Clinical Policy: Ribociclib (Kisqali), Ribociclib/Letrozole (Kisqali Femara)

Reference Number: PA.CP.PHAR.334
Effective Date: 01/18
Last Review Date: 01/19

Coding Implications
Revision Log

Description
Ribociclib (Kisqali®) is an inhibitor of cyclin-dependent kinases 4 and 6 (CDK4/6). Letrozole (Femara®) is an aromatase inhibitor.

FDA Approved Indication(s)
Kisqali (in combination with an aromatase inhibitor) and Kisqali Femara are indicated as initial endocrine-based therapy for the treatment of pre/perimenopausal or postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

Kisqali is also indicated in combination with fulvestrant as initial endocrine based therapy or following disease progression on endocrine therapy for the treatment of postmenopausal women with HR-positive, HER2-negative advanced breast cancer.

Policy/Criteria
It is the policy of health plans affiliated with Pennsylvania Health and Wellness® that Kisqali is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Breast Cancer (must meet all):

1. Diagnosis of breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Disease has all of the following characteristics (a, b, and c):
   a. HR-positive (i.e., estrogen receptor (ER) and/or progesterone receptor (PR) positive);
   b. HER2-negative;
   c. Advanced (locally or recurrent) or metastatic;
5. If request is for Kisqali, therapy is prescribed in combination with one of the following (a, b, or c):
   a. An aromatase inhibitor (e.g., letrozole, anastrozole, exemestane);
   b. Fulvestrant;
   c. Tamoxifen (off-label), and medical justification supports need to use tamoxifen over an aromatase inhibitor or fulvestrant;
6. If male (off-label) and receiving an aromatase inhibitor, therapy is prescribed in combination with an agent that suppresses testicular steroidogenesis (e.g., gonadotropin-releasing hormone agonists);
7. Request meets one of the following (a or b):
   a. Dose does not exceed Kisqali 600 mg per day (3 tablets per day for 21 days) and Femara 2.5 mg per day (1 tablet per day for 28-day cycle);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Breast Cancer (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. Dose of Kisqali is ≥ 200 mg/day;

4. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed Kisqali 600 mg per day (3 tablets per day for 21 days) and Femara 2.5 mg per day (1 tablet per day for 28-day cycle);
   b. New dose is supported by practice guideline or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
   Approval duration: per request or 6 months (whichever is less);

2. Refer to PA.CP.PMN.53

Background

Description/Mechanism of Action:

Kisqali is a cyclin-dependent kinase (CDK) 4 and 6 inhibitor. These kinases are activated upon binding to D-cyclins and play a crucial role in signaling pathways which lead to cell cycle progression and cellular proliferation. The cyclin D-CDK4/6 complex regulates cell cycle progression through phosphorylation of the retinoblastoma protein (pRb).

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CDK: cyclin-dependent kinase
ER: estrogen receptor
FDA: Food and Drug Administration
HER2: human epidermal growth factor receptor 2
HR: hormone receptor
NCCN: National Comprehensive Cancer Network
PR: progesterone receptor

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information

- The NCCN recommends that men with breast cancer be treated similarly to postmenopausal women, except that the use of an aromatase inhibitor is ineffective without concomitant suppression of testicular steroidogenesis.
- When used for the treatment of premenopausal women, the NCCN recommends that patients should also be treated with ovarian ablation/suppression. Ovarian ablation can be achieved with surgical oophorectomy or ovarian irradiation. Ovarian suppression can be achieved with luteinizing hormone-releasing hormone agonists (e.g., goserelin, leuprolide).
- For disease progression while on a CDK4/6 inhibitor, there is no data to support retreatment with another CDK4/6 inhibitor-containing regimen.
- Although the NCCN currently supports the use of Kisqali with tamoxifen (category 1; breast cancer guidelines v1.2018), a warning was recently added to Kisqali's prescribing information noting concerns for increased QT prolongation observed with concomitant use in the MONALEESA-7 trial.

IV. Dosage and Administration

Drug Name	Dosing Regimen*	Maximum Dose
Ribociclib (Kisqali)	600 mg PO QD for 21 consecutive days followed by 7 days off	600 mg/day
Ribociclib/letrozole (Kisqali Femara)	600 mg Kisqali PO QD for 21 consecutive days followed by 7 days off 2.5 mg Femara PO QD for a 28-day cycle	Kisqali: 600 mg/day Femara: 2.5 mg/day

**If the dose of Kisqali is reduced to < 200 mg/day, therapy should be discontinued.*

V. Product Availability

Drug Name	Availability
Ribociclib (Kisqali)	Tablets: 200 mg
Ribociclib/letrozole (Kisqali Femara)	Tablets: 200 mg ribociclib, 2.5 mg letrozole

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
Added requirement for prescriber specialty. Added criteria for off-label use in men. References reviewed and updated.	02/18	
4Q 2018 annual review: criteria added for new FDA indications: use in combination with an aromatase inhibitor for pre- and perimenopausal women and use in combination with fulvestrant for postmenopausal women; age requirement added; clarified that men should receive an aromatase inhibitor with an agent that suppresses testicular steroidogenesis; added option for use in combination with tamoxifen per NCCN; references reviewed and updated.	01/19	

References

1. Kisqali Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2018. Available at https://www.kisqali.com/. Accessed July 18, 2018.
2. Kisqali Femara Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2018. Available at https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/kisqali_copack.pdf. Accessed July 18, 2018.
3. National Comprehensive Cancer Network. Breast Cancer Version 1.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 18, 2018.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 18, 2018.