Interactions	Strong and moderate CYP3A4 inducers and inhibitors

PLACE IN THERAPY	DRUG	VANF	CFU	FDA	GUIDELINES
	Capivasertib + fulvestrant	NF	No	Approved	VA Breast Cancer – Stage IV ER+ or PR+/HER2- Pathway directs to fulvestrant and capivasertib in patients who have progressed on prior endocrine therapy and have a molecular alteration identified in AKT-PTEN NCCN Invasive Breast Cancer Guidelines V4.2025, Category 1, capivasertib and fulvestrant are preferred second or subsequent-line in recurrent, unresectable or metastatic ER+/PR+/HER2- patients with PIK3CA, AKT2 or PTEN alterations and have progressive disease after ≥ 1 prior line of endocrine therapy
	Alpelisib + fulvestrant	PA-F	Yes	Approved	VA Breast Cancer – Stage IV ER+ or PR+/HER2- Pathway directs to fulvestrant and capivasertib in patients who have progressed on prior endocrine therapy and have a molecular alteration identified in PIK3CA NCCN Invasive Breast Cancer Guidelines V4.2025, Category 1, alpelisib and fulvestrant are preferred second or subsequent line in recurrent, unresectable or metastatic ER+/PR+/HER2- patients with PIK3CA activating mutation and have progressive disease after ≥ 1 prior line of endocrine therapy

VHA PLACE IN THERAPY	Potential Use in VHA	<ol style="list-style-type: none"> 1. Patients with hormone-receptor positive, HER2-negative locally advanced or metastatic breast cancer who have progressed on aromatase inhibitors and have specific gene mutations (PIK3CA, AKT1, or PTEN) showed better outcomes when treated with capivasertib and fulvestrant compared to those receiving placebo and fulvestrant. Specifically, they experienced improved progression-free survival (PFS) of 7.3 months versus 3.1 months and a higher overall response rate (ORR) of 26% compared to 8%. 2. Improved outcomes with capivasertib and fulvestrant comes with increased toxicity, particularly diarrhea, cutaneous adverse reactions and hyperglycemia; additionally, reduced lymphocyte count, increased ALT and reduced potassium levels were noted by patients in the treatment arm; regularly scheduled monitoring and patient/caregiver education will be needed for select patients. 3. Patients previously treated with endocrine therapy and possess a PIK3CA, AKT1 or PTEN alteration may be a candidate for capivasertib and fulvestrant. Ensure patients with concomitant conditions, such as diabetes or GI conditions, are educated on monitoring and management as these conditions may be impacted.
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References

1. TRUQAP (capivasertib) tablets [prescribing information]. AstraZeneca Pharmaceuticals, Wilmington, DE 2024.
2. Turner NC, Oliveira M, Howell SJ et al. Capivasertib in hormone receptor-positive advanced breast cancer. *N Engl J Med* 2023;388: 2058-2070.
3. National Comprehensive Cancer Network. Invasive Breast Cancer Guidelines Version 4.2025.
4. VHA Oncology Clinical Pathways. Breast Cancer Stage IV ER+ or PR+/HER2- V2.2025.