PDL NEW DRUG REVIEW

Proprietary Name: Verzenio®
Common Name: abemaciclib
PDL Category: Antineoplastics

Comparable Products	Preferred Drug List Status
Ibrance	Recommended with Conditions
Kisqali	Recommended with Conditions

Summary

Pharmacology/Usage: Abemaciclib, the active ingredient of Verzenio® is a kinase inhibitor, an inhibitor of cyclin-dependent kinases 4 and 6 (CDK4 and CDK6). In breast cancer xenograft models, abemaciclib dosed daily without interruption used as monotherapy or in combination with anti-estrogens resulted in reduction of tumor size.

Indications: 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 AND 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.

There is no pregnancy category for this product; however, based on the findings in animal studies and its mechanism of action, Verzenio® can cause fetal harm when administered to a pregnant woman. There are no available human data informing the drug-associated risk. Advise pregnant women of the potential risk to a fetus. For females of reproductive potential, pregnancy testing is recommended prior to starting treatment and effective contraception should be used during treatment and for at least 3 weeks after the last dose. The safety and efficacy of use in the pediatric population have not been established.

Dosage Forms: Tablets: 50mg, 100mg, 150mg, 200mg

Recommended Dosage: *When used in combination with fulvestrant*, take 150mg PO BID. Pre/perimenopausal women should be treated with a gonadotropin-releasing hormone agonist per current clinical practice standards. *When used as monotherapy*, the recommended dose is 200mg PO BID.

Continue until disease progression or unacceptable toxicity, with or without food. Refer to the prescribing information for additional information regarding dose modifications and management for adverse events, for hematological toxicities, diarrhea, hepatotoxicity, and other toxicities.

Dose adjustments are not required with mild or moderate renal or hepatic impairment. It is recommended to reduce the dosing frequency to once daily in those with severe hepatic impairment. The effects with severe renal impairment, end stage renal disease, or in patients on dialysis is not known.

Drug Interactions: Avoid the concomitant use of ketoconazole or grapefruit products with Verzenio®. Reduce the dose of Verzenio® if use concomitantly with other strong CYP3A4 inhibitors. Refer to prescribing information for additional specific information regarding dose modifications if use Verzenio® concomitantly with other strong CYP3A inhibitors. The concomitant use of Verzenio® with strong CYP3A inducers should be avoided and alternative agents should be considered.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Verzenio® plus fulvestrant) minus reported % incidence for placebo plus fulvestrant for all grades. Please note that an incidence of 0% means the incidence was the same as or that the active drug was less than its comparator.* The most frequently reported adverse events included diarrhea (61%), nausea (22%), abdominal pain (19%), vomiting (16%), stomatitis (5%), infections (18%), neutropenia (42%), anemia (25%), leukopenia (26%), thrombocytopenia (13%), fatigue (14%), edema peripheral (5%), pyrexia (5%), decreased appetite (15%), cough (2%), alopecia (14%), pruritus (7%), rash (7%), headache (5%), dysgeusia (15%), dizziness (6%), and weight decreased (8%). Additional laboratory abnormalities included increased creatinine (24%), decreased white blood cell (57%), decreased neutrophil count (57%), anemia (51%), decreased lymphocyte count (31%), decreased platelet count (38%), increased alanine aminotransferase (9%), and increased aspartate aminotransferase (12%).

In the MONARCH 2 study, venous thromboembolic events (VTEs) were reported in 5% of those treated with Verzenio® plus fulvestrant as compared to 0.9% treated with placebo plus fulvestrant. VTEs included deep vein thrombosis, pulmonary embolism, cerebral venous sinus thrombosis, subclavian and axillary vein thrombosis, and inferior vena cava thrombosis. Monitor for signs and symptoms of venous thrombosis and pulmonary embolism.

As hepatotoxicity has been reported in patients receiving Verzenio®, it is recommended to monitor liver function tests prior to starting treatment, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated. In addition, as neutropenia has been reported with Verzenio® use, it is recommended to monitor complete blood counts at the same frequency as the liver function tests are monitored.

Contraindications: There are currently no contraindications listed with this product.

Manufacturer: Eli Lilly

Analysis: MONARCH 2 was a randomized, placebo-controlled, multicenter study that included women with HR-positive, HER2-negative metastatic breast cancer with disease progression following endocrine therapy who had not received chemotherapy in the metastatic setting to assess the safety and efficacy of Verzenio®, in combination with fulvestrant. Patients (N=669), with a median age of 60 years, were randomized to either Verzenio® plus fulvestrant or placebo plus fulvestrant and remained on continuous treatment until development of progressive disease or unmanageable toxicity.

Median progression free survival (PFS) based on a blinded independent radiologic review was consistent with the investigator assessment. At the time of primary analysis of PFS, overall survival data were not mature (20% of patients had died). The following table illustrates results of this study, which was adapted from the prescribing information.

	Verzenio® + fulvestrant	Placebo + fulvestrant
Progression Free Survival (PFS)		
N	446	223
Number of patients with event (%)	222 (49.8%)	157 (70.4%)

	Verzenio® + fulvestrant	Placebo + fulvestrant
Median, months	16.4	9.3
Hazard ratio, p-value	0.553; p<0.0001	
Objective Response for patients with measurable disease		
N	318	164
Objective response rate	153 (48.1%)	35 (21.3%)

MONARCH 1 was a single-arm, open-label, multicenter study that included women with measurable HR-positive, HER2-negative metastatic breast cancer whose disease progressed during or after endocrine therapy, had received a taxane in any setting, and who received 1 or 2 prior chemotherapy regimens in the metastatic setting to assess the safety and efficacy of Verzenio® used continuously until development of progressive disease or unmanageable toxicity. The median age of patients was 58 years and the median duration of metastatic disease was 27.6 months. Results can be seen in the table below, which was adapted from the prescribing information. Note that all responses were partial responses.

	Verzenio® 200mg (N=132)	
	Investigator Assessed	Independent Review
Objective Response Rate	26 (19.7%)	23 (17.4%)
Median Duration of Response	8.6 months	7.2 months

Place in Therapy: Verzenio® is indicated 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 AND 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. Dose modifications may be required for cases of adverse events, drug interactions, or with severe hepatic impairment. Verzenio® in combination with fulvestrant was found to be significantly more effective than placebo plus fulvestrant for progression-free survival.

It is recommended that Verzenio® be placed on the Recommended Drug List as recommended and require prior authorization to verify diagnosis and prior treatments.

PDL Placement: ☒ **Recommended with Conditions**

References

[1] Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Co; 2017.