HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use VERZENIO safely and effectively. See full prescribing information for VERZENIO.

VERZENIO® (abemaciclib) tablets, for oral use
Initial U.S. Approval: 2017

---------- RECENT MAJOR CHANGES ----------

Indications and Usage (1.1, 1.2)	10/2021
Dosage and Administration (2.1, 2.2, 2.3)	10/2021
Warnings and Precautions (5.5)	10/2021

---------- INDICATIONS AND USAGE ----------

VERZENIO® is a kinase inhibitor indicated:

- in combination with 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 and a Ki-67 score ≥20% as determined by an FDA approved test. (1.1, 2.1, 14.1)
- in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer. (1.2)
- in combination with fulvestrant for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer with disease progression following endocrine therapy. (1.2)
- 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. (1.2)

----------DOSAGE AND ADMINISTRATION----------

VERZENIO tablets are taken orally with or without food. (2.2)

- Recommended starting dose in combination with fulvestrant, tamoxifen, or an aromatase inhibitor: 150 mg twice daily. (2.2)
- Recommended starting dose as monotherapy: 200 mg twice daily. (2.2)
- Dosing interruption and/or dose reductions may be required based on individual safety and tolerability. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------

Tablets: 50 mg, 100 mg, 150 mg, and 200 mg. (3)

---------- CONTRAINDICATIONS ----------

None. (4)

---------- WARNINGS AND PRECAUTIONS ----------

- Diarrhea: VERZENIO can cause severe cases of diarrhea, associated with dehydration and infection. Instruct patients at the first sign of loose stools to initiate antidiarrheal therapy, increase oral fluids, and notify their healthcare provider. (2.3, 5.1)
- Neutropenia: Monitor complete blood counts prior to the start of VERZENIO therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated. (2.3, 5.2)
- Interstitial Lung Disease (ILD)/Pneumonitis: Severe and fatal cases of ILD/pneumonitis have been reported. Monitor for clinical symptoms or radiological changes indicative of ILD/pneumonitis. Permanently discontinue VERZENIO in all patients with Grade 3 or 4 ILD or pneumonitis. (2.3, 5.3)
- Hepatotoxicity: Increases in serum transaminase levels have been observed. Perform liver function tests (LFTs) before initiating treatment with VERZENIO. Monitor LFTs every two weeks for the first two months, monthly for the next 2 months, and as clinically indicated. (2.3, 5.4)
- Venous Thromboembolism: Monitor patients for signs and symptoms of thrombosis and pulmonary embolism and treat as medically appropriate. (2.3, 5.5)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of potential risk to a fetus and to use effective contraception. (5.6, 8.1, 8.3)

---------- ADVERSE REACTIONS ----------

Most common adverse reactions (incidence ≥20%) were diarrhea, neutropenia, nausea, abdominal pain, infections, fatigue, anemia, leukopenia, decreased appetite, vomiting, headache, alopecia, and thrombocytopenia. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Eli Lilly and Company at 1-800-LillyRx (1-800-545-5979) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------

- CYP3A Inhibitors: Avoid concomitant use of ketoconazole. Reduce the VERZENIO dose with concomitant use of other strong and moderate CYP3A inhibitors. (2.3, 7.1)
- CYP3A Inducers: Avoid concomitant use of strong and moderate CYP3A inducers. (7.1)

----------USE IN SPECIFIC POPULATIONS----------

Lactation: Advise not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 10/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Early Breast Cancer

VERZENIO® (abemaciclib) is indicated:

- in combination with 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 and a Ki-67 score ≥20% as determined by an FDA approved test *[see Dosage and Administration (2.1) and Clinical Studies (14.1)].*

1.2 Advanced or Metastatic Breast Cancer

VERZENIO (abemaciclib) is indicated:

- in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.
- in combination with fulvestrant for the treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer with disease progression following endocrine therapy.
- 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.

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Patient Selection for Early Breast Cancer

Select patients for treatment of early breast cancer with VERZENIO in combination with endocrine therapy based on a Ki-67 score ≥20% in tumor specimens *[see Clinical Studies (14.1)].* Information on FDA-approved tests for the measurement of Ki-67 score is available at http://www.fda.gov/CompanionDiagnostics.

2.2 Recommended Dose and Schedule

- When used in combination with fulvestrant, tamoxifen, or an aromatase inhibitor, the recommended dose of VERZENIO is 150 mg taken orally twice daily. Refer to the Full Prescribing Information for the recommended dose of the fulvestrant, tamoxifen, or aromatase inhibitor being used.
- Pre/perimenopausal women and men treated with the combination of VERZENIO plus an aromatase inhibitor should be treated with a gonadotropin-releasing hormone agonist (GnRH) according to current clinical practice standards.
- Pre/perimenopausal women treated with the combination of VERZENIO plus fulvestrant should be treated with a GnRH according to current clinical practice standards
- When used as monotherapy, the recommended dose of VERZENIO is 200 mg taken orally twice daily.
- For early breast cancer, continue VERZENIO until completion of 2 years of treatment or until disease recurrence, or unacceptable toxicity.
- For advanced or metastatic breast cancer, continue treatment until disease progression or unacceptable toxicity.

VERZENIO may be taken with or without food *[see Clinical Pharmacology (12.3)]*.

Instruct patients to take their doses of VERZENIO at approximately the same times every day.

If the patient vomits or misses a dose of VERZENIO, instruct the patient to take the next dose at its scheduled time. Instruct patients to swallow VERZENIO tablets whole and not to chew, crush, or split tablets before swallowing. Instruct patients not to ingest VERZENIO tablets if broken, cracked, or otherwise not intact.

2.3 Dose Modification

Dose Modifications for Adverse Reactions

The recommended VERZENIO dose modifications for adverse reactions are provided in Tables 1-7. Discontinue VERZENIO for patients unable to tolerate 50 mg twice daily.

Table 1: VERZENIO Dose Modification — Adverse Reactions

Dose Level	VERZENIO Dose Combination with Fulvestrant, Tamoxifen, or an Aromatase Inhibitor	VERZENIO Dose for Monotherapy
Recommended starting dose	150 mg twice daily	200 mg twice daily
First dose reduction	100 mg twice daily	150 mg twice daily
Second dose reduction	50 mg twice daily	100 mg twice daily
Third dose reduction	not applicable	50 mg twice daily

Table 2: VERZENIO Dose Modification and Management — Hematologic Toxicities[a]

Monitor complete blood counts prior to the start of VERZENIO therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated.	
CTCAE Grade	**VERZENIO Dose Modifications**
Grade 1 or 2	No dose modification is required.
Grade 3	Suspend dose until toxicity resolves to ≤Grade 2. Dose reduction is not required.
Grade 3 recurrent, or Grade 4	Suspend dose until toxicity resolves to ≤Grade 2. Resume at *next lower dose*.

Abbreviation: CTCAE = Common Terminology Criteria for Adverse Events.

[a] If blood cell growth factors are required, suspend VERZENIO dose for at least 48 hours after the last dose of blood cell growth factor and until toxicity resolves to ≤Grade 2. Resume at *next lower dose* unless already performed for the toxicity that led to the use of the growth factor. Growth factor use as per current treatment guidelines.

Table 3: VERZENIO Dose Modification and Management — Diarrhea

At the first sign of loose stools, start treatment with antidiarrheal agents and increase intake of oral fluids.	
CTCAE Grade	**VERZENIO Dose Modifications**
Grade 1	No dose modification is required.
Grade 2	If toxicity does not resolve within 24 hours to ≤Grade 1, suspend dose until resolution. No dose reduction is required.
Grade 2 that persists or recurs after resuming the same dose despite maximal supportive measures	Suspend dose until toxicity resolves to ≤Grade 1. Resume at *next lower dose*.
Grade 3 or 4 or requires hospitalization	Suspend dose until toxicity resolves to ≤Grade 1. Resume at *next lower dose*.

Table 4: VERZENIO Dose Modification and Management — Hepatotoxicity

Monitor ALT, AST, and serum bilirubin prior to the start of VERZENIO therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated.	
CTCAE Grade for ALT and AST	**VERZENIO Dose Modifications**
Grade 1 (>ULN-3.0 x ULN) Grade 2 (>3.0-5.0 x ULN), WITHOUT increase in total bilirubin above 2 x ULN	No dose modification is required.
Persistent or Recurrent Grade 2, or Grade 3 (>5.0-20.0 x ULN), WITHOUT increase in total bilirubin above 2 x ULN	Suspend dose until toxicity resolves to baseline or Grade 1. Resume at next lower dose.
Elevation in AST and/or ALT >3 x ULN WITH total bilirubin >2 x ULN, in the absence of cholestasis	Discontinue VERZENIO.
Grade 4 (>20.0 x ULN)	Discontinue VERZENIO.

Abbreviations: ALT = alanine aminotransferase, AST = aspartate aminotransferase, ULN = upper limit of normal.

Table 5: VERZENIO Dose Modification and Management — Interstitial Lung Disease/Pneumonitis

CTCAE Grade	VERZENIO Dose Modifications
Grade 1 or 2	No dose modification is required.
Persistent or recurrent Grade 2 toxicity that does not resolve with maximal supportive measures within 7 days to baseline or Grade 1	Suspend dose until toxicity resolves to baseline or ≤Grade 1. Resume at *next lower dose*.
Grade 3 or 4	Discontinue VERZENIO.

Table 6: VERZENIO Dose Modification and Management — Venous Thromboembolic Events (VTEs)

CTCAE Grade	VERZENIO Dose Modifications
Early Breast Cancer	
Any Grade	Suspend dose and treat as clinically indicated. Resume VERZENIO when the patient is clinically stable.
Advanced or Metastatic Breast Cancer	
Grade 1 or 2	No dose modification is required.
Grade 3 or 4	Suspend dose and treat as clinically indicated. Resume VERZENIO when the patient is clinically stable.

Table 7: VERZENIO Dose Modification and Management — Other Toxicities[a]

CTCAE Grade	VERZENIO Dose Modifications
Grade 1 or 2	No dose modification is required.
Persistent or recurrent Grade 2 toxicity that does not resolve with maximal supportive measures within 7 days to baseline or Grade 1	Suspend dose until toxicity resolves to baseline or ≤Grade 1. Resume at *next lower dose*.
Grade 3 or 4	Suspend dose until toxicity resolves to baseline or ≤Grade 1. Resume at *next lower dose*.

[a] Excluding diarrhea, hematologic toxicity, hepatotoxicity, ILD/pneumonitis, and VTEs.

Refer to the Full Prescribing Information for coadministered fulvestrant, tamoxifen, or an aromatase inhibitor for dose modifications and other relevant safety information.

Dose Modification for Use with Strong and Moderate CYP3A Inhibitors

Avoid concomitant use of the strong CYP3A inhibitor ketoconazole.

With concomitant use of strong CYP3A inhibitors other than ketoconazole, in patients with recommended starting doses of 200 mg twice daily or 150 mg twice daily, reduce the VERZENIO dose to 100 mg twice daily. In patients who have had a dose reduction to 100 mg twice daily due to adverse reactions, further reduce the VERZENIO dose to 50 mg twice daily. If a patient taking VERZENIO discontinues a CYP3A inhibitor, increase the VERZENIO dose (after 3-5 half-lives of the inhibitor) to the dose that was used before starting the strong inhibitor *[see Drug Interactions (7.1) and Clinical Pharmacology (12.3)].*

With concomitant use of moderate CYP3A inhibitors, monitor for adverse reactions and consider reducing the VERZENIO dose in 50 mg decrements as demonstrated in Table 1, if necessary.

Dose Modification for Patients with Severe Hepatic Impairment

For patients with severe hepatic impairment (Child Pugh-C), reduce the VERZENIO dosing frequency to once daily *[see Use in Specific Populations (8.7) and Clinical Pharmacology (12.3)].*

Refer to the Full Prescribing Information for the coadministered fulvestrant, tamoxifen, or aromatase inhibitor for dose modification requirements for severe hepatic impairment.

3 DOSAGE FORMS AND STRENGTHS

50 mg tablets: oval beige tablet with “Lilly” debossed on one side and “50” on the other side.
100 mg tablets: oval white to practically white tablet with “Lilly” debossed on one side and “100” on the other side.
150 mg tablets: oval yellow tablet with “Lilly” debossed on one side and “150” on the other side.
200 mg tablets: oval beige tablet with “Lilly” debossed on one side and “200” on the other side.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Diarrhea

Severe diarrhea associated with dehydration and infection occurred in patients treated with VERZENIO.

Across four clinical trials in 3691 patients, diarrhea occurred in 81% to 90% of patients who received VERZENIO. Grade 3 diarrhea occurred in 8% to 20% of patients receiving VERZENIO *[see Adverse Reactions (6.1)].*

Most patients experienced diarrhea during the first month of VERZENIO treatment. The median time to onset of the first diarrhea event ranged from 6 to 8 days; and the median duration of Grade 2 and Grade 3 diarrhea ranged from 6 to 11 days and 5 to 8 days, respectively. Across trials, 19% to 26% of patients with diarrhea required a VERZENIO dose interruption and 13% to 23% required a dose reduction.

Instruct patients to start antidiarrheal therapy such as loperamide at the first sign of loose stools, increase oral fluids, and notify their healthcare provider for further instructions and appropriate follow up *[see Patient Counseling Information (17)].* For Grade 3 or 4 diarrhea, or diarrhea that requires hospitalization, discontinue VERZENIO until toxicity resolves to ≤Grade 1, and then resume VERZENIO at the next lower dose *[see Dosage and Administration (2.3)]*.

5.2 Neutropenia

Neutropenia, including febrile neutropenia and fatal neutropenic sepsis, occurred in patients treated with VERZENIO.

Across four clinical trials in 3691 patients, neutropenia occurred in a 37% to 46% of patients receiving VERZENIO. A Grade ≥3 decrease in neutrophil count (based on laboratory findings) occurred in 19% to 32% of patients receiving VERZENIO. Across trials, the median time to the first episode of Grade ≥3 neutropenia ranged from 29 days to 33 days, and the median duration of Grade ≥3 neutropenia ranged from 11 days to 16 days *[see Adverse Reactions (6.1)]*.

Febrile neutropenia has been reported in <1% of patients exposed to VERZENIO across trials. Two deaths due to neutropenic sepsis were observed in MONARCH 2. Inform patients to promptly report any episodes of fever to their healthcare provider *[see Patient Counseling Information (17)]*.

Monitor complete blood counts prior to the start of VERZENIO therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated. Dose interruption, dose reduction, or delay in starting treatment cycles is recommended for patients who develop Grade 3 or 4 neutropenia *[see Dosage and Administration (2.3)]*.

5.3 Interstitial Lung Disease (ILD) or Pneumonitis

Severe, life-threatening, or fatal interstitial lung disease (ILD) or pneumonitis can occur in patients treated with VERZENIO and other CDK4/6 inhibitors. In VERZENIO-treated patients in early breast cancer (monarchE, N=2791), 3% of patients experienced ILD or pneumonitis of any grade: 0.4% were Grade 3 or 4 and there was one fatality (0.1%). In VERZENIO-treated patients in advanced or metastatic breast cancer (N=900) (MONARCH 1, MONARCH 2, MONARCH 3), 3.3% of VERZENIO-treated patients had ILD or pneumonitis of any grade: 0.6% had Grade 3 or 4, and 0.4% had fatal outcomes. Additional cases of ILD or pneumonitis have been observed in the postmarketing setting, with fatalities reported *[see Adverse Reactions (6.2)]*.

Monitor patients for pulmonary symptoms indicative of ILD or pneumonitis. Symptoms may include hypoxia, cough, dyspnea, or interstitial infiltrates on radiologic exams. Infectious, neoplastic, and other causes for such symptoms should be excluded by means of appropriate investigations.

Dose interruption or dose reduction is recommended for patients who develop persistent or recurrent Grade 2 ILD or pneumonitis. Permanently discontinue VERZENIO in all patients with Grade 3 or 4 ILD or pneumonitis *[see Dosage and Administration (2.3)]*.

5.4 Hepatotoxicity

Grade ≥3 ALT (2% to 6%) and AST (2% to 3%) were reported in patients receiving VERZENIO.

Across three clinical trials in 3559 patients (monarchE, MONARCH 2, MONARCH 3), the median time to onset of Grade ≥3 ALT increases ranged from 57 to 87 days and the median time to resolution to Grade <3 was 13 to 14 days. The median time to onset of Grade ≥3 AST increases ranged from 71 to 185 days and the median time to resolution to Grade <3 ranged from 11 to 15 days.

Monitor liver function tests (LFTs) prior to the start of VERZENIO therapy, every 2 weeks for the first 2 months, monthly for the next 2 months, and as clinically indicated. Dose interruption, dose reduction, dose discontinuation, or delay in starting treatment cycles is recommended for patients who develop persistent or recurrent Grade 2, or any Grade 3 or Grade 4 hepatic transaminase elevation *[see Dosage and Administration (2.3)]*.

5.5 Venous Thromboembolism

Across three clinical trials in 3559 patients (monarchE, MONARCH 2, MONARCH 3), venous thromboembolic events were reported in 2% to 5% of patients treated with VERZENIO. Venous thromboembolic events included deep vein thrombosis, pulmonary embolism, pelvic venous thrombosis, cerebral venous sinus thrombosis, subclavian and axillary vein thrombosis, and inferior vena cava thrombosis. In clinical trials, deaths due to venous thromboembolism have been reported in patients treated with VERZENIO.

VERZENIO has not been studied in patients with early breast cancer who had a history of venous thromboembolism. Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism and treat as medically appropriate. Dose interruption is recommended for early breast cancer patients with any grade venous thromboembolic event and for advanced or metastatic breast cancer patients with a Grade 3 or 4 venous thromboembolic event *[see Dosage and Administration (2.3)]*.

5.6 Embryo-Fetal Toxicity

Based on findings from animal studies and the mechanism of action, VERZENIO can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of abemaciclib to pregnant rats during the period of organogenesis caused teratogenicity and decreased fetal weight at maternal exposures that were similar to the human clinical exposure based on area under the curve (AUC) at the maximum recommended human dose.

Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with VERZENIO and for 3 weeks after the last dose *[see Use in Specific Populations (8.1, 8.3) and Clinical Pharmacology (12.1)]*.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling:

- Diarrhea *[see Warnings and Precautions (5.1)]*.
- Neutropenia *[see Warnings and Precautions (5.2)]*.
- Interstitial Lung Disease (ILD) or Pneumonitis *[see Warnings and Precautions (5.3)]*.
- Hepatotoxicity *[see Warnings and Precautions (5.4)]*.
- Venous Thromboembolism *[see Warnings and Precautions (5.5)]*.

6.1 Clinical Studies Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety population described in the Warnings and Precautions reflect exposure to VERZENIO in 3691 patients from four clinical trials: monarchE, MONARCH 1, MONARCH 2, and MONARCH 3. The safety population includes exposure to VERZENIO as a single agent at 200 mg twice daily in 132 patients in MONARCH 1 and to VERZENIO at 150 mg twice daily in 3559 patients administered in combination with fulvestrant, tamoxifen, or an aromatase inhibitor in monarchE, MONARCH 2, and MONARCH 3. The median duration of exposure ranged from 4.5 months in MONARCH 1 to 24 months in monarchE. The most common adverse reactions (incidence ≥20%) across clinical trials were: diarrhea, neutropenia, nausea, abdominal pain, infections, fatigue, anemia, leukopenia, decreased appetite, vomiting, headache, alopecia, and thrombocytopenia.

Early Breast Cancer

monarchE: VERZENIO in Combination with Tamoxifen or an Aromatase Inhibitor as Adjuvant Treatment

Adult patients with HR-positive, HER2-negative, node-positive early breast cancer at a high risk of recurrence

The safety of VERZENIO was evaluated in monarchE, a study of 5591 adult patients receiving VERZENIO plus endocrine therapy (tamoxifen or an aromatase inhibitor) or endocrine therapy (tamoxifen or an aromatase inhibitor) alone *[see Clinical Studies (14.1)].* Patients were randomly assigned to receive 150 mg of VERZENIO orally, twice daily, plus tamoxifen or an aromatase inhibitor, or tamoxifen or an aromatase inhibitor, for two years or until discontinuation criteria were met. The median duration of VERZENIO treatment was 24 months.

The most frequently reported (≥5%) Grade 3 or 4 adverse reactions were neutropenia, leukopenia, diarrhea, and lymphopenia.

Fatal adverse reactions occurred in 0.8% of patients who received VERZENIO plus endocrine therapy (tamoxifen or an aromatase inhibitor), including: cardiac failure (0.1%), cardiac arrest, myocardial infarction, ventricular fibrillation, cerebral hemorrhage, cerebrovascular accident, pneumonitis, hypoxia, diarrhea and mesenteric artery thrombosis (0.03% each).

Permanent VERZENIO treatment discontinuation due to an adverse reaction was reported in 19% of patients receiving VERZENIO, plus tamoxifen or an aromatase inhibitor. Of the patients receiving tamoxifen or an aromatase inhibitor, 1% permanently discontinued due to an adverse reaction. The most common adverse reactions leading to VERZENIO discontinuations were diarrhea (5%), fatigue (2%), and neutropenia (0.9%).

Dose interruption of VERZENIO due to an adverse reaction occurred in 62% of patients receiving VERZENIO plus tamoxifen or aromatase inhibitors. Adverse reactions leading to VERZENIO dose interruptions in ≥5% of patients were diarrhea (20%), neutropenia (16%), leukopenia (7%), and fatigue (5%).

Dose reductions of VERZENIO due to an adverse reaction occurred in 44% of patients receiving VERZENIO plus endocrine therapy (tamoxifen or an aromatase inhibitor). Adverse reactions leading to VERZENIO dose reductions in ≥5% were diarrhea (17%), neutropenia (8%), and fatigue (5%).

- Pruritus-9%
- Dyspepsia-8%
- Nail disorder-6% (includes nail bed disorder, nail bed inflammation, nail discoloration, nail disorder, nail dystrophy, nail pigmentation, nail ridging, nail toxicity, onychalgia, onychoclasis, onycholysis, onychomadesis)
- Lacrimation increased-6%
- Dysgeusia-5%
- Interstitial lung disease (ILD)/pneumonitis-3% (includes pneumonitis, radiation pneumonitis, interstitial lung disease, pulmonary fibrosis, organizing pneumonia, radiation fibrosis – lung, lung opacity, sarcoidosis)
- Venous thromboembolic events (VTEs)-3% (includes catheter site thrombosis, cerebral venous thrombosis, deep vein thrombosis, device related thrombosis, embolism, hepatic vein thrombosis, jugular vein occlusion, jugular vein thrombosis, ovarian vein thrombosis, portal vein thrombosis, pulmonary embolism, subclavian vein thrombosis, venous thrombosis limb)

Table 9: Laboratory Abnormalities (≥10%) in Patients Receiving VERZENIO Plus Tamoxifen or an Aromatase Inhibitor [with a Difference between Arms of ≥2%] in monarchE

	VERZENIO Plus Tamoxifen or an Aromatase Inhibitor N=2791			**Tamoxifen or an Aromatase Inhibitor N=2800**		
	All Grades %	**Grade 3 %**	**Grade 4 %**	**All Grades %**	**Grade 3 %**	**Grade 4 %**
Creatinine increased	99	0.5	0	91	<0.1	0
White blood cell decreased	89	19	<0.1	28	1.1	0
Neutrophil count decreased	84	18	0.7	23	1.6	0.3
Anemia	68	1.0	0	17	0.1	0
Lymphocyte count decreased	59	13	0.2	24	2.4	0.1
Platelet count decreased	37	0.7	0.2	10	0.1	0.1
Alanine aminotransferase increased	37	2.5	<0.1	24	1.2	0
Aspartate aminotransferase increased	31	1.5	<0.1	18	0.9	0
Hypokalemia	11	1.2	0.1	3.8	0.1	0.1

Advanced or Metastatic Breast Cancer

MONARCH 3: VERZENIO in Combination with an Aromatase Inhibitor (Anastrozole or Letrozole) as Initial Endocrine-Based Therapy

Postmenopausal Women with HR-positive, HER2-negative locoregionally recurrent or metastatic breast cancer with no prior systemic therapy in this disease setting

The safety of VERZENIO was evaluated in MONARCH 3, a study of 488 women receiving VERZENIO plus an aromatase inhibitor or placebo plus an aromatase inhibitor *[see Clinical Studies (14.2)].* Patients were randomly assigned to receive 150 mg of VERZENIO or placebo orally twice daily, plus physician's choice of anastrozole or letrozole once daily. Median duration of treatment was 15.1 months for the VERZENIO arm and 13.9 months for the placebo arm.

The most frequently reported (≥5%) Grade 3 or 4 adverse reactions were neutropenia, diarrhea, leukopenia, increased ALT, and anemia.

Deaths during treatment or during the 30-day follow up, regardless of causality, were reported in 11 cases (3%) of VERZENIO plus an aromatase inhibitor treated patients versus 3 cases (2%) of placebo plus an aromatase inhibitor treated patients. Causes of death for patients receiving VERZENIO plus an aromatase inhibitor included: 3 (0.9%) patient deaths due to underlying disease, 3 (0.9%) due to lung infection, 3 (0.9%) due to VTE, 1 (0.3%) due to pneumonitis, and 1 (0.3%) due to cerebral infarction.

Deaths during treatment or during the 30-day follow up, regardless of causality, were reported in 18 cases (4%) of VERZENIO plus fulvestrant treated patients versus 10 cases (5%) of placebo plus fulvestrant treated patients. Causes of death for patients receiving VERZENIO plus fulvestrant included: 7 (2%) patient deaths due to underlying disease, 4 (0.9%) due to sepsis, 2 (0.5%) due to pneumonitis, 2 (0.5%) due to hepatotoxicity, and one (0.2%) due to cerebral infarction.

Permanent study treatment discontinuation due to an adverse reaction were reported in 9% of patients receiving VERZENIO plus fulvestrant and in 3% of patients receiving placebo plus fulvestrant. Adverse reactions leading to permanent discontinuation for patients receiving VERZENIO plus fulvestrant were infection (2%), diarrhea (1%), hepatotoxicity (1%), fatigue (0.7%), nausea (0.2%), abdominal pain (0.2%), acute kidney injury (0.2%), and cerebral infarction (0.2%).

Dose interruption of VERZENIO due to an adverse reaction occurred in 52% of patients receiving VERZENIO plus fulvestrant. Adverse reactions leading to VERZENIO dose interruptions in ≥5% of patients were diarrhea (19%) and neutropenia (16%).

Dose reductions due to an adverse reaction occurred in 43% of patients receiving VERZENIO plus fulvestrant. Adverse reactions leading to reductions in ≥5% of patients were diarrhea and neutropenia. VERZENIO dose reductions due to diarrhea of any grade occurred in 19% of patients receiving VERZENIO plus fulvestrant compared to 0.4% of patients receiving placebo and fulvestrant. VERZENIO dose reductions due to neutropenia of any grade occurred in 10% of patients receiving VERZENIO plus fulvestrant compared to no patients receiving placebo plus fulvestrant.

The most common adverse reactions reported (≥20%) in the VERZENIO arm were: diarrhea, fatigue, neutropenia, nausea, infections, abdominal pain, anemia, leukopenia, decreased appetite, vomiting, and headache. Adverse reactions are shown in Table 12 and laboratory abnormalities in Table 13.

Table 12: Adverse Reactions (≥10%) in Patients Receiving VERZENIO Plus Fulvestrant [with a Difference Between Arms of ≥2%] in MONARCH 2

	VERZENIO plus Fulvestrant N=441			Placebo plus Fulvestrant N=223		
	All Grades %	Grade 3 %	Grade 4 %	All Grades %	Grade 3 %	Grade 4 %
Gastrointestinal Disorders						
Diarrhea	86	13	0	25	0.4	0
Nausea	45	2.7	0	23	0.9	0
Abdominal pain[a]	35	2.5	0	16	0.9	0
Vomiting	26	0.9	0	10	1.8	0
Stomatitis	15	0.5	0	10	0	0
Infections and Infestations						
Infections[b]	43	5	0.7	25	3.1	0.4
General Disorders and Administration Site Conditions						
Fatigue[c]	46	2.7	0	32	0.4	0
Edema peripheral	12	0	0	7	0	0
Pyrexia	11	0.5	0.2	6	0.4	0
Metabolism and Nutrition Disorders						
Decreased appetite	27	1.1	0	12	0.4	0
Respiratory, Thoracic and Mediastinal Disorders						
Cough	13	0	0	11	0	0
Skin and Subcutaneous Tissue Disorders						
Alopecia	16	0	0	1.8	0	0
Pruritus	13	0	0	6	0	0

Table 19: Efficacy Results in MONARCH 1 (Intent-to-Treat Population)

	VERZENIO 200 mg N=132	
	Investigator Assessed	**Independent Review**
Objective Response Rate[a,b], n (%)	26 (19.7)	23 (17.4)
95% CI (%)	13.3, 27.5	11.4, 25.0
Median Duration of Response	8.6 months	7.2 months
95% CI (%)	5.8, 10.2	5.6, NR

Abbreviations: CI = confidence interval, NR = not reached.

[a] All responses were partial responses.

[b] Based upon confirmed responses.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

VERZENIO 50 mg tablets are oval beige tablet with “Lilly” debossed on one side and “50” on the other side.
VERZENIO 100 mg tablet are oval white to practically white tablet with “Lilly” debossed on one side and “100” on the other side.
VERZENIO 150 mg tablets are oval yellow tablet with “Lilly” debossed on one side and “150” on the other side.
VERZENIO 200 mg tablets are oval beige tablet with “Lilly” debossed on one side and “200” on the other side.

VERZENIO tablets are supplied in 7-day dose pack configurations as follows:

- 200 mg dose pack (14 tablets) – each blister pack contains 14 tablets (200 mg per tablet) (200 mg twice daily) NDC 0002-6216-54
- 150 mg dose pack (14 tablets) – each blister pack contains 14 tablets (150 mg per tablet) (150 mg twice daily) NDC 0002-5337-54
- 100 mg dose pack (14 tablets) – each blister pack contains 14 tablets (100 mg per tablet) (100 mg twice daily) NDC 0002-4815-54
- 50 mg dose pack (14 tablets) – each blister pack contains 14 tablets (50 mg per tablet) (50 mg twice daily) NDC 0002-4483-54

Storage and Handling

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F).

17 PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved Patient Information.

Diarrhea

VERZENIO may cause diarrhea, which may be severe in some cases *[see Warnings and Precautions (5.1)]*.

- Early identification and intervention is critical for the optimal management of diarrhea. Instruct patients that at the first sign of loose stools, they should start antidiarrheal therapy (for example, loperamide) and notify their healthcare provider for further instructions and appropriate follow up.
- Encourage patients to increase oral fluids.
- If diarrhea does not resolve with antidiarrheal therapy within 24 hours to ≤Grade 1, suspend VERZENIO dosing *[see Dosage and Administration (2.3)]*.

Neutropenia

Advise patients of the possibility of developing neutropenia and to immediately contact their healthcare provider should they develop a fever, particularly in association with any signs of infection *[see Warnings and Precautions (5.2)]*.

Interstitial Lung Disease/Pneumonitis

Advise patients to immediately report new or worsening respiratory symptoms *[see Warnings and Precautions (5.3)]*.

Hepatotoxicity

Inform patients of the signs and symptoms of hepatotoxicity. Advise patients to contact their healthcare provider immediately for signs or symptoms of hepatotoxicity *[see Warnings and Precautions (5.4)]*.

Venous Thromboembolism

Advise patients to immediately report any signs or symptoms of thromboembolism such as pain or swelling in an extremity, shortness of breath, chest pain, tachypnea, and tachycardia *[see Warnings and Precautions (5.5)]*.

Embryo-Fetal Toxicity

- Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions (5.6) and Use in Specific Populations (8.1)]*.
- Advise females of reproductive potential to use effective contraception during VERZENIO treatment and for 3 weeks after the last dose *[see Use in Specific Populations (8.1, 8.3)]*.

Lactation

Advise lactating women not to breastfeed during VERZENIO treatment and for at least 3 weeks after the last dose *[see Use in Specific Populations (8.2)]*.

Infertility

Inform males of reproductive potential that VERZENIO may impair fertility *[see Use in Specific Populations (8.3)]*.

Drug Interactions

- Inform patients to avoid concomitant use of ketoconazole. Dose reduction may be required for other strong CYP3A inhibitors or for moderate CYP3A inhibitors *[see Dosage and Administration (2.3) and Drug Interactions (7)]*.
- Grapefruit may interact with VERZENIO. Advise patients not to consume grapefruit products while on treatment with VERZENIO.
- Advise patients to avoid concomitant use of strong and moderate CYP3A inducers and to consider alternative agents *[see Dosage and Administration (2.3) and Drug Interactions (7)]*.
- Advise patients to inform their healthcare providers of all concomitant medications, including prescription medicines, over-the-counter drugs, vitamins, and herbal products *[see Dosage and Administration (2.3) and Drug Interactions (7)]*.

Dosing

- Instruct patients to take the doses of VERZENIO at approximately the same times every day and to swallow whole (do not chew, crush, or split them prior to swallowing) *[see Dosage and Administration (2.2)]*.
- If patient vomits or misses a dose, advise the patient to take the next prescribed dose at the usual time *[see Dosage and Administration (2.2)]*.
- Advise the patient that VERZENIO may be taken with or without food *[see Dosage and Administration 2.2)]*.

Marketed by: Lilly USA, LLC, Indianapolis, IN 46285, USA

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PATIENT INFORMATION
VERZENIO® (ver-ZEN-ee-oh)
(abemaciclib)
tablets

What is the most important information I should know about VERZENIO?

VERZENIO may cause serious side effects including:

- **Diarrhea**. Diarrhea is common with VERZENIO treatment and may sometimes be severe. Diarrhea may cause you to develop dehydration or an infection. The most common time to develop diarrhea is during the first month of VERZENIO treatment. If you develop diarrhea during treatment with VERZENIO, your healthcare provider may tell you to temporarily stop taking VERZENIO, stop your treatment, or decrease your dose.
  - **If you have any loose stools,** start taking an antidiarrheal medicine (such as loperamide), drink more fluids, and tell your healthcare provider right away.
- **Low white blood cell counts (neutropenia).** Low white blood cell counts are common during treatment with VERZENIO and may cause serious infections that can lead to death. Your healthcare provider should check your white blood cell counts before and during treatment. If you develop low white blood cell counts during treatment with VERZENIO, your healthcare provider may tell you to temporarily stop taking VERZENIO, decrease your dose, or wait before starting your next month of treatment. **Tell your healthcare provider right away if you have signs and symptoms of low white blood cell counts or infections, such as fever and chills.**
- **Lung problems.** VERZENIO may cause severe or life-threatening inflammation of the lungs during treatment that can lead to death. If you develop lung problems during treatment with VERZENIO, your healthcare provider may tell you to temporarily stop taking VERZENIO, decrease your dose, or stop your treatment. Tell your healthcare provider right away if you have any new or worsening symptoms, including:
  - trouble breathing or shortness of breath
  - cough with or without mucus
  - chest pain
- **Liver problems.** VERZENIO can cause serious liver problems. Your healthcare provider should do blood tests to check your liver before and during treatment with VERZENIO. If you develop liver problems during treatment with VERZENIO, your healthcare provider may reduce your dose or stop your treatment. Tell your healthcare provider right away if you have any of the following signs and symptoms of liver problems:
  - feeling very tired
  - pain on the upper right side of your stomach area (abdomen)
  - loss of appetite
  - bleeding or bruising more easily than normal
- **Blood clots in your veins, or in the arteries of your lungs.** VERZENIO may cause serious blood clots that have led to death. If you develop blood clots during treatment with VERZENIO, your healthcare provider may tell you to temporarily stop taking VERZENIO. Tell your healthcare provider right away if you get any of the following signs and symptoms of a blood clot:
  - pain or swelling in your arms or legs
  - shortness of breath
  - chest pain
  - rapid breathing
  - rapid heart rate

See "What are the possible side effects of VERZENIO?" for more information about side effects.

What is VERZENIO?

VERZENIO is a prescription medicine used:

- in combination with endocrine therapy (tamoxifen or an aromatase inhibitor) to treat adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer with a high risk of coming back as determined by your healthcare provider.
- in combination with an aromatase inhibitor as the first endocrine-based therapy to treat women who have gone through menopause (postmenopausal), and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer that has worsened or that has spread to other parts of the body (metastatic).
- in combination with fulvestrant to treat adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer that has worsened or spread to other parts of the body (metastatic) and whose disease has progressed after endocrine therapy.
- alone to treat adults with HR-positive, HER2-negative breast cancer that has worsened or that has spread to other parts of the body (metastatic) and whose disease has progressed after endocrine therapy and prior chemotherapy.

When VERZENIO is used in combination with fulvestrant, tamoxifen, or an aromatase inhibitor, also read the Patient Information for the prescribed product. Ask your healthcare provider if you are not sure.

It is not known if VERZENIO is safe and effective in children.

Before taking VERZENIO, tell your healthcare provider about all of your medical conditions, including if you:

- have fever, chills, or any other signs of an infection.
- have a history of blood clots in your veins.
- have lung or breathing problems.
- have liver or kidney problems.
- are pregnant or plan to become pregnant. VERZENIO can harm your unborn baby.

  Females who are able to become pregnant:

  – Your healthcare provider will do a pregnancy test before you start treatment with VERZENIO.
  – You should use effective birth control (contraception) during treatment with VERZENIO and for 3 weeks after the last dose of VERZENIO.
  – Tell your healthcare provider right away if you become pregnant or think you are pregnant during treatment with VERZENIO.
- are breastfeeding or plan to breastfeed. It is not known if VERZENIO passes into your breast milk. Do not breastfeed during treatment with VERZENIO and for at least 3 weeks after the last dose of VERZENIO.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. VERZENIO may affect the way other medicines work, and other medicines may affect how VERZENIO works, causing serious side effects.

Especially tell your healthcare provider if you take a medicine that contains ketoconazole.

Know the medicines you take. Keep a list of them to show your healthcare provider or pharmacist when you get a new medicine.

How should I take VERZENIO?

- Take VERZENIO exactly as your healthcare provider tells you.
- Your healthcare provider may change your dose if needed. Do not stop taking VERZENIO or change the dose without talking to your healthcare provider.
- VERZENIO may be taken with or without food.
- Swallow VERZENIO tablets whole. Do not chew, crush, or split the tablets before swallowing. Do not take VERZENIO tablets if they are broken, cracked, or damaged.
- Take your doses of VERZENIO at about the same time every day.
- If you vomit or miss a dose of VERZENIO, take your next dose at your regular time. Do not take 2 doses of VERZENIO at the same time to make up for the missed dose.

What should I avoid during treatment with VERZENIO?

- Avoid taking ketoconazole during treatment with VERZENIO. Tell your healthcare provider if you take a medicine that contains ketoconazole.
- Avoid grapefruit and products that contain grapefruit during treatment with VERZENIO. Grapefruit may increase the amount of VERZENIO in your blood.

What are the possible side effects of VERZENIO?

VERZENIO may cause serious side effects, including:

- See **"What is the most important information I should know about VERZENIO?"**

The most common side effects of VERZENIO include:

- nausea
- infections
- low red blood cell counts (anemia)
- decreased appetite
- headache
- hair thinning or hair loss (alopecia)
- abdominal pain
- tiredness
- low white blood cell counts (leukopenia)
- vomiting
- low platelet count (thrombocytopenia)

VERZENIO may cause fertility problems in males. This may affect your ability to father a child. Talk to your healthcare provider if this is a concern for you.

These are not all the possible side effects of VERZENIO. For more information, ask your healthcare provider or pharmacist.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store VERZENIO?

- Store VERZENIO at room temperature between 68°F to 77°F (20°C to 25°C).

Keep VERZENIO and all medicines out of the reach of children.

General information about the safe and effective use of VERZENIO.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use VERZENIO for a condition for which it was not prescribed. Do not give VERZENIO to other people, even if they have the same symptoms you have. It may harm them. You can ask your pharmacist or healthcare provider for more information about VERZENIO that is written for health professionals.

What are the ingredients in VERZENIO?

Active ingredient: abemaciclib

Inactive ingredients: microcrystalline cellulose 102, microcrystalline cellulose 101, lactose monohydrate, croscarmellose sodium, sodium stearyl fumarate, silicon dioxide.

Color mixture ingredients: polyvinyl alcohol, titanium dioxide, polyethylene glycol, talc, iron oxide yellow, iron oxide red.

Marketed by: Lilly USA, LLC, Indianapolis, IN 46285, USA

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For more information, go to www.verzenio.com or call 1-800-545-5979.

This Patient Information has been approved by the U.S. Food and Drug Administration. Revised: October 2021