capivasertib (Truqap™)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO301

Description

Capivasertib (Truqap) is an orally administered kinase inhibitor selective for all three isoforms of AKT (*AKT1, AKT2, AKT3*).

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
capivasertib (Truqap)	Breast cancer, HER2-negative, HR-positive, *PIK3CA/AKT1/PTEN*-mutated, advanced, or metastatic	160 mg tablets	64 tablets/28 days
		200 mg tablets	

Initial Evaluation

I. **Capivasertib (Truqap)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an oncologist; **AND**
   C. Medication will be used in combination with fulvestrant (Faslodex); **AND**
   D. Medication will not be used in combination with any other oncology therapy except for fulvestrant (Faslodex); **AND**
   E. A diagnosis of **advanced or metastatic breast cancer** when the following are met:
      1. The breast cancer is HR-positive, and HER2-negative; **AND**
      2. Documentation of at least one phosphatidylinositol 3-kinase (*PIK3CA*), serine/threonine protein kinase (*AKT1*), or phosphatase and tensin homolog (*PTEN*)-mutation; **AND**
         i. The member has had disease progression on at least one prior endocrine therapy for advanced or metastatic breast cancer (e.g., letrozole, anastrozole, exemestane, tamoxifen), unless not tolerated or contraindicated; **AND**
         ii. The member has had disease progression on, or after, treatment with a CDK4/6 inhibitor (e.g., palbociclib [Ibrance], abemaciclib [Verzenio], ribociclib [Kisqali], etc.), unless not tolerated or contraindicated; **OR**
      3. The member has had disease recurrence on or within 12 months of completing endocrine-based (neo)adjuvant therapy (e.g., tamoxifen, anastrozole, exemestane, letrozole), unless not tolerated or contraindicated

II. Capivasertib (Truqap) is considered not medically necessary when criteria above are not met and/or when used for:
   A. Second line treatment and beyond in non-altered *PIK3CA/AKT/PTEN*, HR+, HER2-, advanced or metastatic breast cancer

III. Capivasertib (Truqap) is considered investigational when used for all other conditions, including but not limited to:
   A. Capivasertib (Truqap) used in combination with oncology therapy other than fulvestrant (Faslodex)
   B. Capivasertib (Truqap) used to treat cancers other than breast cancer
   C. Triple negative breast cancer

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Disease response to treatment defined by stabilization of disease or decrease in tumor size or tumor spread

Supporting Evidence

I. Capivasertib (Truqap) is indicated in combination with fulvestrant for the treatment of adult patients with hormone-positive (HR+), human epidermal growth factor receptor 2 negative (HER2-), locally advanced, or metastatic breast cancer with one or more *PIK3CA/AKT1/PTEN*-alterations following progression on at least one endocrine-based regimen in the metastatic setting or recurrence on or within 12 months of completing adjuvant therapy.
II. Capivasertib (Truqap) is not FDA approved and has not been studied in patients under 18 years of age. Safety and efficacy in the pediatric/adolescent population remains undetermined.
III. Given the complexities involved with the diagnosis, treatment approaches, and management of therapy for the indicated population, treatment with capivasertib (Truqap) should be initiated by or in consultation with an oncologist.
IV. Capivasertib (Truqap) is not FDA approved and has not been well studied in combination with oncolytic therapies other than fulvestrant at this time. Safety and efficacy of monotherapy with capivasertib (Truqap) or in combination with regimens other than fulvestrant remains undetermined.

V. Capivasertib (Truqap) was studied in combination with fulvestrant in Phase 2 (FAKTION) and Phase 3 (CAPItello-291) 1:1 randomized, double-blind, placebo-controlled trials in 848 patients with advanced or metastatic HR+, HER2- breast cancer. The Phase 3 trial included about 70% of patients refractory to CDK 4/6 inhibitors while the Phase 2 trial included patients refractory to aromatase inhibitors only. Trial participants were mostly postmenopausal females aged 60 years old with a median of one previous line of therapy for advanced disease. Around 40-45% of patients in both trials had PIK3CA/AKT/PTEN pathway alterations. The primary efficacy outcomes were progression-free survival (PFS) and secondary outcomes included overall survival (OS) and health-related quality of life (HRQoL). In the Phase 3 trial, the primary endpoint, PFS, was statistically significant in favor of capivasertib (Truqap) at 7.3 months vs 3.1 months and OS was not yet reached in the PIK3CA/AKT/PTEN altered population only. In the Phase 2 trial, PFS was 12.8 months vs 4.6 months and median OS was 38.9 months vs 20.0 months in favor of capivasertib (Truqap) in the PIK3CA/AKT/PTEN altered population. HRQoL did not improve or deteriorate significantly in the capivasertib (Truqap) arm, except for worsening diarrhea. The overall confidence in that the therapy brings significant value is low at this time due to unknown impact on overall survival, lack of HRQoL benefit, lack of long-term safety data, and significant safety concerns associated with PI3K inhibitors.

VI. Documentation of one of the following mutations/alterations is required when considering an appropriate patient candidate for treatment with capivasertib (Truqap): *PIK3CA, AKT, or PTEN*. The Phase 3 CAPItello-291 clinical trial demonstrated that capivasertib (Truqap) is active in patients with the aforementioned mutations only. A subgroup analysis of the non-altered cohort did not demonstrate statistically significant differences against placebo.

VII. The CAPItello-291 Phase 3 clinical trial established the place in therapy and population likely to benefit from treatment with capivasertib (Truqap). As such, the place in therapy is as second-line treatment in the recurrent unresectable (advanced) or metastatic breast cancer setting. Treatment with National Comprehensive Cancer Network (NCCN) breast cancer guideline first-line recommended therapies is required prior to capivasertib (Truqap) which includes CKD 4/6 inhibitors in combination with aromatase inhibitors (AI) or fulvestrant. Those with disease recurrence on or within 12 months of completing endocrine-based adjuvant therapy (e.g., tamoxifen, anastrozole, exemestane, letrozole) are also considered appropriate candidates for therapy as this aligns with the inclusion criteria of the CAPItello-291 clinical trial.

Investigational or Not Medically Necessary Uses

I. Capivasertib (Truqap) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Second line treatment and beyond in non-altered *PIK3CA/AKT/PTEN*, HR+, HER2-, advanced or metastatic breast cancer
      i. CAPItello-291 Phase 3 clinical trial established that treatment with capivasertib (Truqap) in patients without the *PIK3CA, AKT,* or *PTEN* mutation did not achieve statistically significant difference in PFS against placebo. Due to lack of efficacy,

use of capivasertib (Truqap) is considered not medically necessary in this population.

B. Capivasertib (Truqap) used in combination with oncology therapy other than fulvestrant (Faslodex)
    i. Capivasertib (Truqap) is being studied in a Phase 3 trial (NCT04862663; CAPItello-292) in combination with a CDK4/6 inhibitor and fulvestrant in the first line setting for advanced/metastatic breast cancer. Study completion is estimated in 2029. Requests in the first line setting or in combination with a CDK4/6 inhibitor are considered experimental and investigational at this time.
C. Capivasertib (Truqap) used to treat cancers other than breast cancer.
    i. Capivasertib (Truqap) is being studied in a Phase 3 trial (NCT05348577; CAPItello 280) in combination with docetaxel in metastatic castration resistant prostate cancer. Study completion is estimated in 2026. Requests for this indication are considered experimental and investigational at this time.
D. Triple negative breast cancer
    i. Capivasertib (Truqap) is being studied in a Phase 3 trial (NCT03997123; CAPItello-290) in combination with paclitaxel as first-line treatment for patients with locally advanced or metastatic triple negative breast cancer. The study is estimated to be completed by 03/2024 with data read out in 2024-2025. Requests for this indication are considered experimental and investigational at this time.

References

1. Truqap. Package Insert. AstraZeneca Pharmaceuticals LP; November 2023.
2. National Comprehensive Cancer Network. Breast Cancer. NCCN. January 25, 2024. Accessed March 8, 2024. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
3. Turner NC, Oliveira M, Howell SJ, et al. Capivasertib in Hormone Receptor-Positive Advanced Breast Cancer. N Engl J Med. 2023;388(22):2058-2070. doi:10.1056/NEJMoa2214131
4. Howell SJ, Casbard A, Carucci M, et al. Fulvestrant plus capivasertib versus placebo after relapse or progression on an aromatase inhibitor in metastatic, oestrogen receptor-positive, HER2-negative breast cancer (FAKTION): overall survival, updated progression-free survival, and expanded biomarker analysis from a randomised, phase 2 trial. Lancet Oncol. 2022;23(7):851-864. doi:10.1016/S1470-2045(22)00284-4
5. Jones RH, Casbard A, Carucci M, et al. Fulvestrant plus capivasertib versus placebo after relapse or progression on an aromatase inhibitor in metastatic, oestrogen receptor-positive breast cancer (FAKTION): a multicentre, randomised, controlled, phase 2 trial. Lancet Oncol. 2020;21(3):345-357. doi:10.1016/S1470-2045(19)30817-4

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
alpelisib (Piqray, Vijoice)	Breast cancer, HR+, HER2-, PIK3CA+, advanced or metastatic
Cyclin-Dependent Kinase (CDK) 4/6 Inhibitors	Breast cancer, HER2-, HR+, advanced or metastatic
elacestrant (Orserdu)	Breast cancer, HR+, HER2-, ESR-1+, advanced or metastatic

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	05/2024