CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL POLICY

Abemaciclib (Verzenio®)

Version: 1.0

EFFECTIVE DATE: 12/1/2024

NantHealth® | Eviti®

Please note the following:

Abemaciclib (Verzenio®)

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within 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.

Abemaciclib (Verzenio): Discussion

Abemaciclib is a selective, and potent ATP-competitive inhibitor of cyclin-dependent kinases (CDKs) 4 and 6 that blocks retinoblastoma (Rb) protein phosphorylation which prevents cancer cell proliferation by arresting the cell cycle in the G1 phase, thereby suppressing DNA synthesis, and inhibiting cancer cell growth.[1] Rb protein phosphorylation plays a key role in regulating the activities of the Rb gene originally identified as the tumor suppressor. In certain types of cancers, Rb function is required for cancer development. The link between the Rb pathway and cancer development suggests that the status of Rb activity can potentially be used to develop targeted therapy.[2] Longer treatment with abemaciclib can lead to prolonged antitumor effects by inducing senescence, apoptosis, and modification of cellular mechanisms.[1]

Abemaciclib has several potential side effects, including diarrhea, neutropenia, interstitial lung disease, pneumonitis, hepatotoxicity, venous thromboembolism, and embryo-fetal toxicity.

Abemaciclib is approved by the Food and Drug Administration (FDA) for breast cancer.[3]

The National Comprehensive Cancer Network (NCCN) endorses abemaciclib in the following cancer types: breast and uterine.[4,5]

Abemaciclib: Definitions

- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than 30 cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.
- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.

Abemaciclib: Policy

Note: Coverage of abemaciclib will be provided for an FDA-approved indication or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation or when all criteria are met.

Abemaciclib will be considered for coverage when the following criteria are met:

Breast Cancer

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

3. In combination with one of the following:
   a) Endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult patients with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative, node-positive, early breast cancer at high risk of recurrence
   b) Aromatase inhibitor as initial endocrine based therapy for hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative advanced or metastatic breast cancer
   c) Fulvestrant for hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative advanced or metastatic breast cancer with disease progression following endocrine therapy; OR
4. As monotherapy for HR positive, HER2 negative advanced or metastatic breast cancer with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting.[3]; OR

For **NCCN** required criteria coverage:

5. Adjuvant therapy for 2 years in combination with endocrine therapy in postmenopausal women or premenopausal women treated with ovarian ablation/suppression with hormone receptor positive, human epidermal growth factor receptor 2 (HER2) negative, high risk (i.e., ≥4 positive lymph nodes, or 1-3 positive lymph nodes with either grade 3 disease or tumor size ≥5 cm; OR
6. Recurrent unresectable (local or regional) or stage IV (M1) hormone receptor positive, human epidermal growth factor receptor 2 (HER2) negative disease with no visceral crisis in postmenopausal women or premenopausal women treated with ovarian ablation/suppression for one of the following:
   a) First-line therapy in combination with fulvestrant for disease progression on adjuvant endocrine therapy (ET) or with early disease relapse within 12 months of adjuvant ET completion

b) First-line therapy in combination with an aromatase inhibitor
c) Second-line or subsequent-line therapy in combination with fulvestrant if CDK4/6 inhibitor is not previously used; OR

7. Subsequent treatment of recurrent unresectable (local or regional) or stage IV (M1) hormone receptor positive, non-visceral or asymptomatic visceral human epidermal growth factor receptor 2 (HER2) negative disease as a single agent if there is progression on prior endocrine therapy and prior chemotherapy in the metastatic setting.

Inflammatory Breast Cancer

For **NCCN** required criteria coverage:

8. For 2 years, as adjuvant therapy in combination with endocrine therapy in patients with HR positive, human epidermal growth factor receptor 2 (HER2) negative, high risk (i.e., ≥4 positive lymph nodes or 1-3 positive lymph nodes with either grade 3 disease or tumor size ≥5 cm; OR
9. Recurrent unresectable or stage IV (M1), hormone receptor positive, human epidermal growth factor receptor 2 (HER2) negative disease with no visceral crisis in postmenopausal women or premenopausal women treated with ovarian ablation/suppression as first-line therapy in combination with fulvestrant; OR
10. Disease progression on adjuvant endocrine therapy (ET) or with early disease relapse within 12 months of adjuvant ET completion for one of the following:
    a) First-line therapy in combination with an aromatase inhibitor
    b) Second-line or subsequent-line therapy in combination with fulvestrant if CDK4/6 inhibitor was not previously used; OR
11. Single agent in subsequent treatment for recurrent unresectable or stage IV (M1) hormone receptor positive, non-visceral or asymptomatic visceral human epidermal growth factor receptor 2 (HER2) negative disease if progression on prior endocrine therapy and prior chemotherapy in the metastatic setting.[4]

Note: Men with breast cancer should be treated similarly to postmenopausal women; however, the use of an aromatase inhibitor is ineffective without concomitant suppression of testicular steroidogenesis.

Uterine Neoplasms - Endometrial Carcinoma

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. In combination with letrozole for estrogen receptor positive tumors typically used for lower grade endometrioid histologies, preferably in patients with small tumor volume or an indolent growth pace for one of the following:

a) Disease that is not suitable for primary surgery in patients with suspected or gross cervical involvement
b) With or without external beam radiation therapy (EBRT), stereotactic body radiation therapy (SBRT), and/or total hysterectomy/bilateral salpingo-oophorectomy for distant metastases that are suitable for primary surgery
c) Sequential EBRT with or without brachytherapy for locoregional extrauterine disease that is not suitable for primary surgery
d) Locoregional extrauterine disease or distant metastases that are not suitable for primary surgery; OR

4. Adjuvant treatment for surgically staged patients in combination with letrozole for estrogen receptor positive tumors (ER+) with or without EBRT and with or without vaginal brachytherapy for stage IV disease; OR
5. In combination with letrozole for estrogen receptor positive tumors typically used for lower grade endometrioid histologies, preferably in patients with small tumor volume or an indolent growth pace for one of the following:
   a) Isolated metastases
   b) Disseminated metastases with or without sequential palliative EBRT.
   c) Sequential EBRT with or without brachytherapy for locoregional recurrence in patients with no prior RT to site of recurrence, or previous vaginal brachytherapy only
   d) After surgical exploration, with sequential EBRT for locoregional recurrence in patients with disease confined to the vagina or paravaginal soft tissue, or in pelvic or para-aortic lymph nodes
   e) After surgical exploration, with or without sequential EBRT for locoregional recurrence in patients with upper abdominal or peritoneal disease
   f) With or without sequential palliative EBRT or brachytherapy for locoregional recurrence in patients who have received prior EBRT to site of recurrence.[5]

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Abemaciclib: References

1. National Library of Medicine. Abemaciclib: CADTH Reimbursement Review: Therapeutic area: Adjuvant treatment of hormone receptor-positive, human epidermal growth factor receptor 2–negative early breast cancer. https://www.ncbi.nlm.nih.gov/books/NBK601722/. Accessed November 12, 2024.
2. Wei Du at el. The Rb pathway and cancer therapeutics. https://pmc.ncbi.nlm.nih.gov/articles/PMC3151466/. Accessed November 12, 2024.
3. Abemaciclib (Verzenio) Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/208716s010s011lbl.pdf. Accessed November 12, 2024.
4. National Comprehensive Cancer Network. Breast Cancer.

https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed November 12, 2024.
5. National Comprehensive Cancer Network. Uterine Neoplasms. https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf. Accessed November 12, 2024.

Abemaciclib: Coding (CPT®, ICD 10 and HCPCS) *

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C50.9	Malignant neoplasm of breast
C54.1	Malignant neoplasm of endometrium
J8999	Abemaciclib

Abemaciclib: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	12/1/2024
2	Policy Review Dates:	
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee:	12/21/2024
6	Revision Changes:	