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

Reference Number: CP.PHAR.334
Effective Date: 05.01.17
Last Review Date: 11.24
Line of Business: Commercial, HIM, 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 (CDK 4/6). Letrozole (Femara®) is an aromatase inhibitor.

FDA Approved Indication(s)

Kisqali (in combination with an aromatase inhibitor) and Kisqali Femara are indicated:

- For the adjuvant treatment of adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative stage II and III early breast cancer at high risk of recurrence
- As initial endocrine-based therapy for the treatment of adults with HR-positive, HER2-negative advanced or metastatic breast cancer

Kisqali is also indicated in combination with fulvestrant as initial endocrine-based therapy or with disease progression following endocrine therapy for the treatment of adults 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.

It is the policy of health plans affiliated with Centene Corporation® 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 both of the following characteristics (a and b):
   a. HR-positive (i.e., estrogen receptor (ER) and/or progesterone receptor (PR) positive);
   b. HER2-negative;
5. Disease meets one of the following (a or b):
   a. Advanced, recurrent, or metastatic;
   b. Stage II or Stage III early breast cancer at high risk of recurrence;

6. 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 or as adjuvant therapy;
   b. Fulvestrant;
7. If request is for Kisqali Femara, prescribed as initial endocrine-based therapy or as adjuvant therapy;
8. If male and receiving an aromatase inhibitor, therapy is prescribed in combination with an agent that suppresses testicular steroidogenesis (e.g., gonadotropin-releasing hormone agonists);
9. If member is a premenopausal or perimenopausal female, member has been treated with ovarian ablation or is receiving ovarian suppression (*see Appendix D*);
10. Member has not previously experienced disease progression on a CDK 4/6 inhibitor therapy (e.g., Verzenio®, Ibrance®);
11. The requested agent is not prescribed concurrently with another CDK 4/6 inhibitor therapy (e.g., Verzenio, Ibrance);
12. For brand Kisqali requests, member must use generic ribociclib, if available, unless contraindicated or clinically significant adverse effects are experienced;
13. Request meets one of the following (a, b, or c):*
    a. For advanced, recurrent, or metastatic breast cancer (i or ii):
       i. For Kisqali: Dose does not exceed Kisqali 600 mg (3 tablets) per day for 21 days of each 28-day cycle;
       ii. For Kisqali Femara: Dose does not exceed Kisqali 600 mg (3 tablets) per day for 21 days of each 28-day cycle and Femara 2.5 mg (1 tablet) per day for each 28-day cycle;
    b. For early breast cancer (i or ii):
       i. For Kisqali: Dose does not exceed 400 mg (2 tablets) per day for 21 consecutive days of each 28-day cycle;
       ii. For Kisqali Femra: Dose does not exceed Kisqali 400 mg (2 tablets) per day for 21 days of each 28-day cycle and Femara 2.5 mg (1 tablet) per day for each 28-day cycle;
    c. 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:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Endometrial Carcinoma (off-label) (must meet all)**:**
1. Diagnosis of endometrial carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Presence of ER-positive tumors;
5. If request is for Kisqali, prescribed in combination with letrozole;
6. Kisqali is not prescribed concurrently with another CDK 4/6 inhibitor therapy (e.g., Verzenio, Ibrance);

7. For brand Kisqali requests, member must use generic ribociclib, if available, unless contraindicated or clinically significant adverse effects are experienced;
8. Dose is within FDA maximum limit for any FDA-approved indication or 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: 6 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Kisqali or Kisqali Femara for a covered indication and has received this medication for at least 21 days;
2. Member is responding positively to therapy;
3. If breast cancer, 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. For brand Kisqali requests, member must use generic ribociclib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. For advanced, recurrent, or metastatic breast cancer (i or ii):
      i. For Kisqali: New dose does not exceed Kisqali 600 mg (3 tablets) per day for 21 days of each 28-day cycle;
      ii. For Kisqali Femara: New dose does not exceed Kisqali 600 mg (3 tablets) per day for 21 days of each 28-day cycle and Femara 2.5 mg (1 tablet) per day for each 28-day cycle;

b. For early breast cancer (i or ii):
   i. For Kisqali: New dose does not exceed 400 mg (2 tablets) per day for 21 consecutive days of each 28-day cycle;
   ii. For Kisqali Femra: New dose does not exceed Kisqali 400 mg (2 tablets) per day for 21 days of each 28-day cycle and Femara 2.5 mg (1 tablet) per day for each 28-day cycle;
c. New 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:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. 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
- 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)	**Advanced or metastatic breast cancer:** 600 mg PO QD for 21 consecutive days followed by 7 days off **Early breast cancer:** 400 mg PO QD for 21 consecutive days followed by 7 days off In patients with early breast cancer, treatment with Kisqali should continue for 3 years or until disease recurrence or unacceptable toxicity occurs.	**Advanced or metastatic breast cancer:** 600 mg/day **Early breast cancer:** 400 mg/day
Ribociclib/letrozole (Kisqali Femara)	**Advanced or metastatic breast cancer:** 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 **Early breast cancer:** 400 mg Kisqali PO QD for 21 consecutive days followed by 7 days off 2.5 mg Femara PO QD for a 28-day cycle	**Advanced or metastatic breast cancer:** Kisqali: 600 mg/day Femara: 2.5 mg/day **Early breast cancer:** Kisqali: 400 mg/day Femara: 2.5 mg/day

Drug Name	Dosing Regimen*	Maximum Dose
	In patients with early breast cancer, treatment with Kisqali should continue for 3 years or until disease recurrence or unacceptable toxicity occurs.	

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

VI. Product Availability

Drug Name	Availability
Ribociclib (Kisqali)	Tablet: 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; September 2024 Available at: https://www.novartis.com/us-en/sites/novartis_us/files/kisqali.pdf. Accessed October 15, 2024.
2. Kisqali Femara Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2024. Available at: https://www.novartis.com/us-en/sites/novartis_us/files/kisqali_copack.pdf. Accessed October 15, 2024.
3. National Comprehensive Cancer Network. Breast Cancer Version 5.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed October 15, 2024.
4. National Comprehensive Cancer Network. Uterine Neoplasms Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed August 6, 2024.
5. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed October 15, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2020 annual review: added HIM line of business; 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
4Q 2021 annual review: no significant changes; references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	08.12.21	11.21
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2022 annual review: no significant changes; revised FDA Approved Indications section per updated language in PI; added standard template verbiage for redirection to generic product, if available; references reviewed and updated. Template changes applied to other diagnoses/indications.	07.29.22	11.22
4Q 2023 annual review: no significant changes; clarified maximum dosing for Kisqali and Kisqali Femara by separating dosing into two criteria for initial approval and continued therapy sections; references reviewed and updated.	07.03.23	11.23
4Q 2024 annual review: RT4: for Kisqali, updated the FDA approved indication for use in combination with fulvestrant to reflect the population expansion from "in postmenopausal women or in men" to "adults"; for initial therapy, added "perimenopausal female" to the requirement for ovarian ablation/suppression; added criteria for endometrial carcinoma as off-label indication is supported by NCCN compendium and guidelines; references reviewed and updated. RT4: for Kisqali and Kisqali Femara, added criteria for newly approved indication for adjuvant treatment of adults with HR-positive, HER2-negative stage II and III early breast cancer at high risk of recurrence.	10.15.24	11.24

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.