POLICY NUMBER UM ONC_1328	SUBJECT Verzenio™ (abemaciclib)		DEPT/PROGRAM UM Dept	PAGE 1 OF 5
DATES COMMITTEE REVIEWED 10/11/17, 10/10/18, 10/09/19, 12/11/19	APPROVAL DATE December 11, 2019	EFFECTIVE DATE December 11, 2019	COMMITTEE APPROVAL DATES (latest version listed last) 10/11/17, 10/10/18, 10/09/19, 12/11/19	
PRIMARY BUSINESS OWNER: UM APPROVED BY: Dr. Andrew Hertler		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS HUM 1		NCQA STANDARDS UM 2	ADDITIONAL AREAS OF IMPACT	
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS All	

I. PURPOSE

To define and describe the accepted indications for Verzenio (abemaciclib) usage in the treatment of cancer.

II. DEFINITIONS

Verzenio (abemaciclib): is a cyclin-dependent kinase (CDK) 4 and 6 inhibitor. When these kinases are activated by cyclin D1 in estrogen receptor-positive breast cancer cells, they promote retinoblastoma protein (Rb) phosphorylation, cell cycle progression, and cell proliferation. Senescence and apoptosis were produced with continuous in vitro exposure to abemaciclib, and tumor size was reduced in xenograft models when administered daily alone or in combination with antiestrogens.

Verzenio (abemaciclib) is FDA approved in combination with fulvestrant for the treatment of women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer with disease progression following endocrine therapy. It is also approved as 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. Also FDA approved in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

Verzenio (abemaciclib) is available in 50 mg, 100 mg, 150 mg, and 200 mg tablets.

III. POLICY

New Century Health is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century Health may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Verzenio (abemaciclib) may be considered medically necessary when any of the following selection criteria are met:

1. **Breast Cancer**
    a. The member has recurrent or metastatic breast cancer and **ALL** the following criteria:
        i. Confirmed ER positive and HER2 negative breast cancer **AND**
        ii. Postmenopausal women OR premenopausal women receiving LHRH agonist **AND**
        iii. Verzenio (abemaciclib) is being used in combination with fulvestrant/aromatase inhihibitor for disease progression following one line of endocrine therapy **OR**
        iv. Being used as a single agent for disease progression following endocrine therapy AND up to 2 prior chemotherapy regimens for metastatic disease

Exclusion Criteria: Verzenio (abemaciclib) is not considered medically necessary when any of the following selection criteria are met:

1. Verzenio (abemaciclib) is being used after disease progression with the same regimen or prior therapy with CDK 4 and 6 inhibitor (i.e. palbociclib or ribociclib).
2. For combination with fulvestrant: Prior treatment with fulvestrant, everolimus, or any CDK4/6 inhibitor.
3. Dosing exceeds single dose limit of Verzenio (abemaciclib) 200 mg.
4. Treatment exceeds the maximum limit of (240) 50 mg, (120) 100 mg, (60)150 mg, and (60) 200 mg tablets/month.
5. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Verzenio (abemaciclib) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration:**
    a. Monotherapy: 200 mg orally twice daily until disease progression or unacceptable toxicity.
    b. In combination with fulvestrant or aromatase inhibitor: 150 mg orally twice daily until disease progression or unacceptable toxicity.
2. **Dosage Adjustments:**
    a. Hepatic impairment, Mild or moderate (Child-Pugh A or B): No adjustment required.
    b. Hepatic impairment, Severe (Child-Pugh C): Reduce dosing frequency to once daily.
    c. Renal impairment, Mild or moderate (CrCl 30 to 89 mL/min): No adjustment required
    d. Concomitant moderate CYP3A inhibitors, during combination therapy with fulvestrant or an aromatase inhibitor: Consider reducing the abemaciclib dose in 50-mg decrements if necessary (first reduction, from 150 to 100 mg orally twice daily; second reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated).
    e. Concomitant moderate CYP3A inhibitors, during abemaciclib monotherapy: Consider reducing the abemaciclib dose in 50-mg decrements if necessary (first reduction, from 200 to 150 mg orally twice daily; second reduction, from 150 to 100 mg twice daily; third reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated).
    f. Concomitant strong CYP3A inhibitors: Avoid ketoconazole. For required use of other strong inhibitor, reduce initial dosage to 100 mg orally twice daily. In patients on 100 mg twice daily because of toxicity, reduce to 50 mg twice daily. Upon discontinuation of strong inhibitor, return abemaciclib to previous dose after 3 to 5 half-lives of the inhibitor.
    g. Diarrhea (Grade 1): No adjustment required. Initiate antidiarrheal agents and increase oral fluid intake with first sign of loose stool.
    h. Diarrhea (Grade 2): If toxicity does not resolve to Grade 1 or less within 24 hours, withhold until resolution. No adjustment is required. Initiate antidiarrheal agents and increase oral fluid intake with first sign of loose stool.

i. Diarrhea (Grade 2, persistent or recurs after resuming same dose despite supportive measures) during combination therapy with fulvestrant: Withhold until resolves to Grade 1 or less and resume at next lower dose (first reduction, from 150 to 100 mg orally twice daily; second reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated). Initiate antidiarrheal agents and increase oral fluid intake with first sign of loose stool.

j. Diarrhea (Grade 2, persistent or recurs after resuming same dose despite supportive measures) during abemaciclib monotherapy: Withhold until resolves to Grade 1 or less and resume at next lower dose (first reduction, from 200 to 150 mg orally twice daily; second reduction, from 150 to 100 mg twice daily; third reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated). Initiate antidiarrheal agents and increase oral fluid intake with first sign of loose stool.

k. Diarrhea (Grade 3, 4, or requiring hospitalization) during combination therapy with fulvestrant: Withhold until resolves to Grade 1 or less and resume at next lower dose (first reduction, from 150 to 100 mg orally twice daily; second reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated). Initiate antidiarrheal agents and increase oral fluid intake with first sign of loose stool.

l. Diarrhea (Grade 3, 4, or requiring hospitalization) during abemaciclib monotherapy: Withhold until resolves to Grade 1 or less and resume at next lower dose (first reduction, from 200 to 150 mg orally twice daily; second reduction, from 150 to 100 mg twice daily; third reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated). Initiate antidiarrheal agents and increase oral fluid intake with first sign of loose stool.

m. Hematologic toxicity (Grade 1 or 2): No adjustment required.

n. Hematologic toxicity (Grade 3): Withhold until resolves to Grade 2 or less. No adjustment is required.

o. Hematologic toxicity (recurrent Grade 3, or Grade 4) during combination therapy with fulvestrant: Withhold until resolves to Grade 2 or less and resume at next lower dose (first reduction, from 150 to 100 mg orally twice daily; second reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated). If growth factor support is required, withhold abemaciclib for at least 48 hours after last dose of growth factor and until resolves to Grade 2 or less; resume at next lower dose unless already preformed for the toxicity that lead to growth factor use.

p. Hematologic toxicity (recurrent Grade 3, or Grade 4) during abemaciclib monotherapy: Withhold until resolves to Grade 2 or less and resume at next lower dose (first reduction, from 200 to 150 mg orally twice daily; second reduction, from 150 to 100 mg twice daily; third reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated). If growth factor support is required, withhold abemaciclib for at least 48 hours after last dose of growth factor and until resolves to Grade 2 or less; resume at next lower dose unless already preformed for the toxicity that lead to growth factor use.

q. Hepatotoxicity (ALT and AST elevation, Grade 1 (greater than ULN to 3 x ULN) or Grade 2 (greater than 3 to 5 x ULN) without total bilirubin greater than 2 x ULN): No adjustment required

r. Hepatotoxicity (ALT and/or AST elevation greater than 3 x ULN with total bilirubin greater than 2 x ULN) in the absence of cholestasis: Discontinue abemaciclib.

s. Hepatoxicity (ALT and AST elevation, persistent or recurrent Grade 2, or Grade 3 (greater than 5 to 20 x ULN) without total bilirubin greater than 2 x ULN) during combination

therapy with fulvestrant: Withhold until resolves to baseline or Grade 1 and resume at next lower dose (first reduction, from 150 to 100 mg orally twice daily; second reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated)

t. Hepatoxicity (ALT and AST elevation, persistent or recurrent Grade 2, or Grade 3 (greater than 5 to 20 x ULN) without total bilirubin greater than 2 x ULN) during abemaciclib monotherapy: Withhold until resolves to baseline or Grade 1 and resume at next lower dose (first reduction, from 200 to 150 mg orally twice daily; second reduction, from 150 to 100 mg twice daily; third reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated)

u. Hepatotoxicity (ALT and AST elevation, Grade 4 (greater than 20 x ULN)): Discontinue abemaciclib.

v. Interstitial lung disease/pneumonitis (Grade 1 or 2): No dosage adjustment necessary.

w. Interstitial lung disease/pneumonitis (Grade 2, persistent or recurrent, without resolving to Grade 1 or baseline with maximal supportive measures within 7 days) during combination therapy with fulvestrant or an aromatase inhibitor: Interrupt therapy until resolution to baseline or Grade 1 or less; resume at next lower dose (first reduction, from 150 to 100 mg orally twice daily; second reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated).

x. Interstitial lung disease/pneumonitis (Grade 2, persistent or recurrent, without resolving to Grade 1 or baseline with maximal supportive measures within 7 days) during abemaciclib monotherapy: Interrupt therapy until resolution to baseline or Grade 1 or less; resume at next lower dose (first reduction, from 200 to 150 mg orally twice daily; second reduction, from 150 to 100 mg twice daily; third reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated).

y. Interstitial lung disease/pneumonitis (Grade 3 or 4): Discontinue use.

z. Other toxicity (Grade 1 or 2): No adjustment required.

aa. Other toxicity (Grade 2 persistent or recurrent, without resolving within 7 days to baseline or Grade 1 despite supportive measures) during combination therapy with fulvestrant: Withhold until resolves to baseline or Grade 1 or less and resume at next lower dose (first reduction, from 150 to 100 mg orally twice daily; second reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated).

bb. Other toxicity (Grade 2 persistent or recurrent, without resolving within 7 days to baseline or Grade 1 despite supportive measures): during abemaciclib monotherapy: Withhold until resolves to baseline or Grade 1 or less and resume at next lower dose (first reduction, from 200 to 150 mg orally twice daily; second reduction, from 150 to 100 mg twice daily; third reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated).

cc. Other toxicity (Grade 3 or 4) during combination therapy with fulvestrant: Withhold until resolves to baseline or Grade 1 or less and resume at next lower dose (first reduction, from 150 to 100 mg orally twice daily; second reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated).

dd. Other toxicity (Grade 3 or 4) during abemaciclib monotherapy: Withhold until resolves to baseline or Grade 1 or less and resume at next lower dose (first reduction, from 200 to 150 mg orally twice daily; second reduction, from 150 to 100 mg twice daily; third reduction, from 100 to 50 mg twice daily; discontinue use if 50 mg twice daily is not tolerated).

3. **Monitoring:**

a. Tumor response may indicate efficacy.

b. CBC: At baseline, every 2 weeks for the first 2 months, monthly for 2 months, and then as clinically indicated, including differential.

c. Liver function tests: At baseline, every 2 weeks for the first 2 months, monthly for 2 months, and then as clinically indicated.

d. Pregnancy status: In females of reproductive potential prior to initiating therapy.

e. Signs and symptoms of thrombosis and pulmonary embolism.

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Verzenio PI prescribing information. Lilly USA, LLC, Indianapolis, IN 2019.
2. Clinical Pharmacology Elsevier Gold Standard. 2019.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2019.
5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2019.