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VERZENIO™
(abemaciclib)
Tablets, for oral use

Open here and tear on perforation for Patient Information Leaflet

NL022IDQR03

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(abemaciclib)
Tablets, for oral use

USPI February 2025

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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 *[see 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 adult patients 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 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.

2.2 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: modified oval beige tablet with "Lilly" debossed on one side and "50" on the other side.

100 mg tablets: modified oval white to practically white tablet with "Lilly" debossed on one side and "100" on the other side.

150 mg tablets: modified oval yellow tablet with "Lilly" debossed on one side and "150" on the other side.

200 mg tablets: modified oval beige tablet with "Lilly" debossed on one side and "200" on the other side.

Not all pack sizes, strengths or presentation may be registered or marketed.

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 (2.2)]*.

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 (2.2)]*.

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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 (2.2)]*.

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 (2.2)]*.

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 (2.2)]*.

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%).

The most common adverse reactions reported (≥20%) in the VERZENIO, plus tamoxifen or an aromatase inhibitor, arm and ≥2% higher than the tamoxifen or an aromatase inhibitor arm were: diarrhea, infections, neutropenia, fatigue, leukopenia, nausea, anemia, and headache. Adverse reactions are shown in Table 8 and laboratory abnormalities are shown in Table 9.

Table 8: Adverse Reactions (≥10%) of 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[a] %	Grade 3 %	Grade 4 %	All Grades[b] %	Grade 3 %	Grade 4 %
Gastrointestinal Disorders						
Diarrhea	84	8	0	9	0.2	0
Nausea	30	0.5	0	9	<0.1	0
Vomiting	18	0.5	0	4.6	0.1	0
Stomatitis[c]	14	0.1	0	5	0	0
Infections and Infestations						
Infections[d]	51	4.9	0.6	39	2.7	0.1
General Disorders and Administration Site Conditions						
Fatigue[e]	41	2.9	0	18	0.1	0
Nervous System Disorders						
Headache	20	0.3	0	15	0.2	0
Dizziness	11	0.1	0	7	<0.1	0
Metabolism and Nutrition Disorders						
Decreased appetite	12	0.6	0	2.4	<0.1	0
Skin and Subcutaneous Tissue Disorders						
Rash[f]	11	0.4	0	4.5	0	0
Alopecia	11	0	0	2.7	0	0

[a] Includes the following fatal adverse reactions: diarrhea (n=1), and infections (n=4)
[b] Includes the following fatal adverse reactions: infections (n=5)
[c] Includes mouth ulceration, mucosal inflammation, oropharyngeal pain, stomatitis.
[d] Includes all reported preferred terms that are part of the Infections and Infestations system organ class. Most common infections (>5%) include upper respiratory tract infection, urinary tract infection, and nasopharyngitis.
[e] Includes asthenia, fatigue.
[f] Includes exfoliative rash, mucocutaneous rash, rash, rash erythematous, rash follicular, rash generalized, rash macular, rash maculo-papular, rash maculovesicular, rash morbilliform, rash papular, rash papulosquamous, rash pruritic, rash vesicular, vulvovaginal rash.

Clinically relevant adverse reactions in <10% of patients who received VERZENIO in combination with tamoxifen or an aromatase inhibitor in monarchE include:

- 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.

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Permanent treatment discontinuation due to an adverse reaction was reported in 13% of patients receiving VERZENIO plus an aromatase inhibitor and in 3% of patients receiving placebo plus an aromatase inhibitor. Adverse reactions leading to permanent discontinuation for patients receiving VERZENIO plus an aromatase inhibitor were diarrhea (2%), ALT increased (2%), infection (1%), venous thromboembolic events (VTE) (1%), neutropenia (0.9%), renal impairment (0.9%), AST increased (0.6%), dyspnea (0.6%), pulmonary fibrosis (0.6%) and anemia, rash, weight decreased and thrombocytopenia (each 0.3%).

Dose interruption of VERZENIO due to an adverse reaction occurred in 56% of patients receiving VERZENIO plus anastrozole or letrozole. Adverse reactions leading to VERZENIO dose interruptions in ≥5% of patients were neutropenia (16%) and diarrhea (15%).

Dose reductions due to an adverse reaction occurred in 43% of patients receiving VERZENIO plus anastrozole or letrozole. Adverse reactions leading to dose reductions in ≥5% of patients were diarrhea and neutropenia. VERZENIO dose reductions due to diarrhea of any grade occurred in 13% of patients receiving VERZENIO plus an aromatase inhibitor compared to 2% of patients receiving placebo plus an aromatase inhibitor. VERZENIO dose reductions due to neutropenia of any grade occurred in 11% of patients receiving VERZENIO plus an aromatase inhibitor compared to 0.6% of patients receiving placebo plus an aromatase inhibitor.

The most common adverse reactions reported (≥20%) in the VERZENIO arm and ≥2% than the placebo arm were: diarrhea, neutropenia, fatigue, infections, nausea, abdominal pain, anemia, vomiting, alopecia, decreased appetite, and leukopenia. Adverse reactions are shown in Table 10 and laboratory abnormalities in Table 11. Diarrhea incidence was greatest during the first month of VERZENIO dosing.

The median time to onset of the first diarrhea event was 8 days, and the median durations of diarrhea for Grades 2 and for Grade 3 were 11 days and 8 days, respectively. Most diarrhea events recovered or resolved (88%) with supportive treatment and/or dose reductions *[see Dosage and Administration (2.2) and Patient Counseling Information (17)]*.

Nineteen percent of patients with diarrhea required a dose omission and 13% required a dose reduction. The median time to the first dose reduction due to diarrhea was 38 days.

Table 10: Adverse Reactions (≥10%) in Patients Receiving VERZENIO Plus Anastrozole or Letrozole [with a Difference between Arms of ≥2%] in MONARCH 3

	VERZENIO plus Anastrozole or Letrozole N=327			Placebo plus Anastrozole or Letrozole N=161		
	All Grades %	Grade 3 %	Grade 4 %	All Grades %	Grade 3 %	Grade 4 %
Gastrointestinal Disorders						
Diarrhea	81	9	0	30	1.2	0
Nausea	39	0.9	0	20	1.2	0
Abdominal pain	29	1.2	0	12	1.2	0
Vomiting	28	1.2	0	12	1.9	0
Constipation	16	0.6	0	12	0	0
Infections and Infestations						
Infections[a]	39	4.0	0.9	29	2.5	0.6
General Disorders and Administration Site Conditions						
Fatigue	40	1.8	0	32	0	0
Influenza like illness	10	0	0	8	0	0
Skin and Subcutaneous Tissue Disorders						
Alopecia	27	0	0	11	0	0
Rash	14	0.9	0	5	0	0
Pruritus	13	0	0	9	0	0
Metabolism and Nutrition Disorders						
Decreased appetite	24	1.2	0	9	0.6	0
Investigations						
Weight decreased	10	0.6	0	3.1	0.6	0
Respiratory, Thoracic, and Mediastinal Disorders						
Cough	13	0	0	9	0	0
Dyspnea	12	0.6	0.3	6	0.6	0
Nervous System Disorders						
Dizziness	11	0.3	0	9	0	0

[a] Includes all reported preferred terms that are part of the Infections and Infestations system organ class. Most common infections (>1%) include upper respiratory tract infection, lung infection, and pharyngitis.

Additional adverse reactions in MONARCH 3 include venous thromboembolic events (deep vein thrombosis, pulmonary embolism, and pelvic venous thrombosis), which were reported in 5% of patients treated with VERZENIO plus anastrozole or letrozole as compared to 0.6% of patients treated with anastrozole or letrozole plus placebo.

Table 11: Laboratory Abnormalities (≥10%) in Patients Receiving VERZENIO Plus Anastrozole or Letrozole [with a Difference Between Arms of ≥2%] in MONARCH 3

Laboratory Abnormality	VERZENIO plus Anastrozole or Letrozole N=327 All Grades %	Grade 3 %	Grade 4 %	Placebo plus Anastrozole or Letrozole N=161 All Grades %	Grade 3 %	Grade 4 %
Creatinine increased	98	2.2	0	84	0	0
White blood cell decreased	82	13	0	27	0.6	0
Anemia	82	1.6	0	28	0	0
Neutrophil count decreased	80	19	2.9	21	2.6	0
Lymphocyte count decreased	53	7	0.6	26	1.9	0
Platelet count decreased	36	1.3	0.6	12	0.6	0
Alanine aminotransferase increased	48	6	0.6	25	1.9	0
Aspartate aminotransferase increased	37	3.8	0	23	0.6	0

Creatinine Increased

Abemaciclib has been shown to increase serum creatinine due to inhibition of renal tubular secretion transporters, without affecting glomerular function *[see Clinical Pharmacology (12.3)]*. Across the clinical studies, increases in serum creatinine (mean increase, 0.2-0.3 mg/dL) occurred within the first 28-day cycle of VERZENIO dosing, remained elevated but stable through the treatment period, and were reversible upon treatment discontinuation. Alternative markers such as BUN, cystatin C, or calculated GFR, which are not based on creatinine, may be considered to determine whether renal function is impaired.

MONARCH 2: VERZENIO in Combination with Fulvestrant

Women with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression on or after prior adjuvant or metastatic endocrine therapy

The safety of VERZENIO (150 mg twice daily) plus fulvestrant (500 mg) versus placebo plus fulvestrant was evaluated in MONARCH 2 *[see Clinical Studies (14.2)]*. The data described below reflect exposure to VERZENIO in 441 patients with HR-positive, HER2-negative advanced breast cancer who received at least one dose of VERZENIO plus fulvestrant in MONARCH 2.

Median duration of treatment was 12 months for patients receiving VERZENIO plus fulvestrant and 8 months for patients receiving placebo plus fulvestrant.

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

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
Rash	11	1.1	0	4.5	0	0
Nervous System Disorders						
Headache	20	0.7	0	15	0.4	0
Dysgeusia	18	0	0	2.7	0	0
Dizziness	12	0.7	0	6	0	0
Investigations						
Weight decreased	10	0.2	0	2.2	0.4	0

[a] Includes abdominal pain, abdominal pain upper, abdominal pain lower, abdominal discomfort, abdominal tenderness.
[b] Includes upper respiratory tract infection, urinary tract infection, lung infection, pharyngitis, conjunctivitis, sinusitis, vaginal infection, sepsis.
[c] Includes asthenia, fatigue.

Additional adverse reactions in MONARCH 2 include venous thromboembolic events (deep vein thrombosis, pulmonary embolism, cerebral venous sinus thrombosis, subclavian vein thrombosis, axillary vein thrombosis, and DVT inferior vena cava), which were reported in 5% of patients treated with VERZENIO plus fulvestrant as compared to 0.9% of patients treated with fulvestrant plus placebo.

Table 13: Laboratory Abnormalities (≥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 %
Creatinine increased	98	1.2	0	74	0	0
White blood cell decreased	90	23	0.7	33	0.9	0
Neutrophil count decreased	87	29	3.5	30	3.7	0.5
Anemia	84	2.6	0	34	0.5	0
Lymphocyte count decreased	63	12	0.2	32	1.8	0
Platelet count decreased	53	0.9	1.2	15	0	0
Alanine aminotransferase increased	41	3.9	0.7	32	1.4	0
Aspartate aminotransferase increased	37	3.9	0	25	3.7	0.5

PATIENT INFORMATION NL022IDQR03
VERZENIO™ (ver-ZEN-ee-oh)
(abemaciclib)
tablets, for oral use

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 adults 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.

How should I store VERZENIO?

- Do not store VERZENIO above 30°C.

Keep VERZENIO and all medicines out of the sight and 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. Do not use this medicine after the expiry date which is stated on the blister and carton after 'EXP'. The expiry date refers to the last day of that month. 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.

How is VERZENIO supplied?
VERZENIO 50 mg tablets are modified, oval beige tablet with "Lilly" debossed on one side and "50" on the other side.
VERZENIO 100 mg tablet are modified, oval white to practically white tablet with "Lilly" debossed on one side and "100" on the other side.
VERZENIO 150 mg tablets are modified, oval yellow tablet with "Lilly" debossed on one side and "150" on the other side.
VERZENIO 200 mg tablets are modified,oval beige tablet with "Lilly" debossed on one side and "200" on the other side.
VERZENIO 50 mg, 100 mg, 150 mg and 200 mg are marketed in blister packs of 14 tablets. Each pack contains 1 blister of 14 tablets.
Not all pack sizes, strengths or presentation may be marketed/registered.

Marketing Authorization Holder:
Eli Lilly and Company, Lilly Corporate Center, Indianapolis, Indiana (IN) 46285, United States (USA)

Manufactured by:
Lilly del Caribe, Inc. 12.6 KM 65th Infantry Road, Carolina, Puerto Rico (PR) 00985, United States (USA)

Packaged and released by:
Eli Lilly and Company, Lilly Corporate Center, Indianapolis, Indiana (IN) 46285, United States (USA)

Revised: February 2025

THIS IS A MEDICAMENT
- A medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.

Council of Arab health ministers
Union of Arab Pharmacists

Layout Used to Develop Artwork: INDL7547C00

PPD Information Box

Technical Information: Black DIECUT DIE PERFORATION

Previous Item Code (to be destroyed)
NL022IDQR02

Creatinine Increased

Abemaciclib has been shown to increase serum creatinine due to inhibition of renal tubular secretion transporters, without affecting glomerular function *[see Clinical Pharmacology (12.3)]*. In clinical studies, increases in serum creatinine (mean increase, 0.2-0.3 mg/dL) occurred within the first 28-day cycle of VERZENIO dosing, remained elevated but stable through the treatment period, and were reversible upon treatment discontinuation. Alternative markers such as BUN, cystatin C, or calculated glomerular filtration rate (GFR), which are not based on creatinine, may be considered to determine whether renal function is impaired.

MONARCH 1: VERZENIO Administered as a Monotherapy in Metastatic Breast Cancer

Patients with HR-positive, HER2-negative breast cancer who received prior endocrine therapy and 1-2 chemotherapy regimens in the metastatic setting

The safety of VERZENIO was evaluated in MONARCH 1, a single-arm, open-label, multicenter study in 132 women with measurable HR-positive, HER2-negative metastatic breast cancer *[see Clinical Studies (14.2)]*. Patients received 200 mg VERZENIO orally twice daily until development of progressive disease or unmanageable toxicity. Median duration of treatment was 4.5 months.

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

Deaths due to adverse reactions during treatment or during the 30-day follow up were reported in 2% of patients. Cause of death in these patients was due to infection (2 patients) or pneumonitis (1 patient).

Ten patients (8%) discontinued study treatment from adverse reactions due to (1 patient each), abdominal pain, arterial thrombosis, aspartate aminotransferase (AST) increased, blood creatinine increased, chronic kidney disease, diarrhea, ECG QT prolonged, fatigue, hip fracture, and lymphopenia.

Dose interruption of VERZENIO due to an adverse reaction occurred in 58% of patients. The most frequent (≥5%) adverse reactions leading to dose interruptions were diarrhea (24%), neutropenia (16%), fatigue (10%), vomiting (6%), and nausea (5%).

Forty-nine percent of patients had dose reductions due to an adverse reaction. The most frequent adverse reactions that led to dose reductions were diarrhea (20%), neutropenia (11%), and fatigue (9%).

The most common reported adverse reactions (≥20%) were: diarrhea, fatigue, nausea, decreased appetite, abdominal pain, neutropenia, vomiting, infections, anemia, headache, and thrombocytopenia. Adverse reactions are shown in Table 14 and laboratory abnormalities in Table 15.

Table 14: Adverse Reactions (≥10%) of Patients in MONARCH 1

	VERZENIO N=132		
	All Grades %	**Grade 3 %**	**Grade 4 %**
Gastrointestinal Disorders			
Diarrhea	90	20	0
Nausea	64	4.5	0
Abdominal pain	39	2.3	0
Vomiting	35	1.5	0
Constipation	17	0.8	0
Dry mouth	14	0	0
Stomatitis	14	0	0
Infections and Infestations			
Infections	31	4.5	0
General Disorders and Administration Site Conditions			
Fatigue[a]	65	13	0
Pyrexia	11	0	0
Metabolism and Nutrition Disorders			
Decreased appetite	45	3.0	0
Dehydration	10	2.3	0
Respiratory, Thoracic and Mediastinal Disorders			
Cough	19	0	0
Musculoskeletal and Connective Tissue Disorders			
Arthralgia	15	0	0
Nervous System Disorders			
Headache	20	0	0
Dysgeusia	12	0	0
Dizziness	11	0	0
Skin and Subcutaneous Tissue Disorders			
Alopecia	12	0	0
Investigations			
Weight decreased	14	0	0

[a] Includes asthenia, fatigue.

Table 15: Laboratory Abnormalities for Patients Receiving VERZENIO in MONARCH 1

	VERZENIO N=132		
	All Grades %	**Grade 3 %**	**Grade 4 %**
Creatinine increased	99	0.8	0
White blood cell decreased	91	28	0
Neutrophil count decreased	88	22	4.6
Anemia	69	0	0
Lymphocyte count decreased	42	13	0.8
Platelet count decreased	41	2.3	0
ALT increased	31	3.1	0
AST increased	30	3.8	0

Creatinine Increased

Abemaciclib has been shown to increase serum creatinine due to inhibition of renal tubular secretion transporters, without affecting glomerular function *[see Clinical Pharmacology (12.3)]*. In clinical studies, increases in serum creatinine (mean increase, 0.2-0.3 mg/dL) occurred within the first 28-day cycle of VERZENIO dosing, remained elevated but stable through the treatment period, and were reversible upon treatment discontinuation. Alternative markers such as BUN, cystatin C, or calculated GFR, which are not based on creatinine, may be considered to determine whether renal function is impaired.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of VERZENIO. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Respiratory disorders: Interstitial lung disease (ILD)/pneumonitis *[see Warnings and Precautions (5.3)]*.

7 DRUG INTERACTIONS

7.1 Effect of Other Drugs on VERZENIO

CYP3A Inhibitors

Strong and moderate CYP3A4 inhibitors increased the exposure of abemaciclib plus its active metabolites to a clinically meaningful extent and may lead to increased toxicity.

Ketoconazole

Avoid concomitant use of ketoconazole. Ketoconazole is predicted to increase the AUC of abemaciclib by up to 16-fold *[see Clinical Pharmacology (12.3)]*.

Other Strong CYP3A Inhibitors

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 with concomitant use of strong CYP3A inhibitors other than ketoconazole. 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 with concomitant use of strong CYP3A inhibitors. If a patient taking VERZENIO discontinues a strong CYP3A inhibitor, increase the VERZENIO dose (after 3-5 half-lives of the inhibitor) to the dose that was used before starting the inhibitor. Patients should avoid grapefruit products *[see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)]*.

Moderate CYP3A Inhibitors

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.

Strong and Moderate CYP3A Inducers

Coadministration of strong or moderate CYP3A inducers decreased the plasma concentrations of abemaciclib plus its active metabolites and may lead to reduced activity. Avoid concomitant use of strong or moderate CYP3A inducers and consider alternative agents *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings in animals and its mechanism of action, VERZENIO can cause fetal harm when administered to a pregnant woman *[see Clinical Pharmacology (12.1)]*. There are no available human data informing the drug-associated risk. Advise pregnant women of the potential risk to a fetus. In animal reproduction studies, administration of abemaciclib during organogenesis was teratogenic and caused decreased fetal weight at maternal exposures that were similar to human clinical exposure based on AUC at the maximum recommended human dose (*see* Data). Advise pregnant women of the potential risk to a fetus.

The background risk of major birth defects and miscarriage for the indicated population is unknown. However, the background risk in the U.S. general population of major birth defects is 2 to 4% and of miscarriage is 15 to 20% of clinically recognized pregnancies.

Data

Animal Data

In an embryo-fetal development study, pregnant rats received oral doses of abemaciclib up to 15 mg/kg/day during the period of organogenesis. Doses ≥4 mg/kg/day caused decreased fetal body weights and increased incidence of cardiovascular and skeletal malformations and variations. These findings included absent innominate artery and aortic arch, malpositioned subclavian artery, unossified sternebra, bipartite ossification of thoracic centrum, and rudimentary or nodulated ribs. At 4 mg/kg/day in rats, the maternal systemic exposures were approximately equal to the human exposure (AUC) at the recommended dose.

8.2 Lactation

Risk Summary

There are no data on the presence of abemaciclib in human milk, or its effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed infants from VERZENIO, advise lactating women not to breastfeed during VERZENIO treatment and for 3 weeks after the last dose.

8.3 Females and Males of Reproductive Potential

Based on animal studies, VERZENIO can cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]*.

Pregnancy Testing

Verify pregnancy status in females of reproductive potential prior to initiating treatment with VERZENIO.

Contraception

Females

Advise females of reproductive potential to use effective contraception during VERZENIO treatment and for 3 weeks after the last dose.

Infertility

Males

Based on findings in animals, VERZENIO may impair fertility in males of reproductive potential *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

The safety and effectiveness of VERZENIO have not been established in pediatric patients.

The safety and effectiveness of VERZENIO in combination with chemotherapy was assessed but not established in an open label, dose-finding trial (NCT04238819) in 43 pediatric patients aged 1 to < 17 years with relapsed/refractory solid tumors. No new safety signals were observed in pediatric patients in this study. Abemaciclib exposure in pediatric patients was within the range of the values previously observed in adults given a similar dose per body surface area.

8.5 Geriatric Use

Of the 2791 VERZENIO-treated patients in monarchE, 15% were 65 years of age or older and 2.7% were 75 years of age or older.

Of the 900 patients who received VERZENIO in MONARCH 1, MONARCH 2, and MONARCH 3, 38% were 65 years of age or older and 10% were 75 years of age or older. The most common adverse reactions (≥5%) Grade 3 or 4 in patients ≥65 years of age across MONARCH 1, 2, and 3 were: neutropenia, diarrhea, fatigue, nausea, dehydration, leukopenia, anemia, infections, and ALT increased.

No overall differences in safety or effectiveness of VERZENIO were observed between these patients and younger patients.

8.6 Renal Impairment

No dosage adjustment is required for patients with mild or moderate renal impairment (CLcr ≥30-89 mL/min, estimated by Cockcroft-Gault [C-G]). The pharmacokinetics of abemaciclib in patients with severe renal impairment (CLcr <30 mL/min, C-G), end stage renal disease, or in patients on dialysis is unknown *[see Clinical Pharmacology (12.3)]*.

8.7 Hepatic Impairment

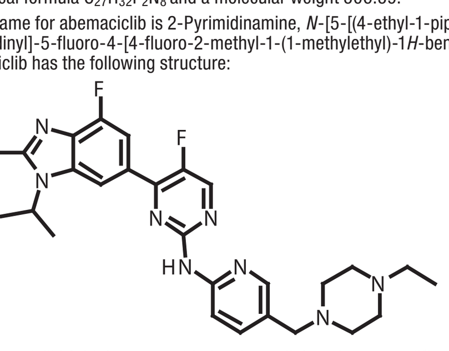
No dosage adjustments are necessary in patients with mild or moderate hepatic impairment (Child-Pugh A or B).

Reduce the dosing frequency when administering VERZENIO to patients with severe hepatic impairment (Child-Pugh C) *[see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)]*.

11 DESCRIPTION

Abemaciclib is a kinase inhibitor for oral administration. It is a white to yellow powder with the empirical formula $C_{27}H_{32}F_2N_8$ and a molecular weight 506.59.

The chemical name for abemaciclib is 2-Pyrimidinamine, *N*-[5-[(4-ethyl-1-piperazinyl) methyl]-2-pyridinyl]-5-fluoro-4-[4-fluoro-2-methyl-1-(1-methylethyl)-1*H*-benzimidazol-6-yl]-. Abemaciclib has the following structure:



VERZENIO (abemaciclib) tablets are provided as immediate-release, modified, oval white, beige, or yellow tablets. Inactive ingredients are as follows: Excipients—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, and iron oxide red.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Abemaciclib is an inhibitor of cyclin-dependent kinases 4 and 6 (CDK4 and CDK6). These kinases are activated upon binding to D-cyclins. In estrogen receptor-positive (ER+) breast cancer cell lines, cyclin D1 and CDK4/6 promote phosphorylation of the retinoblastoma protein (Rb), cell cycle progression, and cell proliferation. In vitro, continuous exposure to abemaciclib inhibited Rb phosphorylation and blocked progression from G1 into S phase of the cell cycle, resulting in senescence and apoptosis. In breast cancer xenograft models, abemaciclib dosed daily without interruption as a single agent or in combination with antiestrogens resulted in reduction of tumor size.

12.2 Pharmacodynamics

Cardiac Electrophysiology

Based on evaluation of the QTc interval in patients and in a healthy volunteer study, abemaciclib did not cause large mean increases (i.e., 20 ms) in the QTc interval.

12.3 Pharmacokinetics

The pharmacokinetics of abemaciclib were characterized in patients with solid tumors, including breast cancer, and in healthy subjects.

Following single and repeated twice daily dosing of 50 mg (0.3 times the approved recommended 150 mg dosage) to 200 mg of abemaciclib, the increase in plasma exposure (AUC) and C_{max} was approximately dose proportional. Steady state was achieved within 5 days following repeated twice daily dosing, and the estimated geometric mean accumulation ratio was 2.3 (50% CV) and 3.2 (59% CV) based on C_{max} and AUC, respectively.

Absorption

The absolute bioavailability of abemaciclib after a single oral dose of 200 mg is 45% (19% CV). The median T_{max} of abemaciclib is 8.0 hours (range: 4.1-24.0 hours).

Effect of Food

A high-fat, high-calorie meal (approximately 800 to 1000 calories with 150 calories from protein, 250 calories from carbohydrate, and 500 to 600 calories from fat) administered to healthy subjects increased the AUC of abemaciclib plus its active metabolites by 9% and increased C_{max} by 26%.

Distribution

In vitro, abemaciclib was bound to human plasma proteins, serum albumin, and alpha-1-acid glycoprotein in a concentration independent manner from 152 ng/mL to 5066 ng/mL. In a clinical study, the mean (standard deviation, SD) bound fraction was 96.3% (1.1) for abemaciclib, 93.4% (1.3) for M2, 96.8% (0.8) for M18, and 97.8% (0.6) for M20. The geometric mean systemic volume of distribution is approximately 690.3 L (49% CV).

In patients with advanced cancer, including breast cancer, concentrations of abemaciclib and its active metabolites M2 and M20 in cerebrospinal fluid are comparable to unbound plasma concentrations.

Elimination

The geometric mean hepatic clearance (CL) of abemaciclib in patients was 26.0 L/h (51% CV), and the mean plasma elimination half-life for abemaciclib in patients was 18.3 hours (72% CV).

Metabolism

Hepatic metabolism is the main route of clearance for abemaciclib. Abemaciclib is metabolized to several metabolites primarily by cytochrome P450 (CYP) 3A4, with formation of N-desethylabemaciclib (M2) representing the major metabolism pathway. Additional metabolites include hydroxyabemaciclib (M20), hydroxy-N-desethylabemaciclib (M18), and an oxidative metabolite (M1). M2, M18, and M20 are

equipotent to abemaciclib and their AUCs accounted for 25%, 13%, and 26% of the total circulating analytes in plasma, respectively.

Excretion

After a single 150 mg oral dose of radiolabeled abemaciclib, approximately 81% of the dose was recovered in feces and approximately 3% recovered in urine. The majority of the dose eliminated in feces was metabolites.

Specific Populations

Age, Gender, and Body Weight

Based on a population pharmacokinetic analysis in patients with cancer, age (range 24-91 years), gender (134 males and 856 females), and body weight (range 36-175 kg) had no effect on the exposure of abemaciclib.

Patients with Renal Impairment

In a population pharmacokinetic analysis of 990 individuals, in which 381 individuals had mild renal impairment (60 mL/min ≤ CLcr <90 mL/min) and 126 individuals had moderate renal impairment (30 mL/min ≤ CLcr <60 mL/min), mild and moderate renal impairment had no effect on the exposure of abemaciclib *[see Use in Specific Populations (8.6)]*. The effect of severe renal impairment (CLcr <30 mL/min) on pharmacokinetics of abemaciclib is unknown.

Patients with Hepatic Impairment

Following a single 200 mg oral dose of abemaciclib, the relative potency adjusted unbound AUC_{0-INF} of abemaciclib plus its active metabolites (M2, M18, M20) in plasma increased 1.2-fold in subjects with mild hepatic impairment (Child-Pugh A, n=9), 1.1-fold in subjects with moderate hepatic impairment (Child-Pugh B, n=10), and 2.4-fold in subjects with severe hepatic impairment (Child-Pugh C, n=6) relative to subjects with normal hepatic function (n=10) *[see Use in Specific Populations (8.7)]*. In subjects with severe hepatic impairment, the mean plasma elimination half-life of abemaciclib increased to 55 hours compared to 24 hours in subjects with normal hepatic function.

Drug Interaction Studies

Effects of Other Drugs on Abemaciclib

Strong CYP3A Inhibitors: Ketoconazole (a strong CYP3A inhibitor) is predicted to increase the AUC of abemaciclib by up to 16-fold.

Coadministration of 500 mg twice daily doses of clarithromycin (a strong CYP3A inhibitor) with a single 50 mg dose of VERZENIO (0.3 times the approved recommended 150 mg dosage) increased the relative potency adjusted unbound AUC_{0-INF} of abemaciclib plus its active metabolites (M2, M18, and M20) by 2.5-fold relative to abemaciclib alone in cancer patients.

Moderate CYP3A Inhibitors: Verapamil and diltiazem (moderate CYP3A inhibitors) are predicted to increase the relative potency adjusted unbound AUC of abemaciclib plus its active metabolites (M2, M18, and M20) by approximately 1.6-fold and 2.4-fold, respectively.

Strong CYP3A Inducers: Coadministration of 600 mg daily doses of rifampin (a strong CYP3A inducer) with a single 200 mg dose of VERZENIO decreased the relative potency adjusted unbound AUC_{0-INF} of abemaciclib plus its active metabolites (M2, M18, and M20) by approximately 70% in healthy subjects.

Moderate CYP3A Inducers: Efavirenz, bosentan, and modafinil (moderate CYP3A inducers) are predicted to decrease the relative potency adjusted unbound AUC of abemaciclib plus its active metabolites (M2, M18, and M20) by 53%, 41%, and 29%, respectively.

Loperamide: Co-administration of a single 8 mg dose of loperamide with a single 400 mg dose of abemaciclib in healthy subjects increased the relative potency adjusted unbound AUC_{0-INF} of abemaciclib plus its active metabolites (M2 and M20) by 12%, which is not considered clinically relevant.

Endocrine Therapies: In clinical studies in patients with breast cancer, there was no clinically relevant effect of fulvestrant, anastrozole, letrozole, exemestane, or tamoxifen on abemaciclib pharmacokinetics.

Effects of Abemaciclib on Other Drugs

Loperamide: In a clinical drug interaction study in healthy subjects, coadministration of a single 8 mg dose of loperamide with a single 400 mg abemaciclib (2.7 times the approved recommended 150 mg dosage) increased loperamide AUC_{0-INF} by 9% and C_{max} by 35% relative to loperamide alone. These increases in loperamide exposure are not considered clinically relevant.

Metformin: In a clinical drug interaction study in healthy subjects, coadministration of a single 1000 mg dose of metformin, a clinically relevant substrate of renal OCT2, MATE1, and MATE2-K transporters, with a single 400 mg dose of abemaciclib (2.7 times the approved recommended 150 mg dosage) increased metformin AUC_{0-INF} by 37% and C_{max} by 22% relative to metformin alone. Abemaciclib reduced the renal clearance and renal secretion of metformin by 45% and 62%, respectively, relative to metformin alone, without any effect on glomerular filtration rate (GFR) as measured by iohexol clearance and serum cystatin C.

Endocrine Therapies: In clinical studies in patients with breast cancer, there was no clinically relevant effect of abemaciclib on the pharmacokinetics of fulvestrant, anastrozole, letrozole, exemestane, or tamoxifen.

CYP Metabolic Pathways: In a clinical drug interaction study in patients with cancer, multiple doses of abemaciclib (200 mg twice daily for 7 days) did not result in clinically meaningful changes in the pharmacokinetics of CYP1A2, CYP2C9, CYP2D6 and CYP3A4 substrates. Abemaciclib is a substrate of CYP3A4, and time-dependent changes in pharmacokinetics of abemaciclib as a result of autoinhibition of its metabolism were not observed.

In Vitro Studies

Transporter Systems: Abemaciclib and its major active metabolites inhibit the renal transporters OCT2, MATE1, and MATE2-K at concentrations achievable at the approved recommended dosage. The observed serum creatinine increase in clinical studies with abemaciclib is likely due to inhibition of tubular secretion of creatinine via OCT2, MATE1, and MATE2-K [see Adverse Effects (6.1)]. Abemaciclib and its major metabolites at clinically relevant concentrations do not inhibit the hepatic uptake transporters OCT1, OATP1B1, and OATP1B3 or the renal uptake transporters OAT1 and OAT3.

Abemaciclib is a substrate of P-gp and BCRP. Abemaciclib and its major active metabolites, M2 and M20, are not substrates of hepatic uptake transporters OCT1, organic anion transporting polypeptide 1B1 (OATP1B1), or OATP1B3.

Abemaciclib inhibits P-gp and BCRP. The clinical consequences of this finding on sensitive P-gp and BCRP substrates are unknown.

P-gp and BCRP Inhibitors: In vitro, abemaciclib is a substrate of P-gp and BCRP. The effect of P-gp or BCRP inhibitors on the pharmacokinetics of abemaciclib has not been studied.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Abemaciclib was assessed for carcinogenicity in a 2-year rat study. Abemaciclib was not carcinogenic in male and female rats at oral doses up to 3 mg/kg/day (approximately 1 time the exposure at the maximum recommended human dose based on AUC).

Abemaciclib and its active human metabolites M2 and M20 were not mutagenic in a bacterial reverse mutation (Ames) assay or clastogenic in an in vitro chromosomal aberration assay in Chinese hamster ovary cells or human peripheral blood lymphocytes. Abemaciclib, M2, and M20 were not clastogenic in an in vivo rat bone marrow micronucleus assay.

Abemaciclib may impair fertility in males of reproductive potential. In repeat-dose toxicity studies up to 3-months duration, abemaciclib-related findings in the testis, epididymis, prostate, and seminal vesicle at doses ≥10 mg/kg/day in rats and ≥0.3 mg/kg/day in dogs included decreased organ weights, intratubular cellular debris, hypospermia, tubular dilatation, atrophy, and degeneration/necrosis. These doses in rats and dogs resulted in approximately 2 and 0.02 times, respectively, the exposure (AUC) in humans at the maximum recommended human dose. In a rat male fertility study, abemaciclib had no effects on mating and fertility at oral doses up to 10 mg/kg/day (approximately 2 times the exposure at the maximum recommended human dose based on AUC).

In a rat female fertility and early embryonic development study, abemaciclib did not affect mating and fertility at doses up to 20 mg/kg/day (approximately 3 times the exposure at the maximum recommended human dose based on AUC).

13.2 Animal Toxicology and/or Pharmacology

In repeat-dose toxicity studies up to 6-months duration, oral administration of abemaciclib resulted in retinal atrophy of the eyes in mice at a dose of 150 mg/kg/day (approximately 10 times the exposure at the maximum recommended human dose based on AUC) and in rats at a dose of 30 mg/kg/day (approximately 5 times the exposure at the maximum recommended human dose based on AUC). In a 2-year rat carcinogenicity study, oral administration of abemaciclib resulted in retinal atrophy in the eyes at doses ≥0.3 mg/kg/day (approximately 0.05 times the exposure at the maximum recommended human dose based on AUC).

14 CLINICAL STUDIES

14.1 Early Breast Cancer

VERZENIO in Combination with Standard Endocrine Therapy (monarchE)

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

monarchE (NCT03155997) was a randomized (1:1), open-label, two cohort, multicenter study in adult women and men with HR-positive, HER2-negative, node-positive, resected, early breast cancer with clinical and pathological features consistent with a high risk of disease recurrence. To be enrolled, patients had to have HR-positive HER2-negative early breast cancer with tumor involvement in at least 1 axillary lymph node (pALN) and to be enrolled in cohort 1 had to have either:

- ≥4 pALN or
- 1-3 pALN and at least one of:
  - tumor grade 3 or
  - tumor size ≥50 mm

Patients enrolled in cohort 2 could not have met the eligibility criteria for cohort 1. To be enrolled in cohort 2, patients had to have 1-3 pALN and Ki-67 score ≥20%. Breast tumor samples were tested at central sites using the Ki-67 IHC MIB-1 pharmDx (Dako Omnis) assay to establish if the Ki-67 score was ≥20%.

Patients were randomized to receive 2 years of VERZENIO plus physician's choice of standard endocrine therapy or standard endocrine therapy alone. Randomization to treatment was stratified by prior treatment (neoadjuvant chemotherapy versus adjuvant chemotherapy versus no chemotherapy); menopausal status (premenopausal versus postmenopausal); and region (North America/Europe versus Asia versus other). Men were stratified as postmenopausal. After the end of the study treatment period, standard adjuvant endocrine therapy was continued for a duration of at least 5 years if deemed medically appropriate.

The major efficacy outcome measure was invasive disease–free survival (IDFS). IDFS was defined as the time from randomization to the first occurrence of: ipsilateral invasive breast tumor recurrence, regional invasive breast cancer recurrence, distant recurrence, contralateral invasive breast cancer, second primary non-breast invasive cancer, or death attributable to any cause. Overall survival (OS) was an additional outcome measure.

A statistically significant difference in IDFS was observed in the intent-to-treat (ITT) population which was primarily attributed to the patients treated in cohort 1. While the OS data in cohort 2 remains immature, more deaths were observed among those receiving VERZENIO plus standard endocrine therapy compared to those receiving standard endocrine therapy alone (10/253 vs. 5/264).

Of 5637 patients randomized, 5120 (91%) were randomized in cohort 1. Patient median age was 51 years (range, 22-89 years), 99% were women, 70% were White, 24% were Asian, 1.7% were Black or African American, 2.1% were American Indian or Alaska Native, and 0.1% were Native Hawaiian or Other Pacific Islander. Forty-three percent of patients were premenopausal. Most patients received prior chemotherapy (37% neoadjuvant, 59% adjuvant) and prior radiotherapy (96%). Sixty-five percent of the patients had 4 or more positive lymph nodes with 22% having ≥10 positive lymph nodes, 41% had Grade 3 tumor, and 24% had pathological tumor size ≥50 mm. The majority of patients (99%) had estrogen receptor positive disease and 87% had progesterone receptor positive disease. Initial endocrine therapy received by patients included letrozole (39%), tamoxifen (31%), anastrozole (22%), or exemestane (8%).

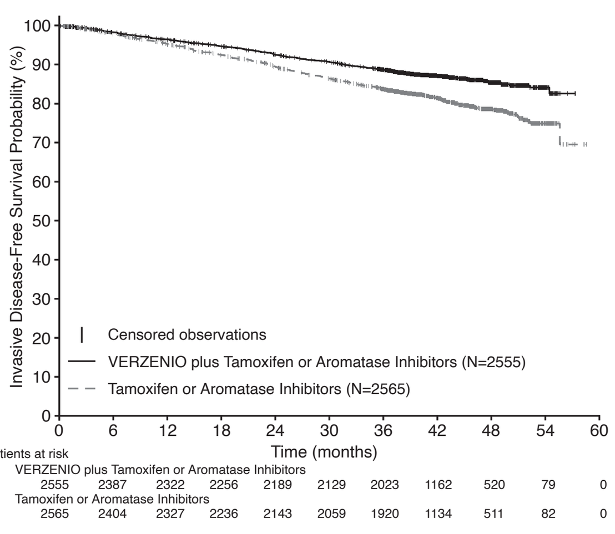
Efficacy results for cohort 1 are summarized in Table 16 and Figure 1. At the time of OS interim analysis 2, OS was immature and a total of 315 (6%) of patients had died in cohort 1.

Table 16: Efficacy Results in monarchE in Cohort 1

	VERZENIO Plus Tamoxifen or an Aromatase Inhibitor N=2555	**Tamoxifen or an Aromatase Inhibitor N=2565**
Invasive Disease–Free Survival (IDFS)		
Number of patients with an event, n (%)	317 (12)	474 (18)
Hazard ratio (95% CI)	0.65 (0.57, 0.75)	
IDFS at 48 months, % (95% CI)	85.5 (83.8, 87.0)	78.6 (76.7, 80.4)

Abbreviation: CI = confidence interval.

Figure 1: Kaplan-Meier Curves of Invasive Disease–Free Survival VERZENIO plus Tamoxifen or an Aromatase Inhibitor versus Tamoxifen or an Aromatase Inhibitor in Cohort 1 (monarchE)



14.2 Advanced or Metastatic Breast Cancer

VERZENIO in Combination with an Aromatase Inhibitor (Anastrozole or Letrozole) (MONARCH 3)

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

MONARCH 3 (NCT02246621) was a randomized (2:1), double-blinded, placebo-controlled, multicenter study in postmenopausal women with HR-positive, HER2-negative advanced or metastatic breast cancer in combination with a nonsteroidal aromatase inhibitor as initial endocrine-based therapy, including patients not previously treated with systemic therapy for breast cancer.

Randomization was stratified by disease site (visceral, bone only, or other) and by prior (neo)adjuvant endocrine therapy (aromatase inhibitor versus other versus no prior endocrine therapy). A total of 493 patients were randomized to receive 150 mg VERZENIO or placebo orally twice daily, plus physician's choice of letrozole (80% of patients) or anastrozole (20% of patients). Patient median age was 63 years (range, 32-88 years) and the majority were White (58%) or Asian (30%). A total of 51% had received prior systemic therapy and 39% of patients had received chemotherapy, 53% had visceral disease, and 22% had bone-only disease.

Efficacy results are summarized in Table 17 and Figure 2. PFS was evaluated according to RECIST version 1.1 and PFS assessment based on a blinded independent radiologic review was consistent with the investigator assessment.

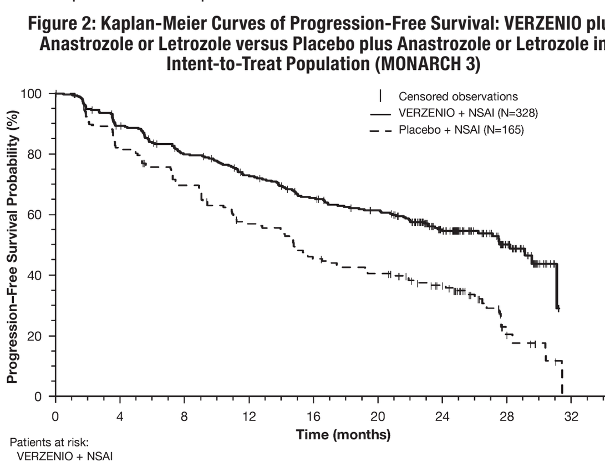
Consistent PFS results were observed across patient stratification subgroups of disease site and prior (neo)adjuvant endocrine therapy.

Table 17: Efficacy Results in MONARCH 3 (Investigator Assessment, Intent-to-Treat Population)

	VERZENIO plus Anastrozole or Letrozole	**Placebo plus Anastrozole or Letrozole**
Progression-Free Survival	**N=328**	**N=165**
Number of patients with an event, n (%)	138 (42)	108 (65)
Median in months (95% CI)	28.2 (23.5, NR)	14.8 (11.2, 19.2)
Hazard ratio (95% CI)	0.54 (0.42, 0.70)	
p-value	<0.0001	
Overall Survival	**N=328**	**N=165**
Number of patients with an event, n (%)	198 (60)	116 (70)
Median in months (95% CI)	66.8 (59.2, 74.8)	53.7 (44.7 59.3)
Hazard ratio (95% CI)	0.80 (0.64, 1.02)	
p-value	NS	
Objective Response for Patients with Measurable Disease[a]	**N=267**	**N=132**
Objective response rate, n (%)[a,b]	148 (55)	53 (40)
95% CI	49, 61	32, 49

Abbreviations: CI = confidence interval; OS = overall survival; NR = not reached; NS = not statistically significant.
[a] Complete response + partial response.
[b] Based upon confirmed responses.

Figure 2: Kaplan-Meier Curves of Progression-Free Survival: VERZENIO plus Anastrozole or Letrozole versus Placebo plus Anastrozole or Letrozole in Intent-to-Treat Population (MONARCH 3)



VERZENIO in Combination with Fulvestrant (MONARCH 2)

Patients with HR-positive, HER2-negative advanced or metastatic breast cancer with disease progression on or after prior adjuvant or metastatic endocrine therapy

MONARCH 2 (NCT02107703) was a randomized, placebo-controlled, multicenter study in women with HR-positive, HER2-negative metastatic breast cancer in combination with fulvestrant in patients with disease progression following endocrine therapy who had not received chemotherapy in the metastatic setting. Randomization was stratified by disease site (visceral, bone only, or other) and by sensitivity to prior endocrine therapy (primary or secondary resistance). Primary endocrine therapy resistance was defined as relapse while on the first 2 years of adjuvant endocrine therapy or progressive disease within the first 6 months of first line endocrine therapy for metastatic breast cancer. A total of 669 patients were randomized to receive VERZENIO or placebo orally twice daily plus intramuscular injection of 500 mg fulvestrant on days 1 and 15 of cycle 1 and then on day 1 of cycle 2 and beyond (28-day cycles). Pre/perimenopausal women were enrolled in the study and received the gonadotropin-releasing hormone agonist goserelin for at least 4 weeks prior to and for the duration of MONARCH 2. Patients remained on continuous treatment until development of progressive disease or unmanageable toxicity.

Patient median age was 60 years (range, 32-91 years), and 37% of patients were older than 65. The majority were White (56%), and 99% of patients had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Twenty percent (20%) of patients had de novo metastatic disease, 27% had bone-only disease, and 56% had visceral disease. Twenty-five percent (25%) of patients had primary endocrine therapy resistance. Seventeen percent (17%) of patients were pre- or perimenopausal.

The efficacy results from the MONARCH 2 study are summarized in Table 18, Figure 3, and Figure 4. PFS assessment based on a blinded independent radiologic review was consistent with the investigator assessment. Consistent results were observed across patient stratification subgroups of disease site and endocrine therapy resistance for PFS and OS.

Table 18: Efficacy Results in MONARCH 2 (Intent-to-Treat Population)

	VERZENIO plus Fulvestrant	**Placebo plus Fulvestrant**
Progression-Free Survival (Investigator Assessment)	**N=446**	**N=223**
Number of patients with an event, n (%)	222 (50)	157 (70)
Median in months (95% CI)	16.4 (14.4, 19.3)	9.3 (7.4, 12.7)
Hazard ratio (95% CI)[a]	0.55 (0.45, 0.68)	
p-value[a]	p<.0001	
Overall Survival[b]		
Number of deaths, n (%)	211 (47)	127 (57)
Median OS in months (95% CI)	46.7 (39.2, 52.2)	37.3 (34.4, 43.2)
Hazard ratio (95% CI)[a]	0.76 (0.61, 0.95)	
p-value[a]	p=.0137	
Objective Response for Patients with Measurable Disease	**N=318**	**N=164**
Objective response rate, n (%)[c]	153 (48)	35 (21)
95% CI	43, 54	15, 28

Abbreviation: CI = confidence interval, OS = overall survival.
[a] Stratified by disease site (visceral metastases vs. bone-only metastases vs. other) and endocrine therapy resistance (primary resistance vs. secondary resistance)
[b] Data from a pre-specified interim analysis (77% of the number of events needed for the planned final analysis) with the p-value compared with the allocated alpha of 0.021.
[c] Complete response + partial response.

Figure 3: Kaplan-Meier Curves of Progression-Free Survival: VERZENIO plus Fulvestrant versus Placebo plus Fulvestrant (MONARCH 2)

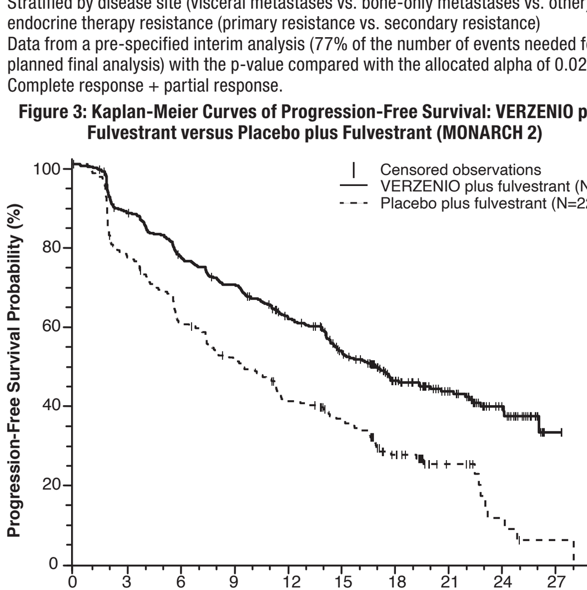
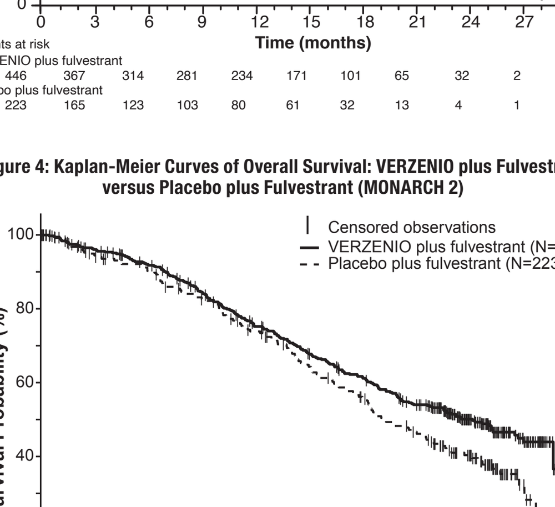


Figure 4: Kaplan-Meier Curves of Overall Survival: VERZENIO plus Fulvestrant versus Placebo plus Fulvestrant (MONARCH 2)



VERZENIO Administered as a Monotherapy in Metastatic Breast Cancer (MONARCH 1)

Patients with HR-positive, HER2-negative breast cancer who received prior endocrine therapy and 1-2 chemotherapy regimens in the metastatic setting

MONARCH 1 (NCT02102490) was a single-arm, open-label, multicenter study in 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. A total of 132 patients received 200 mg VERZENIO orally twice daily on a continuous schedule until development of progressive disease or unmanageable toxicity.

Patient median age was 58 years (range, 36-89 years), and the majority of patients were White (85%). Patients had an Eastern Cooperative Oncology Group performance status of 0 (55% of patients) or 1 (45%). The median duration of metastatic disease was 27.6 months. Ninety percent (90%) of patients had visceral metastases, and 51% of patients had 3 or more sites of metastatic disease. Fifty-one percent (51%) of patients had had one line of chemotherapy in the metastatic setting. Sixty-nine percent (69%) of patients had received a taxane-based regimen in the metastatic setting and 55% had received capecitabine in the metastatic setting. Table 19 provides the efficacy results from MONARCH 1.

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 (20)	23 (17)
95% CI	13, 28	11, 25
Median Duration of Response in months	8.6	7.2
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 modified, oval beige tablet with "Lilly" debossed on one side and "50" on the other side.

VERZENIO 100 mg tablet are modified, oval white to practically white tablet with "Lilly" debossed on one side and "100" on the other side.

VERZENIO 150 mg tablets are modified, oval yellow tablet with "Lilly" debossed on one side and "150" on the other side.

VERZENIO 200 mg tablets are modified, 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)
- 150 mg dose pack (14 tablets) – each blister pack contains 14 tablets (150 mg per tablet) (150 mg twice daily)
- 100 mg dose pack (14 tablets) – each blister pack contains 14 tablets (100 mg per tablet) (100 mg twice daily)
- 50 mg dose pack (14 tablets) – each blister pack contains 14 tablets (50 mg per tablet) (50 mg twice daily)

Not all pack sizes, strengths or presentation may be registered or marketed.

Storage and Handling

Do not store above 30°C.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the approved patient labeling (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 (2.2)]*.

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 (2.2) 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 (2.2) 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 (2.2) 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 (2.1)]*.
- If patient vomits or misses a dose, advise the patient to take the next prescribed dose at the usual time *[see Dosage and Administration (2.1)]*.
- Advise the patient that VERZENIO may be taken with or without food *[see Dosage and Administration (2.1)]*.

Marketing Authorization Holder:
Eli Lilly and Company, Lilly Corporate Center, Indianapolis, Indiana (IN) 46285, United States (USA)
Manufactured by:
Lilly del Caribe, Inc. 12.6 KM 65th Infantry Road, Carolina, Puerto Rico (PR) 00985, United States (USA)
Packaged and released by:
Eli Lilly and Company, Lilly Corporate Center, Indianapolis, Indiana (IN) 46285, United States (USA)

THIS IS A MEDICAMENT
- A medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.

Council of Arab health ministers
Union of Arab Pharmacists

معلومات للمريض
فيرزينيو ™
(أبيماسيكليب)
أقراص، للاستعمال عن طريق الفم

ما هي المعلومات الأهمّ التي يجب أن أعرفها عن فيرزينيو؟

يمكن أن يسبّب فيرزينيو آثارًا جانبيّة خطيرة تتضمّن:

- **الإسهال.** الإسهال شائع مع العلاج بفيرزينيو وقد يكون حادًا أحيانًا. بسبب الإسهال، قد تُصاب بالتجفاف أو بعدوى. والفترة الأكثر شيوعًا للإصابة بالإسهال هي خلال الشهر الأوّل من العلاج بفيرزينيو. وإذا أُصبت بالإسهال خلال فترة علاجك بفيرزينيو، قد يطلب منك طبيبك التوقّف مؤقّتًا عن أخذ فيرزينيو أو إيقاف علاجك أو تخفيض جرعتك.
  - **إذا كان برازك رخوًا،** ابدأ بأخذ دواء مضاد للإسهال (مثل لوبيراميد)، اشرب المزيد من السوائل وأعلم طبيبك على الفور.
- **انخفاض عدد كريات الدم البيضاء (قلّة العدلات).** انخفاض عدد كريات الدم البيضاء أمر شائع خلال العلاج بفيرزينيو وقد يسبّب هذا الانخفاض حالات إنتان خطيرة يمكن أن تؤدّي إلى الوفاة. لذلك يجب على طبيبك التحقق من تعداد كريات الدم البيضاء قبل العلاج وخلاله. إذا انخفضت كريات الدم البيضاء في دمك خلال العلاج بفيرزينيو، قد يطلب منك طبيبك التوقّف مؤقّتًا عن أخذ فيرزينيو أو قد يخفّض جرعتك أو قد ينتظر قبل البدء بشهرك التالي من العلاج. **أعلم طبيبك على الفور إذا أُصبتَ بعلامات وأعراض تدلّ على انخفاض عدد كريات الدم البيضاء أو على حالات إنتان، مثل الحمى والقشعريرة.**
- **مشاكل رئويّة.** يمكن لفيرزينيو أن يتسبب بالتهاب شديد أو مهدد للحياة في الرئتين خلال العلاج والذي يمكن أن يؤدّي إلى الوفاة. إذا أُصبت بمشاكل رئويّة أثناء العلاج بفيرزينيو فقد يطلب منك مقدّم الرعاية الصحيّة الذي يتابعك التوقف مؤقّتًا عن تناول فيرزينيو، أو تخفيض الجرعة أو إيقاف العلاج. قم بإعلام طبيبك فوراً في حال حدوث أي أعراض رئوية جديدة أو في حال ازدياد الأعراض سوءاً، ويتضمن ذلك:
  - صعوبة أو ضيق في التنفس
  - سعال مصحوب أو غير مصحوب بمفرزات مخاطية
  - ألم في الصدر
- **مشاكل في الكبد.** يمكن أن يسبّب فيرزينيو مشاكل خطيرة في الكبد. لذلك يجب على طبيبك إجراء فحوصات دم للتحقق من سلامة كبدك قبل العلاج بفيرزينيو وخلاله. إذا أُصبت بمشاكل في الكبد خلال العلاج بفيرزينيو، قد يخفّض طبيبك جرعتك أو يوقف علاجك. أعلم طبيبك على الفور إذا أُصبت بأيٍّ من علامات وأعراض مشاكل الكبد التالية:
  - الشعور بتعب كبير
  - فقدان الشهيّة
  - ألم في الجانب العلوي الأيمن من معدتك (البطن)
  - التعرّض لنزيف أو لكدمات بسهولة أكثر من المعتاد
- **الخثرات الدمويّة في الأوردة أو في شرايين رئتيْك.** يمكن أن يسبّب فيرزينيو خثرات دمويّة خطيرة تؤدّي إلى الوفاة. إذا أُصبت بجلطات دمويّة أثناء العلاج بفيرزينيو، قد يطلب منك مقدّم الرعاية الصحيّة الذي يتابعك التوقف مؤقّتًا عن تناول فيرزينيو. أعلم طبيبك على الفور إذا أُصبت بأيٍّ من علامات وأعراض الخثرات الدمويّة التالية:
  - ألم أو تورّم في ذراعيك أو ساقيك
  - تسرّع في معدّل التنفّس
  - تسرّع في معدّل نبضات القلب
  - ضيق في التنفّس
  - ألم في الصدر

راجع فقرة "ما هي الآثار الجانبيّة المحتملة لفيرزينيو؟" للمزيد من المعلومات حول الآثار الجانبيّة.

ما هو فيرزينيو؟

فيرزينيو دواء يُصرف بناء على وصفة طبيّة ويُستعمل:

- بالاشتراك مع المعالجة الهرمونيّة (تاموكسيفين أو مثبّط لأنزيم الأروماتاز) لعلاج البالغين الذين يعانون من سرطان الثدي المبكر الإيجابي مستقبل الهرمون (HR) – السلبيّ مستقبل عامل نمو البشرة البشري 2 (HER2)، الإيجابيّ العقدة، مع وجود مخاطر عالية لعودة مرض السرطان على النحو الذي يحدّده مقدّم الرعاية الصحية الذي يتابعك.
- بالاشتراك مع مثبّط لأنزيم الأروماتاز كأوّل معالجة هرمونيّة لعلاج البالغين المصابين بسرطان الثدي الإيجابي مستقبل الهرمون (HR) – السلبيّ مستقبل عامل نمو البشرة البشري 2 (HER2) الذي ازداد سوءًا أو انتشر إلى أجزاء أخرى من الجسم (المنتقل).
- بالاشتراك مع فولفسترانت لعلاج البالغين المصابين بسرطان الثدي الذي ازداد سوءًا أو انتشر إلى أجزاء أخرى من الجسم (المنتقل)، والذين لديهم المستقبل الهرموني إيجابي (HR)، ومستقبل عامل نموّ البشرة 2 (HER2) سلبي، والذين تقدّم مرضهم بعد العلاج الهورموني.
- بمفرده لعلاج البالغين المصابين بسرطان الثدي الذي ازداد سوءًا أو الذي انتشر إلى أجزاء أخرى من الجسم(المنتقل)، والذين لديهم المستقبل الهرموني إيجابي (HR)، مستقبل عامل نموّ البشرة 2 (HER2) سلبي والذين تقدّم مرضهم بعد العلاج الهورموني أو العلاج الكيميائي السابق.

عند استعمال فيرزينيو مع فولفسترانت أو تاموكسيفين أو مثبّط لأنزيم الأروماتاز، اقرأ أيضًا نشرة معلومات المريض الخاصة بالمنتج الموصوف. اسأل مقدّم الرعاية الصحية الذي يتابعك إذا لم تكن متأكّدًا.
من غير المعروف ما إذا كان فيرزينيو آمنًا وفعّالاً لدى الأطفال.

قبل أن تأخذ فيرزينيو، أعلم طبيبك بكلّ الحالات الطبيّة التي تعاني منها، بما في ذلك:

- إذا أُصبت بحمى أو بقشعريرة أو بعوارض عدوى.
- إذا لديك تاريخ من جلطات الدم في الأوردة.
- إذا كان لديك مشاكل في الرئة أو التنفس.
- إذا كنت تعاني من مشاكل في الكبد أو الكليتين.
- إذا كنتِ حاملاً أو كنت تخططين للحمل لأنّ فيرزينيو يمكن أن يؤذي الجنين.
  الإناث القادرات على الحمل:
  - سيُجري لكِ طبيبك فحص حمل قبل أن تبدأي العلاج بفيرزينيو.
  - يجب عليك استعمال وسيلة فعّالة لمنع الحمل خلال العلاج بفيرزينيو ولمدّة 3 أسابيع بعد الجرعة الأخيرة من فيرزينيو.
  - أعلمي مقدّم الرعاية الصحيّة الذي يتابعك على الفور إذا أصبحت حاملاً أو إذا كنتِ تعتقدين أنّك حامل أثناء العلاج بفيرزينيو.
- إذا كنتِ تُرضعين أو كنتِ تنوين الإرضاع. من غير المعروف ما إذا كان فيرزينيو ينتقل عبر حليب الثدي. لا تُرضعي خلال العلاج بفيرزينيو ولمدّة 3 أسابيع على الأقلّ بعد الجرعة الأخيرة من فيرزينيو.

أعلم طبيبك بكلّ الأدوية التي تأخذها، بما فيها الأدوية التي تُصرف بوصفة طبيّة والأدوية التي تحصل عليها بدون وصفة طبيّة والفيتامينات والمكملات العشبيّة. قد يؤثّر فيرزينيو على طريقة عمل أدوية أخرى، وقد تؤثّر أدوية أخرى على طريقة عمل فيرزينيو، مما يتسبب في آثار جانبية خطيرة.
أعلم طبيبك بشكل خاص إذا كنت تأخذ دواءً يحتوي على الكيتوكونازول.
إعرف الأدوية التي تأخذها. احتفظ بقائمة بها لتستشير طبيبك أو الصيدليّ الخاص بك عندما يصف لك دواءً جديداً.

كيف يجب عليّ أن آخذ فيرزينيو؟

- خذ فيرزينيو تمامًا حسب ارشادات طبيبك المعالج.
- يمكن أن يعدّل طبيبك جرعتك عند الحاجة. لا تتوقّف عن أخذ فيرزينيو ولا تغيّر الجرعة بدون استشارة طبيبك.
- يمكن أن تأخذ فيرزينيو خلال وجبة الطعام أو خارجها.
- إبلع أقراص فيرزينيو كاملة. لا تمضغها أو تسحقها أو تقسمها قبل البلع. لا تأخذ أقراص فيرزينيو إذا كانت مكسورة أو مشقوقة أو متضرّرة.
- خذ جرعاتك من فيرزينيو في التوقيت ذاته تقريبًا كلّ يوم.
- إذا تقيّأت فيرزينيو أو فوّت جرعة منه، خذ جرعتك التالية في موعدها الاعتياديّ. لا تأخذ جرعتين من فيرزينيو في الوقت ذاته للتعويض عن الجرعة التي لم تأخذها.

ما الذي عليّ تجنّبه خلال العلاج بفيرزينيو؟

- تجنّب أخذ الكيتوكونازول خلال العلاج بفيرزينيو. إستشير طبيبك إذا كنت تأخذ دواءً يحتوي على الكيتوكونازول.
- تجنّب تناول فاكهة الجريب فروت والمنتجات التي تحتوي على الجريب فروت خلال العلاج بفيرزينيو، لأنّ الجريب فروت قد يزيد كميّة فيرزينيو في الدم.

ما هي الآثار الجانبيّة المحتملة لفيرزينيو؟

يمكن أن يسبّب فيرزينيو آثارًا جانبيّة خطيرة تتضمّن:

- راجع فقرة **"ما هي المعلومات الأهمّ التي يجب أن أعرفها حول فيرزينيو؟"**

تتضمّن الآثار الجانبيّة الأكثر شيوعًا لفيرزينيو ما يلي:

- غثيان
- ألم في المعدة
- حالات إنتان
- تعب
- انخفاض عدد كريات الدم الحمراء (فقر دم)
- انخفاض عدد كريات الدم البيضاء (قلّة الكريات البيضاء)
- شهيّة متناقصة
- تقيّؤ
- صداع
- انخفاض عدد الصفيحات (قلّة الصفيحات)
- ترقق الشعر أو تساقطه (الصلع)

يمكن أن يسبّب فيرزينيو مشاكل خصوبة لدى الرجال مما يمكن أن يؤثّر على قدرتك على الإنجاب. استشر طبيبك إذا كان هذا الأمر مصدر قلق بالنسبة إليك.

ليست هذه كلّ الآثار الجانبيّة التي يسبّبها فيرزينيو. للمزيد من المعلومات، استشر طبيبك أو الصيدليّ الخاص بك.
استشر طبيبك لتحصل على مشورة طبيّة حول الآثار الجانبيّة.

كيف عليّ أن أحفظ فيرزينيو؟

- لا تحفظ فيرزينيو على حرارة تتعدى 30 درجة مئويّة.

إحفظ فيرزينيو وكلّ الأدوية بعيدًا عن متناول الأطفال ونظرهم.

معلومات عامة حول الاستعمال الآمن والفعّال لفيرزينيو.

توصف الأدوية أحيانًا لغايات تختلف عن تلك المذكورة في نشرة معلومات المريض. لا تستعمل فيرزينيو لحالة لم يوصف لأجلها. لا تعطِ فيرزينيو لأشخاص آخرين حتّى ولو كان لديهم العوارض نفسها التي تعاني منها أنت، فقد يؤذيهم. لا تستخدم هذا الدواء بعد انتهاء تاريخ انتهاء الصلاحية المدون على العلبة و الظرف بعد كلمة ' **EXP** '. يشير تاريخ انتهاء الصلاحيةً إلى اليوم الأخير من الشهر المذكور. يمكن طلب المزيد من المعلومات حول فيرزينيو تكون موجّهة إلى أخصّائيي الرعاية الصحيّة، من الصيدليّ الخاص بك أو من طبيبك.

ما هي مكوّنات فيرزينيو؟

المادة الفاعلة: أبيماسيكليب
المكوّنات غير الفاعلة: سلولوز دقيق البلوريّة 102، سلولوز دقيق البلوريّة 101، لاكتوز أحادي الهيدرات، كروسكارميلوز الصوديوم، فومارات ستياريل الصوديوم، ثاني أكسيد السيليكون.
مكوّنات خليط اللون: كحول عديد الفاينيل، ثاني أكسيد التيتانيوم، غليكول بولي إيثيلين، طلق، أكسيد الحديد الأصفر، أكسيد الحديد الأحمر.

كيف يتوفّر فيرزينيو؟

أقراص فيرزينيو 50 ملغ، هي أقراص معدّلة بيضاويّة الشكل لونها بيج، تحمل علامة "ليلي" « Lilly » على جهة والرقم "50" على الجهة الأخرى.
أقراص فيرزينيو 100 ملغ، هي أقراص معدّلة بيضاويّة الشكل لونها أبيض أو مائل الى البياض، تحمل علامة "ليلي" « Lilly » على جهة والرقم "100" على الجهة الأخرى.
أقراص فيرزينيو 150 ملغ، هي أقراص معدّلة بيضاويّة الشكل لونها أصفر، تحمل علامة "ليلي" « Lilly » على جهة والرقم "150" على الجهة الأخرى.
أقراص فيرزينيو 200 ملغ، هي أقراص معدّلة بيضاويّة الشكل لونها بيج، تحمل علامة "ليلي" « Lilly » على جهة والرقم "200" على الجهة الأخرى.
يُسوَّق فيرزينيو 50 ملغ، 100 ملغ، 150 ملغ و 200 ملغ في علب شرائط من 14 قرصاً. كل علبة تحتوي على شريط واحد من 14 قرص.

قد لا تكون أحجام العبوات أو العيارات أو الأشكال كلّها مسوّقة/مسجّلة.

حامل ترخيص التسويق:
ايلي ليلي أند كومباني، ليلي كوربورايت سنتر، إنديانابوليس، إنديانا (إن) 46285، الولايات المتحدة الأمريكية
صنع:
ليلي ديل كاريب ، Inc. 12.6 KM ، 65th شارع انفانتري، كارولينا، بويرتو ريكو (PR) 00985، الولايات المتحدة الأمريكية
تعبئة وتحرير:
ايلي ليلي أند كومباني، ليلي كوربورايت سنتر، إنديانابوليس، إنديانا (إن) 46285، الولايات المتحدة الأمريكية

تاريخ المراجعة: فبراير/شباط 2025

إن هذا دواء
- الدواء مستحضر يؤثّر على صحتك واستهلاكه خلافاً للتعليمات يعرّضك للخطر.
- اتّبع بدقّة وصفة الطبيب وطريقة الاستعمال المنصوص عليها وتعليمات الصيدلاني الذي صرفها لك.
- فالطبيب والصيدلاني هما الخبيران بالدواء وبنفعه وضرره.
- لا تقطع مدة العلاج المحدّدة لك من تلقاء نفسك.
- لا تكرر صرف الدواء بدون وصفة طبية.
- لا تترك الأدوية في متناول أيدي الأطفال.

مجلس وزراء الصحة العرب
واتحاد الصيادلة العرب

FPO

Layout Used to Develop Artwork: INDL7547C00

PPD Information Box

Technical Information: Black; DIECUT; DIE PERFORATION

Previous Item Code *(to be destroyed)*
NL022IDQR02

Lilly