Washington State Health Care Authority

Cyclin-Dependent Kinase (CDK) 4/6 Inhibitors – abemaciclib, palbociclib, ribociclib

Medical policy no. **.**.**-* Effective Date: Month, 1, Year

Related medical policies:

Policy Name	Indications
N/A	N/A

Note: *New-to-market drugs included in this class based on the Apple Health Preferred Drug List are non-preferred and subject to this prior authorization (PA) criteria. Non-preferred agents in this class require an inadequate response or documented intolerance due to severe adverse reaction or contraindication to at least TWO preferred agents. If there is only one preferred agent in the class documentation of inadequate response to ONE preferred agent is needed. If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling.*

To see the list of the current Apple Health Preferred Drug List (AHPDL), please visit: https://www.hca.wa.gov/assets/billers-and-providers/apple-health-preferred-drug-list.xlsx

Medical necessity

Drug	Medical Necessity
Abemaciclib (Verzenio) Palbociclib (Ibrance) Ribociclib (Kisqali) Ribociclib/letrozole (Kisqali/Femara)	**Cyclin-Dependent Kinase (CDK) Inhibitors** may be considered medically necessary in patients who meet the criteria described in the clinical policy below. If all criteria are not met, the clinical reviewer may determine there is a medically necessary need and approve on a case-by-case basis. The clinical reviewer may choose to use the reauthorization criteria when a patient has been previously established on therapy and is new to Apple Health.

Clinical policy:

Clinical Criteria	
Adjuvant therapy of early-stage (stage I-III) breast cancer (EBC) Abemaciclib (Verzenio)	Abemaciclib (Verzenio) may be approved when all of the following documented criteria are met: 1. Patient is 18 years of age or older, **AND** 2. Prescribed by, or in consultation with, an oncologist; **AND** 3. Patient has <u>not</u> previously progressed on, or after treatment with another CDK4/6 inhibitor (e.g., ribociclib [Kisqali], abemaciclib [Verzenio]); **AND**

4. Diagnosis of hormone receptor-positive (HR+) and HER2-negative (HER2-) breast cancer; **AND**
5. The request is for adjuvant therapy of early-stage (stage I- III) breast cancer (EBC); **AND**
6. Provider attests the patient has high-risk breast cancer based on one the following:
    - **a.** Histopathological tests showing four or more (≥ 4) axillary lymph nodes are affected (pALN N2 or N3 disease); **OR**
    - b. Histopathological tests showing one to three axillary lymph nodes are affected, and one of the following:
        - i. Tumor size is ≥ 5 cm; **OR**
        - ii. Histopathological grade 3 disease (G3); **OR**
        - iii. The patient has a Ki-67 score ≥ 20% as determined by an FDA-approved test; **AND**
7. The patient has undergone definitive surgical resection of the primary tumor; **AND**
8. History of failure or intolerance using one of the following treatment modalities:
    - a. Radiotherapy; **OR**
    - b. Taxane-based (e.g., docetaxel) or anthracycline-based (e.g., doxorubicin) chemotherapy; **AND**
9. Abemaciclib (Verzenio) will be used in combination with aromatase inhibitor (e.g., letrozole, anastrozole, exemestane) or tamoxifen; **AND**
10. Will not be used in combination with any additional oncology therapy.

If ALL criteria are met, the request will be authorized for **6 months.**

Criteria (Reauthorization)

Abemaciclib (Verzenio) may be approved when all of the following documented criteria are met:

1. Not used in combination with any other oncolytic medication with the exception of an aromatase inhibitor (e.g., anastrozole, letrozole) or estrogen receptor antagonist (e.g., tamoxifen, fulvestrant); **AND**
2. Documentation is submitted demonstrating disease stability or a positive clinical response [e.g., decrease in tumor size or tumor spread].

If ALL criteria are met, the request will be authorized for **6 months.**

Systemic therapy of recurrent, advanced, or metastatic breast cancer Abemaciclib (Verzenio) Palbociclib (Ibrance) Ribociclib (Kisqali) Ribociclib/letrozole (Kisqali/Femara)	Abemaciclib (Verzenio), palbociclib (Ibrance), ribociclib (Kisqali), and ribociclib/letrozole (Kisqali/Femara) may be approved when all of the following documented criteria are met: 1. Patient is 18 years of age or older, **AND** 2. Prescribed by, or in consultation with, an oncologist; **AND** 3. Patient has <u>not</u> previously progressed on, or after treatment with another CDK4/6 inhibitor (e.g., ribociclib [Kisqali], abemaciclib [Verzenio]); **AND** 4. Diagnosis of hormone receptor-positive (HR+) and HER2-negative (HER2-) breast cancer; **AND** 5. Patient has a diagnosis of advanced (stage III), or metastatic (stage IV) breast cancer; **AND** 6. The medication is being prescribed as a <u>first-line systemic therapy</u>; **AND** a. The medication will be used in combination with an aromatase inhibitor (e.g., letrozole, anastrozole, exemestane) or fulvestrant; **AND** b. Will not be used in combination with any additional oncology therapy; **AND** c. The patient is a postmenopausal female, premenopausal or perimenopausal female receiving ovarian suppression/ablation (e.g., surgical ablation, suppression with GnRH therapy [e.g., leuprolide], etc.); **OR** i. The patient is hormone suppressed male (e.g., GnRH therapy [e.g., leuprolide] used concomitantly); **OR** 7. The medication is being prescribed as a <u>second-line systemic therapy</u>; **AND** a. The medication will be used in combination with fulvestrant (Faslodex); **AND** b. Will not be used in combination with any additional oncology therapy; **AND** c. The patient had disease progression on, or after primary endocrine therapy (as adjuvant or first-line systemic therapy); **AND** d. The patient is a postmenopausal female, premenopausal or perimenopausal female receiving ovarian suppression/ablation (e.g., surgical ablation, suppression with GnRH therapy [e.g., leuprolide], etc.); **OR** i. The patient is hormone suppressed male (e.g., GnRH therapy [e.g., leuprolide] used concomitantly); **OR**

	8. The medication is being prescribed for subsequent-line (3rd line or later) systemic therapy in metastatic (stage IV, M1) setting; **AND** a. Patient had disease progression on, or after endocrine therapy AND systemic chemotherapy (not containing a CDK 4/6 inhibitor) in the metastatic (stage IV) setting; **AND** b. The request is for abemaciclib (Verzenio) monotherapy. If ALL criteria are met, the request will be authorized for **6 months.**
	Criteria (Reauthorization) Abemaciclib (Verzenio), palbociclib (Ibrance), ribociclib (Kisqali), and ribociclib/letrozole (Kisqali/Femara) may be approved when all of the following documented criteria are met: 1. Not used in combination with any other oncolytic medication with the exception of an aromatase inhibitor (e.g., anastrozole, letrozole) or estrogen receptor antagonist (e.g., tamoxifen, fulvestrant); **AND** 2. Documentation is submitted demonstrating disease stability or a positive clinical response [e.g., decrease in tumor size or tumor spread]. If ALL criteria are met, the request will be authorized for **6 months.**

Dosage and quantity limits

Drug	Indication	FDA Approved Dosing	Dosage Form and Quantity Limit
Abemaciclib (Verzenio)	Breast cancer, HER2-negative, HR-positive, advanced or metastatic; early-stage breast cancer	150 mg to 200 mg twice daily	• 50 mg tablets: 56 tablets per 28 days • 100 mg tablets: 56 tablets per 28 days • 150 mg tablets: 56 tablets per 28 days • 200 mg tablets: 56 tablets per 28 days
Palbociclib (Ibrance)	Breast cancer, HER2-negative, HR-positive, advanced or metastatic	125 mg once daily (21 consecutive days on, 7 days off)	• 75 mg capsule/tablet: 21 capsules or tablets per 28 days • 100 mg capsule/tablet: 21 capsules or tablets per 28 days

			• 125 mg capsule/tablet: 21 capsules or tablets per 28 days
Ribociclib (Kisqali)	Breast cancer, HER2-negative, HR-positive, advanced or metastatic	600 mg once daily (21 consecutive days on, 7 days off)	• 200 mg tablet dose pack: 21 tablets per 28 days • 400 mg tablet dose pack: 42 tablets per 28 days • 600 mg tablet dose pack: 64 tablets per 28 days
Ribociclib/ letrozole (Kisqali/ Femara)	Breast cancer, HER2-negative, HR-positive, advanced or metastatic	600 mg once daily (21 consecutive days on, 7 days off) Letrozole 2.5 mg once daily	• 200 mg and 2.5 mg tablet dose pack: 49 tablets per 28 days • 400 mg and 2.5 mg tablet dose pack: 70 tablets per 28 days • 600 mg and 2.5 mg tablet dose pack: 91 tablets per 28 days

Coding:

HCPCS Code	Description
N/A	N/A

Background:

Many treatment options exist for advanced and metastatic breast cancer. Abemaciclib (Verzenio), palbociclib (Ibrance), and ribociclib (Kisqali) are cyclin-dependent kinase 4 and 6 (CDK 4/6) inhibitors which promote senescence and tumor cell apoptosis. Abemaciclib (Verzenio) was evaluated in the MONARCH-E trial as an early-stage adjuvant therapy for female subjects with HR+, HER2- breast cancer with a high risk of recurrence or metastasis. High risk was defined based on the following key factors: ≥ 4 pALN disease, or 1 to 3 positive ALN in the setting of a tumor of at least 5 cm or larger, or histologic grade 3 disease. A Ki-67 index ≥ 20% in untreated breast tissue as determined by an FDA approved test was required as a marker for high-risk recurrence (Ki-67 is a cancer antigen protein and serves as a marker for tumor cell mitosis). This definition of high-risk breast cancer is consistent with the NCCN guidelines for invasive breast cancer. This study demonstrated a significant improvement in the primary endpoint of invasive disease-free survival (IDFS) in Verzenio versus endocrine therapy alone. Abemaciclib (Verzenio) was also studied in advanced or metastatic HR+, HER2- breast cancer in other MONARCH trials which demonstrated a progression free survival (PFS) and overall survival (OS) benefit. Palbociclib (Ibrance) was evaluated as a first-line or subsequent-line systemic chemotherapy in adult male and female subjects with HR+, HER2-, advanced or metastatic breast cancer in the PALOMA trials demonstrating either a PFS or OS benefit. Ribociclib (Kisqali) was evaluated in adults with HR+, HER2- advanced or metastatic breast cancer in the MONALEESA trials demonstrating either a PFS or OS benefit. The natural incidence of breast cancer in men is rare (<1%), therefore the recommendations are generally extrapolated from the findings of clinical trials in women. All of the CDK4/6 inhibitors above have received FDA approval for treatment of breast cancer in men. Clinical trials to date have not included significant numbers of subjects previously treated with other CDK4/6 inhibitors; thus, safety and efficacy of subsequent administration is unknown at this time. Further, NCCN guidelines note a lack of data to support use of an additional CDK4/6 inhibitor after progression on a CDK4/6 regimen. NCCN guidelines do not currently distinguish a preference between currently available CDK4/6 inhibitors.

References

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History

Approved Date	Effective Date	Version	Action and Summary of Changes
MM/DD/YYY	MM/DD/YYYY	XX.XX.XX-X	Pending Approval (draft/unpublished version) -Updated clinical criteria for indication A to require Lab A. -Added indication for X. -Added new products in class which include Drug A and Drug B. -Updating dosing for Drug A.

			-Updating language at header note to include "If a drug within this policy receives a new indication approved by the Food and Drug Administration (FDA), medical necessity for the new indication will be determined on a case-by-case basis following FDA labeling."
MM/DD/YYY	MM/DD/YYYY	XX.XX.XX-X	Approved by HCA. Updated dosing limits for expanded indication for drug X.
MM/DD/YYY	MM/DD/YYYY	XX.XX.XX-X	Approved by DUR Board.

Appendix

Definitions	
Tumor, node, metastasis (TNM) system	• The tumor, node, metastasis (TNM) TNM system is the most common method of cancer staging in breast cancer. Numbers or letters after T, N, and M give more details about each characteristic. Higher numbers mean the cancer is more advanced. ○ T refers to the size and extent of the main (primary) tumor. ▪ Tis: non-invasive cancer found only in ducts (carcinoma in situ) ▪ TX: Main tumor cannot be measured ▪ T0: Main tumor cannot be found ▪ T1, T2, T3, T4: Refers to the size and/or extent of the main tumor. The higher the number after the T, the larger the tumor or the more it has grown into nearby tissues. T's may be further divided to provide more detail, such as T3a and T3b. ○ The N refers to the number of nearby lymph nodes involved that have cancer ▪ NX: Cancer in nearby lymph nodes cannot be measured (e.g., previously removed, etc.) ▪ N0: There is no cancer in nearby lymph nodes ▪ N1, N2, N3: Refers to the number and location of lymph nodes that contain cancer. The higher the number after the N, the more lymph nodes that contain cancer ○ The M refers to whether the cancer has metastasized ▪ MX: Metastasis cannot be measured ▪ M0: Cancer has not spread to other parts of the body ▪ M1: Cancer has spread to other parts of the body (distant metastasis)

Breast cancer staging	• Breast cancer is often staged before and after surgery. Clinical staging (c) is referred to staging before treatment (cTNM) and pathologic stage (p) is based on the results of tissue samples removed during surgery (pTNM).
Tumor grading	• Tumor grade is dependent on tumor histology. A low-grade tumor has a lower risk of recurrence. A high-grade tumor tend to grow/spread faster and have a higher risk for recurrence.
Ki-67	• A cancer antigen protein and serves as a marker for tumor cell mitosis
Axillary lymph nodes (ALN)	• Receive the majority of lymphatic drainage from all quadrants of the breast and are one of the nodes most likely to be involved in patients with metastatic breast cancer.

Washington State Health Care Authority

CDK Inhibitors

Please provide the information below, please print your answer, attach supporting documentation, sign, date, and return to our office as soon as possible to expedite this request. **Without this information, we may deny the request in seven (7) working days.**

Date of request:	Reference #:	MAS:	
Patient	Date of birth	ProviderOne ID	
Pharmacy name	Pharmacy NPI	Telephone number	Fax number
Prescriber	Prescriber NPI	Telephone number	Fax number
Medication and strength	Directions for use	Qty/Days supply	

1. Is this request for a continuation of existing therapy? ☐ Yes ☐ No
   If yes, is there documentation demonstrating disease stability or a positive clinical response?
   ☐ Yes ☐ No

2. Indicate patient's diagnosis:
   ☐ Adjuvant therapy of early-stage (stage I-III) breast cancer (EBC)
   ☐ Systemic therapy of recurrent, advanced, or metastatic breast cancer
   ☐ Other, specify: _____

3. Indicate stage: _____

4. What is the patients hormone reception and HER2 status?
   Hormone receptor: ☐ Positive ☐ Negative
   HER2: ☐ Positive ☐ Negative

5. Is this being prescribed by or in consultation with an oncologist? ☐ Yes ☐ No

6. Will this medication be used in combination with other agents for the treatment of this diagnosis?
   ☐ No
   ☐ Yes, specify regimen: _____

7. Has patient previously progressed on, or after treatment with another CDK4/6 inhibitor (e.g., ribociclib [Kisqali], abemaciclib [Verzenio])?
   ☐ No
   ☐ Yes, explain: _____

Request for Adjuvant therapy of early-stage (stage I-III) breast cancer (EBC) answer the following:

8. Provider attests the patient has high-risk breast cancer based on which of the following? Check all that apply:
   ☐ Histopathological tests showing four or more (≥ 4) axillary lymph nodes are affected (pALN N2 or N3 disease)
   ☐ Histopathological tests showing one to three axillary lymph nodes are affected
      ☐ Tumor size is ≥ 5 cm
      ☐ Histopathological grade 3 disease (G3)
      ☐ Ki-67 score ≥ 20% as determined by an FDA-approved test
   ☐ Other. Specify: _____

9. Has the patient undergone surgical resection of the primary tumor? ☐ Yes ☐ No

10. Does the patient have a history of failure or intolerance using one of the following treatment modalities? Check all that apply.
    - ☐ Radiotherapy
    - ☐ Taxane (e.g., docetaxel)
    - ☐ Anthracycline (e.g., doxorubicin) based chemotherapy

Request for Systemic therapy of recurrent, advanced, or metastatic breast cancer, answer the following:

11. Is the treatment being prescribed as a first-line systemic therapy? ☐ Yes ☐ No
    If yes, please select all that apply:
    - ☐ The patient is a postmenopausal female, premenopausal or perimenopausal female receiving ovarian suppression/ablation (e.g., surgical ablation, suppression with GnRH therapy [e.g., leuprolide], etc.)
    - ☐ The patient is hormone suppressed male (e.g., GnRH therapy [e.g., leuprolide] used concomitantly)

12. Is the treatment being prescribed as a second-line systemic therapy? ☐ Yes ☐ No
    If yes, please select all that apply:
    - ☐ The medication will be used in combination with fulvestrant (Faslodex)
    - ☐ The patient had disease progression on, or after primary endocrine therapy (as adjuvant or first-line systemic therapy)
    - ☐ The patient is a postmenopausal female, premenopausal or perimenopausal female receiving ovarian suppression/ablation (e.g., surgical ablation, suppression with GnRH therapy [e.g., leuprolide]
    - ☐ The patient is hormone suppressed male (e.g., GnRH therapy [e.g., leuprolide] used concomitantly)

13. Is the treatment being prescribed as a subsequent-line (3rd line or later) systemic therapy in metastatic (stage IV, M1) setting? ☐ Yes ☐ No
    If yes, please select all that apply:
    - ☐ Patient had disease progression on, or after endocrine therapy AND systemic chemotherapy (not containing a CDK 4/6 inhibitor) in the metastatic setting.
    - ☐ The request is for abemaciclib (Verzenio) monotherapy.

CHART NOTES & LABS ARE REQUIRED WITH THIS REQUEST

Prescriber signature	Prescriber specialty	Date