talazoparib (Talzenna®)

EOCCO POLICY

Policy Type: PA Pharmacy Coverage Policy: EOCCO065

Description

Talazoparib (Talzenna) is an orally administered poly (ADP-ribose) polymerase (PARP) inhibitor.

Length of Authorization

- Initial: Three months
- Renewal: Twelve months

Quantity limits

Product Name	Indication	Dosage Form	Quantity Limit
talazoparib (Talzenna)	Breast cancer, locally advanced or metastatic, BRCA-mutated	0.25mg capsules	30 capsules/ 30 days*
		0.5 mg capsules	
		0.75 mg capsules	
		1 mg capsules	

** Quantity limit exceptions are limited to dose reductions and clinician review*

Initial Evaluation

I. **Talazoparib (Talzenna)** may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a specialist in oncology; **AND**
   C. Medication will be used as monotherapy; **AND**
   D. Member has not had disease progression on prior PARP inhibitor therapy (e.g., niraparib [Zejula], rucaparib [Rubraca], olaparib [Lynparza]); **AND**
   E. A diagnosis of **locally advanced (stage III) or metastatic (stage IV) breast cancer** when the following are met:
      1. Documented deleterious (pathogenic) or suspected deleterious (likely pathogenic) germline BRCA mutation as determined by FDA approved diagnostic testing; **AND**
      2. Prior treatment with an anthracycline (e.g., doxorubicin) and/or a taxane (e.g., paclitaxel) was ineffective, unless contraindicated; **AND**
      3. For hormone receptor-positive (ER/PR+) disease, member has had disease progression on endocrine therapy; **OR**
         i. Endocrine therapy has been deemed inappropriate by the treating healthcare provider

II. Talazoparib (Talzenna) is considered investigational when used for all other conditions, including but not limited to:
   A. When used in combination with any other chemotherapy or targeted therapy
   B. Early-stage breast cancer
   C. Ovarian cancer, fallopian tube, and peritoneal cancer
   D. Lung cancer
   E. Prostate 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. Talazoparib (Talzenna) will not be used in combination with other anti-cancer agents (outside of gonadotropin releasing hormone agonist [e.g., leuprolide] or endocrine therapy [e.g., anastrozole, tamoxifen, fulvestrant]); **AND**
IV. Clinical documentation of response to treatment (e.g., stabilization of disease or decrease in tumor size, or tumor spread).

Supporting Evidence

I. Talazoparib (Talzenna) is FDA-approved for the treatment of adults with germline BRCA mutated (gBRCAm), HER2-negative, locally advanced or metastatic disease.
II. The efficacy and safety of talazoparib (Talzenna) monotherapy was demonstrated in an open-label randomized, trial (EMBRACA) which enrolled adult patients that had a deleterious or suspected deleterious germline BRCA1/2 mutation detected by testing with BRACAnalysis.
III. Overall, 431 patients were randomized 2:1 to receive talazoparib or chemotherapy of the provider's choice (capecitabine, eribulin, gemcitabine or vinorelbine); 287 patients received talazoparib and 144, chemotherapy. Baseline characteristics of both groups were generally similar, but the talazoparib included a higher number of patients with a baseline Eastern Cooperative Oncology Group (ECOG) performance score of 1 or 2 and a higher number of patients whose disease progressed to advanced within 12 months of initial diagnosis.
IV. To be included in the EMBRACA study, patients had received no more than three previous cytotoxic regimens for advanced breast cancer, and they had received previous treatment with a

taxane or an anthracycline, or both, unless contraindicated. Additionally, previous neoadjuvant or adjuvant platinum-based therapy was allowed, provided the patient had a disease-free interval for at least six months after the last dose. Patients were excluded if they had disease progression while receiving platinum chemotherapy for advanced breast cancer (i.e., progression of disease within approximately eight weeks after the last dose). Third, patients included in the study had no more than three prior therapies in the advanced breast cancer setting. More than two therapies in other settings (e.g. neoadjuvant, adjuvant) do not apply. However, as current guidelines move to testing for targeted therapies once diagnosed, the likelihood of patients using over one line of therapy is rare.

V. The primary endpoint of the study was radiologic progression-free survival (PFS) done via imaging at baseline, every 6 weeks until week 30, and then every 9 weeks after. The median progression-free survival was significantly longer among patients in the talazoparib group than among patients in the standard-therapy group (8.6 months [95% confidence interval {CI}, 7.2 to 9.3] vs. 5.6 months [95% CI, 4.2 to 6.7]; hazard ratio for disease progression or death, 0.54; 95% CI, 0.41 to 0.71; P<0.001).

VI. Although prior endocrine-based therapy was not required in the EMBRACA trial, 90.4% of patients had progressed on endocrine-based therapy before being treated with talazoparib (Talzenna), and 100% had received prior chemotherapy for HR+ disease. The standard treatment approach for HR+ disease is to first target the hormone pathway (unless considered inappropriate), then consider single agent chemotherapy or PARP inhibitor if there is a progression on endocrine-based therapy.

VII. The National Comprehensive Cancer Network (NCCN) breast cancer guideline lists the PARP inhibitors [talazoparib (Talzenna) and olaparib (Lynparza)] as Category 1 options for previously treated recurrent or metastatic germline BRCA mutated breast cancer. EMBRACA clinical program included 56% patients with ER/PR+, HER2- advanced or metastatic breast cancer, while 44% had triple-negative breast cancer (TNBC). Thus, talazoparib (Talzenna) may be considered a practical treatment option for patients with TNBC. However, presence of germline BRCA1 or BRCA2 mutation is a pre-requisite for initiating treatment with talazoparib (Talzenna).

VIII. In the EMBRACA trial, adverse reactions were reported at a higher incidence in those receiving talazoparib than placebo-chemotherapy arm. Sixty-five percent of patients taking talazoparib versus 50% chemotherapy experienced ADE and dose reductions due to any cause occurred in 53% of talazoparib patients versus chemotherapy patients. Due to the high incidence of this, split fill is applied to the medication upon initial approval.

IX. Dose adjustments are common with talazoparib (Talzenna) and the as the product it is flat priced (i.e., there is a single fixed price for *each* tablet regardless of dosage strength). When possible, patients should be dose optimized to once a day dosing of an appropriate strength versus allowing multiple tablets of a lower dose.

Investigational or Not Medically Necessary Uses

I. The efficacy and safety of talazoparib (Talzenna) in combination with other chemotherapy or immunotherapy agents have not been evaluated. Talazoparib (Talzenna) is indicated as monotherapy.
II. There is no evidence to support the use of a subsequent PARP inhibitor following the progression of disease on another PARP inhibitor.
III. Due to its mechanism of action, there is interest in using talazoparib (Talzenna) in other cancers such as ovarian cancer, prostate cancer, and lung cancer; however, studies are still ongoing and use outside of BRCA mutated advanced or metastatic breast cancer is considered investigational.
IV. Additionally, there is a lack of evidence supporting the use of talazoparib (Talzenna) in early breast cancer (e.g., neoadjuvant or adjuvant treatment).

References

1. Talzenna [Prescribing Information]. New York, NY: Pfizer. October 2018. Revised 9/2021
2. Litton J, Rugo H, Ettl J, et al. Talazoparib in patients with advanced breast cancer and germline BRCA mutation. N Engl J Med 2018;379:753-63
3. NCCN Clinical Practice Guideline in Oncology: Breast Cancer. Version 2.2022-December 20,2021 National Comprehensive Cancer Network. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Updated 12/2021. Accessed April 18, 2022.
4. UpToDate, Inc. Systemic treatment of metastatic breast cancer in women: Chemotherapy. UpToDate [database online]. Waltham, MA. Available at: http://www.uptodate.com/home/index.html. Updated August 21, 2017. Accessed December 27, 2018.
5. National Institutes of Health, Clinicaltrials.gov [website]. [cited periodically]; Available from: www.clinicaltrials.gov

Related Policies

Policy Name	Disease state
Cyclin-Dependent Kinase (CDK) 46 Inhibitors	Breast cancer, HER2-negative, HR-positive, advanced or metastatic, early-stage breast cancer
alpelisib (Piqray)	PIK3CA mutation, HR+, HER2-, advanced or metastatic breast cancer
lapatinib (Tykerb)	Breast cancer, HER2 over expression, advanced or metastatic in combination with capecitabine after prior therapy OR postmenopausal women, in combination with letrozole
neratinib (Nerlynx)	Breast cancer, early stage, HER2-positive, following trastuzumab OR advanced, metastatic
olaparib (Lynparza)	Breast cancer, metastatic, HER2-negative, germline BRCA-mutated (gBRCAm)
tucatinib (Tukysa)	Metastatic breast cancer

Policy Implementation/Update:

Action and Summary of Changes	Date
Streamlined clinical criteria to better reflect our current PARP policies. Removed requirement of HER2 negative disease. Removed confirmation member is not platinum refractory. Removed requirement of maximum number of prior cytotoxic regimens. Improved supporting evidence section for better clinical support. Added related policies.	08/2022
Previous Reviews	02/2019