INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

NPF Coverage Policy

Cigna covers palbociclib capsules and tablets (Ibrance®) as medically necessary when the following criteria are met for FDA Indications or Other Uses with Supportive Evidence:

Prior authorization is recommended for prescription benefit coverage of Ibrance. All approvals are provided for 3 years in duration unless otherwise noted below. In the clinical criteria, as appropriate, an asterisk (*) is noted next to the specified gender. In this context, the specified gender is defined as follows: a woman is defined as an individual with the biological traits of a woman, regardless of the individual’s gender identity or gender expression; men are defined as individuals with the biological traits of a man, regardless of the individual’s gender identity or gender expression.

FDA Indication(s)

1. Breast Cancer in Postmenopausal Women*. Approve for 3 years if the individual meets the following criteria (A, B, C, and D):
   A) Individual has advanced or metastatic hormone receptor positive (HR+) [i.e., estrogen receptor positive (ER+) and/or progesterone receptor positive (PR+)] disease; AND
   B) Individual has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
   C) The individual meets ONE of the following criteria (i or ii):
i. Ibrance will be used in combination with anastrozole, exemestane, or letrozole; OR
ii. Ibrance will be used in combination with fulvestrant; AND

D) The individual has not had disease progression while on Ibrance, Kisqali (ribociclib tablets), or Verzenio (abemaciclib tablets).

* Refer to the Policy Statement.

2. Breast Cancer in Pre/Perimenopausal Women*. Approve for 3 years if the individual meets the following criteria (A, B, C, D, and E):
   A) Individual has advanced or metastatic hormone receptor positive (HR+) [i.e., estrogen receptor positive (ER+) and/or progesterone receptor positive (PR+)] disease; AND
   B) Individual has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
   C) The individual is receiving ovarian suppression/ablation with a gonadotropin-releasing hormone (GnRH) agonist (e.g., Lupron [leuprolide], Trelstar [triptorelin], Zoladex (goserelin)), or has had surgical bilateral oophorectomy or ovarian irradiation; AND
   D) Individual meets ONE of the following conditions (i or ii):
      i. Ibrance will be used in combination with anastrozole, exemestane, or letrozole; OR
      ii. Ibrance will be used in combination with fulvestrant; AND
   E) Individual has not had disease progression while on Ibrance, Kisqali (ribociclib tablets), or Verzenio (abemaciclib tablets).

* Refer to the Policy Statement.

3. Breast Cancer in Men*. Approve for 3 years if the individual meets the following criteria (A, B, C, and D):
   A) Individual has advanced or metastatic hormone receptor positive (HR+) [i.e., estrogen receptor positive (ER+) and/or progesterone receptor positive (PR+)] disease; AND
   B) Individual has human epidermal growth factor receptor 2 (HER2)-negative breast cancer; AND
   C) Individual meets ONE of the following criteria (i or ii):
      i. Individual meets BOTH of the following criteria (a and b):
         a) Individual is receiving a gonadotropin-releasing hormone (GnRH) agonist (e.g., Lupron [leuprolide], Trelstar [triptorelin], Zoladex (goserelin)); AND
         b) Ibrance will be used in combination with anastrozole, exemestane, or letrozole; OR
      ii. Ibrance will be used in combination with fulvestrant; AND
   D) Individual has not had disease progression while on Ibrance, Kisqali (ribociclib tablets), or Verzenio (abemaciclib tablets).

* Refer to the Policy Statement.

Other Uses with Supportive Evidence

4. Liposarcoma. Approve for 3 years if the individual has well-differentiated/dedifferentiated liposarcoma (WD-DDLS).

Conditions Not Covered
Palbociclib capsules and tablets (Ibrance®) is considered experimental, investigational or unproven for ANY other use.

Background

Overview
Ibrance, a cyclin-dependent kinase (CDK) 4/6 inhibitor, is indicated for the treatment of adult patients with hormone receptor positive (HR+), human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in combination with:
1. An aromatase inhibitor (AI) as initial endocrine-based therapy in postmenopausal women or in men1-3; or
2. Fulvestrant in patients with disease progression following endocrine therapy.1,4-5
**Disease Overview**

Based on molecular profiling, breast cancer is classified as HR+ (estrogen receptor positive [ER+] and/or progesterone receptor positive [PgR+]), HER2+, or triple negative (ER-negative, PgR-negative, and HER2-negative). Most breast cancers in women (71%) are HR+, HER2-negative; these cancers tend to be slow-growing and less aggressive than other subtypes. HER+, HER2-negative tumors are associated with the most favorable prognosis compared with other subtypes, particularly in the short-term, in part because expression of hormone receptors is predictive of a favorable response to hormonal therapy. In men, about 85% of breast cancers are ER+ and 70% are PgR+. About 12% of breast cancers are HR+ and HER2+, and tend to be higher grade and more aggressive than HR+ cancers. About 5% of breast cancers are HER2+ and do not express hormone receptors. These cancers tend to be more aggressive than other breast cancers and have a poorer short-term prognosis compared with ER+ breast cancers. About 12% of breast cancers in women are triple negative and have a poorer short-term prognosis than other subtypes.

**Guidelines**

The National Comprehensive Cancer Network (NCCN) guidelines on breast cancer (version 3.2020 – March 6, 2020) recommend any of the CDK4/6 inhibitors in combination with an AI or fulvestrant as a first-line treatment option for recurrent or Stage IV HR+ and HER2-negative disease in postmenopausal women or premenopausal patient receiving ovarian ablation or suppression (category 1). The compendium recommend that men with breast cancer be treated similarly to postmenopausal women, except that the use of an AI is ineffective without concomitant suppression of testicular steroidogenesis. The NCCN guidelines state in a footnote that if there is disease progression on CDK4/6 inhibitor therapy, there are limited data to support an additional line of therapy with another CDK4/6-containing regimen. The limited data are based on a multicenter analysis which evaluated clinical outcomes in patients (n = 58) with HR+/HER2-negative metastatic breast cancer who received Verzenio after disease progression on Ibrance or Kisqali. At data cutoff, 34% of patients (n = 20/58) had progressive disease, while 36% of patients (n = 21/58) had treatment duration exceeding 6 months. The median PFS was 5.8 months. There are no published data with additional line of therapy with Ibrance or Kisqali, if the patient has progressed on Verzenio.

In men with breast cancer, tamoxifen is generally used rather than an AI, because the data supporting use of an AI in men are limited. The use of AI therapy with LHRH has been reported. Only limited data are available with Kisqali use in men with breast cancer as first-line endocrine therapy in combination with anastrozole, exemestane, or letrozole or for combination use with fulvestrant. However, available real-world data suggest comparable efficacies and safety profiles in men as in women; it is reasonable to recommend CDK4/6 inhibitors in combination with an aromatase inhibitor or fulvestrant, everolimus, and PIK3CA inhibitors for men based on extrapolation of data from studies comprised largely of female participants with advanced breast cancer.


**References**


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**Last Revision Details**

| Annual revision | Added Ibrance “tablets” to drug targets. Use of Ibrance in men is an FDA approved use, so moved it under “FDA-approved Indications”. | 04/15/2020 |

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