09-J3000-21

Original Effective Date: 03/15/19

Reviewed: 02/13/19

Revised: 00/00/00

Subject: Talazoparib (Talzenna®)

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DESCRIPTION:

Approximately 266,000 new cases of breast cancer are predicted to be diagnosed in the United States in 2018. It is estimated that 20 to 50% of those diagnosed with early stage breast cancer will eventually progress to metastatic breast cancer.

Talazoparib (Talzenna), a poly (ADP-ribose) polymerase (PARP) inhibitor, was approved by the U.S. Food and Drug Administration (FDA) in 2018 for the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm), HER2-negative locally advanced or metastatic breast cancer.

The safety and efficacy of talazoparib were evaluated in subjects with locally advanced or metastatic breast cancer that was HER2-negative open label study (EMBRACA). All patients were required to have a known deleterious or suspected deleterious gBRCA mutation and must have received no more than 3 prior cytotoxic chemotherapy regimens for locally advanced or metastatic disease. Patients were required to have received treatment with an anthracycline and/or a taxane (unless contraindicated) in the neoadjuvant, adjuvant, and/or metastatic treatment setting.

Subjects (n=431) were randomized to receive talazoparib 1 mg daily or standard single-agent chemotherapy (capecitabine, eribulin, gemcitabine, or vinorelbine). The primary efficacy outcome was progression-free survival (PFS) according to Response Evaluation Criteria in Solid Tumors (RECIST) 1.1, as assessed by blinded independent central review.

Talazoparib compared with standard single-agent chemotherapy significantly prolonged progression-free survival determined by independent review (8.6 vs 5.6 months; HR 0.54; 95% CI, 0.41 to 0.71) in the randomized, open-label EMBRACA trial of women with locally advanced or metastatic breast cancer and a germline BRCA1/2 mutation. Hormone-receptor status included triple-negative (45.3% with talazoparib and 41.7% with standard therapy) and hormone-receptor positive (54.7% vs 58.3%). At interim analysis, median overall survival was not significantly different with talazoparib versus standard therapy (22.3 vs 19.5 months); 62% and 68% of patients received anticancer therapy after the trial. The response rate

determined by investigators was 62.6% versus 27.2%; median time to response 2.6 versus 1.7 months, and median duration of response was 5.4 versus 3.1 months. Clinical benefit rate at 24 weeks was 68.6% versus 36.1%. Adverse effects were reported in 98.6% with talazoparib and 97.6% with standard therapy and included serious events (31.8% vs 29.4%), Grade 3 or 4 hematologic events (55% vs 38%), and Grade 3 nonhematologic events (32% vs 38%).

National Comprehensive Cancer Network (NCCN) Guidelines for Breast Cancer (Version 3.2018) recommend talazoparib for treatment of treatment of recurrent or stage IV HER2-negative, BRCA 1/2 – germline mutated disease.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of talazoparib (Talzenna) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with recurrent, locally advanced, or metastatic breast cancer
2. Member has human epidermal growth factor receptor 2 (HER2)-negative disease – laboratory documentation must be provided
3. Member has BRCA 1/2-germline mutated disease – laboratory documentation must be provided
4. Member's disease meets ONE of the following:
    a. Hormone receptor-negative
    b. Hormone receptor-positive AND refractory to endocrine therapy (anastrozole, letrozole, exemestane, tamoxifen)
    c. Symptomatic visceral disease or visceral crisis
5. Talazoparib will be used as a single agent
6. Talazoparib dose does not exceed 1 mg/day – dosage will be achieved using the fewest number of capsules per day

Approval duration: 6 months

Continuation of talazoparib (Talzenna) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of breast cancer, **OR** the member has previously met all indication-specific criteria
2. Member's disease has not progressed during treatment with talazoparib
3. Dose does not exceed 1 mg/day – dosage will be achieved using the fewest number of capsules per day

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

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FDA-approved

- 1 mg taken as a single oral daily dose, with or without food

Dose Adjustments

- To manage adverse reactions, consider interruption of treatment with or without dose reduction based on severity and clinical presentation
- Reduce the dose to 0.75 mg once daily when coadministered with certain P-gp inhibitors

Drug Availability

- Capsules: 0.25 mg, 1 mg

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML)
- Myelosuppression
- Embryo-Fetal Toxicity

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8999	Prescription drug, oral, chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnosis Codes That Support Medical Necessity

C50.011 – C50.929	Malignant neoplasm of breast

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

DEFINITIONS:

Adjuvant Treatment: Additional cancer treatment given after the primary treatment to lower the risk that the cancer will return. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, targeted therapy, or biologic therapy. Adjuvant therapy can be used after or in combination with another form of cancer therapy and is commonly used following removal of a cancerous tumor to further help in treatment.

DPD: deoxypyridinoline, also called D-Pyrilinks or Pyrilinks-D, is a crosslink of type I collagen present in bone which is excreted unmetabolized in urine and is a specific marker of bone resorption. It is measured in a urine tests in members when osteoporosis is suspected.

Metastatic cancer: when cancer spreads from the primary site (place where it started) to other places in the body.

Neoadjuvant treatment: Treatment given as a first step to shrink a tumor before the main treatment, which is usually surgery, is given. Examples of neoadjuvant therapy include chemotherapy, radiation therapy, and hormone therapy. It is a type of induction therapy

RELATED GUIDELINES:

Ado-trastuzumab emtansine (Kadcyla) Injection, 09-J1000-90

Docetaxel (Taxotere®) IV, 09-J0000-95

Palbociclib (Ibrance), 09-J2000-34

Pertuzumab (Perjeta) IV, 09-J1000-75

Trastuzumab (Herceptin®) Injection, 09-J0000-86

OTHER:

None

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the BCBSF Pharmacy Policy Committee on 02/13/19.

GUIDELINE UPDATE INFORMATION:

03/15/19	New Medical Coverage Guideline.