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

Reference Number: CP.PHAR.334
Effective Date: 05.01.17
Last Review Date: 11.20
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 (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.

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 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);
   b. 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. Member has not previously experienced disease progression on a CDK 4/6 inhibitor therapy (e.g., Verzenio®, Ibrance®);
8. 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:
Medicaid/HIM – 6 months
Commercial – Length of Benefit

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, 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. 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:
Medicaid/HIM – 12 months
Commercial – Length of Benefit

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 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.PHAR.21 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.

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 July 14, 2020.
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 July 14, 2020.
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 July 14, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04.17	04.17
1Q18 annual review: Combined with CP.CPA.222. Converted to new template Added requirement for prescriber specialty Added criteria for off-label use in men References reviewed and updated.	11.17	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; commercial: modified approval durations to length of benefit; references reviewed and updated.	08.28.18	11.18
4Q 2019 annual review: no significant changes; references reviewed and updated.	08.12.19	11.19
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

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.