Clinical Policy Title:	ribociclib, ribociclib-letrozole
Policy Number:	RxA.181
Drug(s) Applied:	Kisqali®, Kisqali® Femara® Co-Pack
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

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

Ribociclib, in combination with an aromatase inhibitor, and ribociclib-letrozole 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.

Ribociclib 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
ribociclib (Kisqali®)	Breast cancer	600 mg orally once a day for 21 consecutive days followed by 7 days off	600 mg/day
ribociclib/letrozole (Kisqali® Femara® Co-Pack)	Breast cancer	600 mg ribociclib orally once a day for 21 consecutive days followed by 7 days off 2.5 mg letrozole orally once a day for a 28-day cycle	ribociclib: 600 mg/day letrozole: 2.5 mg/day

*If the dose of ribociclib is reduced to less than 200 mg/day, therapy should be discontinued.

Dosage Forms

- Ribociclib (Kisqali®): Tablets: 200 mg
- Ribociclib/letrozole (Kisqali® Femara® Co-Pack): Tablets: 200 mg ribociclib, 2.5 mg letrozole

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the

terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

1. Diagnosis of recurrent or stage IV breast cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years of age or older;
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 recurrent) or metastatic;
5. If request is for ribociclib, 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 ribociclib 600 mg per day (3 tablets per day for 21 days) and letrozole 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: 12 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is currently receiving ribociclib or ribociclib-letrozole for breast cancer and has received this medication for at least 21 days;
3. Member is responding positively to therapy;
4. Dose of ribociclib is at least 200 mg per day;
5. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed ribociclib 600 mg per day (3 tablets per day for 21 days) and letrozole 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: 12 months
Medicaid: 12 months

III. Appendices

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):
  - None.

- Boxed Warning(s): None
  - None.

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.
- 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.

References

1. Kisqali® Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020. Available at: https://www.kisqali.com/. Accessed March 31, 2021.
2. Kisqali® Femara® Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2020. Available at: https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/kisqali_copack .pdf. Accessed March 31, 2021.
3. National Comprehensive Cancer Network. Breast Cancer Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed March 31, 2021.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed March 31, 2021.
5. Kisqali® Femara®. In: Lexicomp Online Drug Database [database on the Internet]. Hudson, Ohio: Lexicomp, Inc.; 2021 [updated March 17, 2021]. Available at: http://online.lexi.com. Subscription required to view. Accessed March 31, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	03/2020	02/07/2020
Policy updated. 1. Formatting updated.	07/28/2020	09/14/2020

2. Clinical title updated. 3. Continued criteria for approval updated. 4. Approval duration updated. 5. Reference updated.		
Policy was reviewed: 1. Clinical policy section standard verbiage was updated to include “The provision of prescriber samples…”. 2. Continued therapy approval criteria II.A.1 was updated to “Member is currently receiving medication…”. 3. References were updated.	03/31/2021	06/10/2021