Pharmacy Policy Bulletin: J-0891 CDK Inhibitors - Commercial and Healthcare Reform	
Number: J-0891	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes with Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0891-016	**Original Date:** 06/04/2003
Effective Date: 07/18/2025	**Review Date**: 06/25/2025

Drugs Product(s):	• Ibrance (palbociclib) • Kisqali (ribociclib) • Kisqali Femara Co-Pack (ribociclib; letrozole) • Verzenio (abemaciclib)

FDA-Approved Indication(s):	• Ibrance (palbociclib)
	  ○ Treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:
	  ▪ An aromatase inhibitor as initial endocrine-based therapy
	  ▪ Fulvestrant in patients with disease progression following endocrine therapy
	  ○ In combination with inavolisib and fulvestrant for the treatment of adult patients with endocrine-resistant, *PIK3CA*-mutated, HR-positive, HER2-negative, locally advanced or metastatic breast cancer, as detected by an FDA-approved test, following recurrence on or after completing adjuvant endocrine therapy.
	• Kisqali (ribociclib)
	  ○ In combination with an aromatase inhibitor for the adjuvant treatment of adults with HR-positive, HER2-negative stage II and III early breast cancer at high risk of recurrence.
	  ○ Treatment of adults with HR-positive, HER2-negative advanced or metastatic breast cancer in combination with:
	  ▪ An aromatase inhibitor as initial endocrine-based therapy; or
	  ▪ Fulvestrant as initial endocrine-based therapy or with disease progression following endocrine therapy
	• Kisqali Femara Co-Pack (ribociclib; letrozole)
	  ○ Adjuvant treatment of adults with HR-positive, HER2-negative stage II and III early breast cancer at high risk of recurrence.
	  ○ Initial endocrine-based therapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer.
	• Verzenio (abemaciclib)

	○ In combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with HR-positive, HER2-negative, node-positive, early breast cancer at high risk of recurrence. ○ In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer. ○ In combination with fulvestrant for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy. ○ Monotherapy for the treatment of adult patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting.

Background:	• Ibrance, Kisqali, Kisqali Femara Co-Pack, and Verzenio are inhibitors of cyclin-dependent kinase (CDK) 4 and 6. Cyclin D1 and CDK4/6 are downstream of signaling pathways which lead to cellular proliferation. These medications block progression of the cell from G1 into S phase of the cell cycle and reduce breast cancer proliferation. • Endocrine-based therapy includes drugs such as aromatase inhibitors (anastrozole, exemestane, letrozole), fulvestrant, and tamoxifen, among others. • For information regarding FDA-approved companion diagnostics, please visit: https://www.fda.gov/medical-devices/vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-vitro-and-imaging-tools. • Prescribing Considerations: ○ Pre/perimenopausal women treated with Verzenio plus fulvestrant should be treated with a gonadotropin-releasing hormone (GnRH) agonist according to current clinical practice standards. ○ Kinase inhibitors should be prescribed under the supervision of a hematologist/oncologist. ○ NCCN guidelines state that if there is disease progression while using CDK4/6 therapy, there are limited data available to support additional therapy of another CDK4/6 agent. ○ The safety and efficacy of Ibrance, Kisqali, Kisqali Femara Co-Pack, or Verzenio in pediatric patients have not been established.

Approval Criteria

I. Initial Authorization

A. Ibrance

1. Use in Combination with an Aromatase Inhibitor or fulvestrant

When a benefit, coverage of Ibrance may be approved when all of the following criteria are met **(a. through e.)**:

a. The member is 18 years of age or older.

b. The member has a diagnosis of advanced or metastatic breast cancer (ICD-10: C50).

c. Disease is HR-positive, HER2-negative.

d. The member meets one (1) of the following criteria **(i. or ii.)**:

i. The member meets all of the following criteria **(A) and B))**:

A) Ibrance is being used as initial endocrine-based therapy.

B) Ibrance is being used in combination with an aromatase inhibitor (e.g., letrozole, exemestane).

ii. The member meets all of the following criteria **(A) and B))**:

A) Ibrance is being used in patients with disease progression following endocrine-based therapy.
B) Ibrance is being used in combination with fulvestrant.

e. The member has experienced therapeutic failure, contraindication, or intolerance to one (1) of the following plan-preferred products **(i. or ii.)**:
i. Kisqali
ii. Verzenio

2. Use in Combination with Itovebi and fulvestrant
When a benefit, coverage of Ibrance may be approved when all of the following criteria are met **(a. through f.)**:
a. The member is 18 years of age or older.
b. The member has a diagnosis of endocrine-resistant, locally advanced or metastatic breast cancer (ICD-10: 50).
c. Disease is HR-positive, HER2-negative.
d. Disease is *PIK3CA*-mutated, as detected by an FDA-approved test.
e. The member is using Ibrance in combination with all of the following **(i. and ii.)**:
i. inavolisib (Itovebi)
ii. fulvestrant
f. The member has experienced recurrence on or after completing adjuvant endocrine therapy.

B. Kisqali

1. Stage II and III Early Breast Cancer at High Risk of Recurrence
When a benefit, coverage of Kisqali may be approved when all of the following criteria are met **(a. through f.):**
a. The member is 18 years of age or older.
b. The member has a diagnosis of early breast cancer (ICD-10: C50), classified as one (1) of the following **(i. or ii)**:
i. Stage II
ii. Stage III
c. Disease is HR-positive, HER2-negative.
d. Disease is at high risk of recurrence.
e. The member is using Kisqali in combination with an aromatase inhibitor.
f. Kisqali is being used as adjuvant treatment.

2. Advanced or Metastatic Breast Cancer
When a benefit, coverage of Kisqali may be approved when all of the following criteria are met **(a. through d.):**
a. The member is 18 years of age or older.
b. The member has a diagnosis of advanced or metastatic breast cancer (ICD-10: C50).
c. Disease is HR-positive, HER2-negative.
d. The member meets one (1) of the following criteria **(i. or ii.):**
i. The member is using Kisqali in combination with an aromatase inhibitor as initial endocrine-based therapy.
ii. The member is using Kisqali in combination with fulvestrant and meets one (1) of the following criteria **(A). or B)):**
A) The member is using fulvestrant as initial endocrine-based therapy.
B) The member has experienced disease progression on endocrine therapy.

C. Kisqali Femara Co-Pack

1. Stage II and III Early Breast Cancer at High Risk of Recurrence
When a benefit, coverage of Kisqali Femara Co-Pack may be approved when all of the following criteria are met **(a. through e.):**
a. The member is 18 years of age or older.

b. The member has a diagnosis of early breast cancer (ICD-10: C50), classified as one (1) of the following **(i. or ii)**:
  i. Stage II
  ii. Stage III
c. Disease is HR-positive, HER2-negative.
d. Disease is at high risk of recurrence.
e. The member is using Kisqali Femara Co-Pack as adjuvant treatment.

2. Advanced or Metastatic Breast Cancer
When a benefit, coverage of Kisqali Femara Co-Pack may be approved when all of the following criteria are met **(a. through d.):**
a. The member is 18 years of age or older.
b. The member has a diagnosis of advanced or metastatic breast cancer (ICD-10: C50).
c. Disease is HR-positive, HER2-negative.
d. Kisqali Femara Co-Pack is being used as initial endocrine-based therapy.

D. Verzenio
When a benefit, coverage of Verzenio may be approved when all of the following criteria are met **(1., 2., and 3.):**
1. The member is 18 years of age or older.
2. Disease is HR-positive, HER2-negative.
3. The member meets one (1) of the following criteria **(a. through d.):**
  a. The member meets all of the following criteria **(i., ii., and iii.)**:
    i. The member has a diagnosis of early breast cancer (ICD-10: C50) meeting all of the following criteria **(A) and B))**:
      A) Disease is at high risk of recurrence.
      B) Disease is node-positive.
    ii. Verzenio is being used in combination with endocrine therapy (tamoxifen or an aromatase inhibitor).
    iii. Verzenio is being used as adjuvant treatment.
  b. The member meets all of the following criteria **(i., ii., and iii.)**:
    i. The member has a diagnosis of advanced or metastatic breast cancer (ICD-10: C50).
    ii. Verzenio is being used as initial endocrine-based therapy.
    iii. Verzenio is being used in combination with an aromatase inhibitor (e.g., letrozole, exemestane)
  c. The member meets all of the following criteria **(i., ii., and iii.)**:
    i. The member has a diagnosis of advanced or metastatic breast cancer (ICD-10: C50).
    ii. Verzenio is being used after disease progression following endocrine therapy.
    iii. Verzenio is being used in combination with fulvestrant.
  d. The member meets all of the following criteria **(i. through iv.)**:
    i. The member has a diagnosis of advanced or metastatic breast cancer (ICD-10: C50).
    ii. Verzenio is being used after disease progression.
    iii. Verzenio is being used following endocrine therapy and prior chemotherapy in the metastatic setting.
    iv. Verzenio will be used as monotherapy.

II. Reauthorization
When a benefit, reauthorization of a CDK inhibitor may be approved when the following criterion is met **(A.)**:
A. The prescriber attests that the member is tolerating therapy and has experienced a therapeutic response defined as either one (1) of the following **(1. or 2.)**:
  1. Disease improvement
  2. Delayed disease progression

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology medications listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

Refer to J-699 and J-650 for previous versions.

References:

1. Ibrance [package insert]. New York, NY: Pfizer Labs.; April 2025.
2. Itovebi [package insert]. San Francisco, CA: Genentech USA, Inc.; October 2024.
3. Kisqali [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2024.
4. Kisqali Femara Co-Pack [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2024.
5. Verzenio [package insert]. Indianapolis, IN; Eli Lilly and Company; March 2023.
6. NCCN Guidelines. Breast Cancer. v.1.2024 National Comprehensive Cancer Network. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast_blocks.pdf. Accessed February 22, 2024.