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

Reference Number: ERX.SPA.51
Effective Date: 06.01.17
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 or metastatic breast cancer.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Kisqali and Kisqali Femara are **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, recurrent, or metastatic;
5. If request is for Kisqali, therapy is prescribed in combination with one of the following (a or b):
   a. An aromatase inhibitor (e.g., letrozole, anastrozole, exemestane) as part of initial endocrine based therapy;
   b. Fulvestrant;
6. If request is for Kisqali Femara, prescribed as initial endocrine based therapy;
7. 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);
8. If member is a premenopausal female, member has been treated with ovarian ablation or is receiving ovarian suppression (*see Appendix D*);
9. Member has not previously experienced disease progression on a CDK 4/6 inhibitor therapy (e.g., Verzenio®, Ibrance®);

10. The requested agent is not prescribed concurrently with another CDK 4/6 inhibitor therapy (e.g., Verzenio, Ibrance);
11. 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 6 months

B. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Breast Cancer (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Kisqali or Kisqali Femara for breast cancer and has received this medication for at least 21 days;
2. Member is responding positively to therapy;
3. Dose of Kisqali is ≥ 200 mg per day;
4. The requested agent is not prescribed concurrently with another CDK 4/6 inhibitor therapy (e.g., Verzenio, Ibrance);
5. 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CDK: cyclin-dependent kinase
ER: progesterone 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
- Contraindication(s): Kisqali Femara only – known hypersensitivity to letrozole, or to any excipients of Femara
- Boxed warning(s): none reported

Appendix D: General Information
- For disease progression while on a CDK4/6 inhibitor, there is no data to support retreatment with another CDK4/6 inhibitor-containing regimen.
- The NCCN no longer supports the use of Kisqali with tamoxifen (previously category 1; removed from the breast cancer guidelines as of v1.2020). In addition, there is a warning in Kisqali's prescribing information noting concerns for increased QT prolongation observed with concomitant use in the MONALEESA-7 trial.
- Ovarian ablation may be accomplished by surgical oophorectomy or by ovarian irradiation. Ovarian suppression utilizes luteinizing hormone-releasing hormone (LHRH) agonists that result in suppression of luteinizing hormone and release of follicle-stimulating hormone from pituitary and reduction in ovarian estrogen production. LHRH agonists include goserelin and leuprolide.

V. 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 a dose reduction to < 200 mg/day is required, therapy should be discontinued.*

VI. Product Availability

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

VII. References

1. Kisqali Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020. Available at: https://www.kisqali.com/. Accessed June 30, 2021.
2. Kisqali Femara Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/209935s008lbl.pdf. Accessed June 30, 2021.
3. National Comprehensive Cancer Network. Breast Cancer Version 4.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed July 14, 2020.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed June 30, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	03.17	05.17
1Q18 annual review: Converted to new template. Added requirement for prescriber specialty. Added criteria for off-label use in men. Approval durations modified to length of benefit.	11.17	02.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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.	08.28.18	11.18
4Q 2019 annual review: no significant changes; added Medicaid line of business with 6/12 month approval durations; references reviewed and updated.	08.12.19	11.19
4Q 2020 annual review: removed option for combination use with tamoxifen as this is no longer NCCN supported; added that member has not previously failed another CDK 4/6 inhibitor therapy; references reviewed and updated.	07.15.20	11.20
Clarified that combination use with an aromatase inhibitor should be for initial endocrine based therapy per FDA/NCCN and added that premenopausal women should be treated with ovarian ablation/suppression per NCCN; added requirement for no concurrent use with another CDK 4/6 inhibitor therapy.	06.30.21	08.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.