09-J2000-75

Original Effective Date: 0**6/15/17**

Reviewed: 03/13/19

Revised: 03/15/20

Subject: Ribociclib (Kisqali®)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Approximately 255,000 new cases of breast cancer are predicted to be diagnosed in the United States in 2017. It is estimated that 20 to 50% of those diagnosed with early stage breast cancer will eventually progress to metastatic breast cancer.

Ribociclib (Kisqali), a cyclin-dependent kinase inhibitor, was approved by the U.S. Food and Drug Administration (FDA) in 2017 for use in combination with letrozole for the treatment of postmenopausal women with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced breast cancer as initial endocrine-based therapy for their metastatic disease.

The safety and efficacy of ribociclib were evaluated in subjects with previously untreated advanced hormone receptor (HR)-positive, HER2-negative disease in a randomized, double-blind, placebo-controlled Phase III study (MONALEESA-2). Subjects were randomized 1:1 to receive with ribociclib plus letrozole (n=334) or placebo plus letrozole (n=334). Letrozole 2.5 mg was given orally once daily for 28 days, with either ribociclib 600 mg or placebo orally once daily for 21 consecutive days followed by 7 days off until disease progression or unacceptable toxicity. The major efficacy outcome measure for the study was investigator-assessed progression-free survival (PFS) using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.

At a median follow-up of 15.3 months, treatment with ribociclib plus letrozole compared with placebo plus letrozole resulted in significantly prolonged PFS (not reached vs 14.7 months) in an interim analysis. Ribociclib plus letrozole was also associated with a significantly greater 18-month PFS rate (63% vs 42.2%) and an overall response rate (40.7% vs 27.5%). Overall survival data is not yet available.

Adverse events associated with the combination treatment included Grade 3 or 4 neutropenia (59.3% vs 0.9%; febrile neutropenia 1.5% vs 0%), leukopenia (21% vs 0.6%) and an increase of more than 60 msec

in the QTcF interval (2.7% vs 0%). Permanent discontinuation due to adverse events occurred in 7.5% of patients receiving ribociclib plus letrozole.

National Comprehensive Cancer Network (NCCN) Guidelines for Breast Cancer (Version 4.2018) recommend ribociclib for treatment of treatment of recurrent or stage IV HR-positive/HER2-negative 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 **does not meet the definition of medical necessity**.

NOTE: Palbociclib (Ibrance) and Abemaciclib (Verzenio) are the preferred CDK4/6 inhibitors.

Initiation of ribociclib (Kisqali) **meets the definition of medical necessity** for members diagnosed with **ANY** of the following conditions when ALL associated criteria are met:

1. Breast Cancer
    a. Member is diagnosed with recurrent or metastatic breast cancer
    b. Member has hormone receptor (HR)-positive disease – laboratory documentation must be provided
    c. Member has human epidermal growth factor receptor 2 (HER2)-negative disease – laboratory documentation must be provided
    d. Ribociclib will be used in combination with **ONE** of the following:
        i. Aromatase inhibitor (anastrazole (Arimidex), letrozole (Femara; available separately, or as part of Kisqali-Femara Co-Pack), or exemestane (Aromasin))
        ii. Fulvestrant (Faslodex)
        iii. Tamoxifen
    e. Member meets one of the following:
        i. Postmenopausal
        ii. Premenopausal AND receiving ovarian ablation/suppression
        iii. Use will be in combination with an agent that suppress testicular steroidogenesis (e.g., leuprolide, goserelin)
    f. **ONE** of the following:
        i. Member has a contraindication to both palbociclib and abemaciclib – specific contraindication must be provided
        ii. Prescriber has provided information in support of use of ribociclib over palbociclib and abemaciclib for the requested indication

g. Member has not previously had disease progression while on a CDK4/6 inhibitor (e.g., palbociclib)

h. Dose does not exceed **ALL** of the following:

i. 600 mg/day – dosage will be achieved using the fewest number of tablets per day

ii. 63 tablets/28 days

2. Other FDA-approved or NCCN supported diagnosis (not previously listed above)

a. Member meets one of the following:

i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)

ii. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation

b. Dose does not exceed **ALL** of the following:

i. 600 mg/day – dosage will be achieved using the fewest number of tablets per day

ii. 63 tablets/28 days

Approval duration: 6 months

Continuation of ribociclib (Kisqali) **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 other FDA-approved or NCCN supported diagnosis, OR the member has previously met all indication-specific initiation criteria
2. Member's disease has not progressed during treatment with ribociclib
3. Dose does not exceed **ALL** of the following:

a. 600 mg/day – dosage will be achieved using the fewest number of tablets per day

b. 63 tablets/28 days

Approval duration: 6 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- 600 mg orally (three 200 mg tablets) taken once daily with or without food for 21 consecutive days followed by 7 days off treatment

Dose Adjustments

- Dose interruption, reduction, and/or discontinuation may be required based on individual safety and tolerability

Drug Availability

- Tablets: 200 mg
- Kisqali Femara Co-Pack contains:
    - Kisqali Tablets: 200 mg
    - Femara Tablets: 2.5 mg

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- None

Precautions/Warnings

- QT interval prolongation
- Hepatobiliary toxicity: Increases in serum transaminase levels have been observed
- Neutropenia
- 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: Florida Blue 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

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2019 [cited 2/28/19]. Available from: http://www.clinicalpharmacology.com/.
2. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 2/28/19]. Available from: http://clinicaltrials.gov/.
3. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2/28/19]. Available from: http://www.thomsonhc.com/.

4. National Comprehensive Cancer Network®. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). Breast Cancer, v. 4.2018 [cited 2/28/19]. Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp.
5. NCCN Drugs & Biologics Compendium [Internet]. Fort Washington (PA): National Comprehensive Cancer Network; 2019 [cited 2/28/19]. Available from: http://www.nccn.org/professionals/drug_compendium/content/contents.asp/.
6. Novartis. Kisqali (ribociclib) tablet, film coated. 2017 [cited 2/28/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=aaeaef94-f3f5-4367-8ea2-b181d7be2da8/.
7. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2019 [cited 2/28/19]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/13/19.

GUIDELINE UPDATE INFORMATION:

06/15/17	New Medical Coverage Guideline.
7/15/17	Revision to guideline; Updated position statement with new Kisqali Femara Co-Pack formulation.
01/15/18	Revision to guideline; updated position statement with NCCN recommendations.
04/15/18	Review and revision to guideline; updated description and references.
12/15/18	Revision to guideline; updated position statement.
04/15/19	Review and revision to guideline; updated description and references.
12/15/19	Revision to position statement
3/15/20	Revision to position statement