everyday
Verzenio®
abemaciclib
50 | 100 | 150 | 200 mg tablets
twice a day

# Dosing and Administration Guide

**VERZENIO® is a kinase inhibitor indicated[1]:**

- **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.
- **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.

## SELECT IMPORTANT SAFETY INFORMATION

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. 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. 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.

**Please see Select Important Safety Information throughout and full Prescribing Information for Verzenio.**

*In patients with HR+, HER2− MBC and patients with HR+, HER2−, node-positive EBC at high risk of recurrence*

# Verzenio can be taken every day in both the adjuvant and metastatic settings[1]

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twice a day

**150 mg** | TWICE DAILY
IN COMBINATION WITH ET[1]*

**200-mg tablet twice daily:** single agent[1]

**EBC:** 2 years of treatment or until disease recurrence or unacceptable toxicity.[1]

**MBC:** Until disease progression or unacceptable toxicity.[1]

*Tamoxifen or an AI in EBC and fulvestrant or an AI in MBC. Please refer to the full Prescribing Information for the recommended dose of the ET selected.

**VERZENIO IS SUPPLIED IN BLISTER PACKS OF**

**50 mg | 100 mg | 150 mg | 200 mg**

**The following should receive a gonadotropin-releasing hormone agonist (GnRH) according to current clinical practice standards[1]:**

- Pre/perimenopausal women treated with Verzenio plus an AI or fulvestrant
- Men treated with Verzenio plus an AI

**Dose modification is recommended based on individual safety and tolerability.[1]**

- If necessary, reduce Verzenio by 50 mg at a time[1]
- Discontinue Verzenio for patients unable to tolerate 50 mg twice daily[1]

Please refer to the full Prescribing Information for additional guidance.

AI=aromatase inhibitor; EBC=early breast cancer; ET=endocrine therapy; MBC=metastatic breast cancer.

## SELECT IMPORTANT SAFETY INFORMATION (CONT'D)

**Strong and moderate CYP3A inhibitors** increased the exposure of abemaciclib plus its active metabolites to a clinically meaningful extent and may lead to increased toxicity. Avoid concomitant use of ketoconazole. Ketoconazole is predicted to increase the AUC of abemaciclib by up to 16-fold. 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 to 5 half-lives of the inhibitor) to the dose that was used before starting the inhibitor. With concomitant use of moderate CYP3A inhibitors, monitor for adverse reactions and consider reducing the Verzenio dose in 50 mg decrements. Patients should avoid grapefruit products.

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# Dosing considerations[1]

### Verzenio should be taken at approximately the same times every day

If the patient vomits or misses a dose, they should take the next dose of Verzenio at its scheduled time.

### Verzenio should be swallowed whole

Patients should not ingest chewed, crushed, or otherwise not intact tablets.

### Verzenio has no meal requirements and may be taken with or without food

Patients should avoid grapefruit products when taking Verzenio.

Please refer to the full Prescribing Information for additional guidance.

## SELECT IMPORTANT SAFETY INFORMATION (CONT'D)

**Avoid concomitant use of strong or moderate CYP3A inducers and consider alternative agents.** Coadministration of strong or moderate CYP3A inducers decreased the plasma concentrations of abemaciclib plus its active metabolites and may lead to reduced activity.

**With severe hepatic impairment** (Child-Pugh C), reduce the Verzenio dosing frequency to once daily. The pharmacokinetics of Verzenio in patients with **severe renal impairment** (CLcr <30 mL/min), end stage renal disease, or in patients on dialysis **is unknown**. No dosage adjustments are necessary in patients with mild or moderate hepatic (Child-Pugh A or B) and/or renal impairment (CLcr ≥30-89 mL/min).

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# Dose modifications[1]

## Dose modification is recommended based on individual safety and tolerability[1]

If dose reduction is necessary, reduce the Verzenio dose by 50 mg at a time. Discontinue Verzenio for patients unable to tolerate 50 mg twice daily.

| | VERZENIO IN COMBINATION WITH FULVESTRANT, TAMOXIFEN, OR AN AI | VERZENIO SINGLE AGENT |
|---|---|---|
| **Recommended starting dose** | 150 mg twice daily | 200 mg twice daily |
| **1st dose reduction** | 100 mg twice daily | 150 mg twice daily |
| **2nd dose reduction** | 50 mg twice daily | 100 mg twice daily |
| **3rd dose reduction** | Not applicable | 50 mg twice daily |

**Please see pages 5-11 for dose modification instructions for hematologic toxicities, diarrhea, hepatotoxicity, interstitial lung disease/pneumonitis, venous thromboembolic events, and other toxicities.**

*In the monarchE, MONARCH 2, and MONARCH 3 trials.

**Across Verzenio trials*, dose reductions were common[1]**
Verzenio efficacy was maintained following dose reduction[1,3,4]
44% of patients received a dose reduction to help them remain on treatment[1,3,4]

### SELECT IMPORTANT SAFETY INFORMATION (CONT'D)

**Neutropenia,** including febrile neutropenia and fatal neutropenic sepsis, occurred in patients treated with Verzenio. Across four clinical trials in 3691 patients, neutropenia occurred in 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 first episode of Grade ≥3 neutropenia ranged from 29 to 33 days, and the median duration of Grade ≥3 neutropenia ranged from 11 to 16 days. 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.

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.

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# Dose modifications[1,2]

## Hematologic toxicities*†

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 | SEVERITY OF NEUTROPENIA (ANC) | DOSE MODIFICATIONS |
|---|---|---|
| **Grade 1** or **Grade 2** | <LLN-1.5 x $10^9$/L<br>**<1.5-1.0** x $10^9$/L | No dose modification is required. |
| **Grade 3** | <1.0-0.5 x $10^9$/L | Suspend dose until toxicity resolves to ≤Grade 2. Dose reduction is not required. |
| **Grade 3** recurrent or **Grade 4** | <1.0-0.5 x $10^9$/L<br><0.5 x $10^9$/L | Suspend dose until toxicity resolves to ≤Grade 2. Resume at *next lower dose.* |

*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.
†Neutropenia was the most common hematologic toxicity in Verzenio-treated patients.
ANC=absolute neutrophil count; CTCAE=Common Terminology Criteria for Adverse Events; LLN=lower level of normal.

### SELECT IMPORTANT SAFETY INFORMATION (CONT'D)

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 EBC (monarchE), 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 MBC (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.

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 in 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.

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# Dose modifications[1,2]

## Diarrhea*

| CTCAE GRADE | SEVERITY OF DIARRHEA | DOSE MODIFICATIONS |
|---|---|---|
| **Grade 1** | <4 stools/day over baseline | No dose modification required. |
| **Grade 2** that does not resolve within 24 hours | 4-6 stools/day over baseline | If toxicity does not resolve within 24 hours to ≤Grade 1, suspend dose until resolution. No dose reduction required. |
| **Grade 2** that persists or recurs after the same dose despite maximal supportive measures | 4-6 stools/day over baseline | Suspend dose until toxicity resolves to ≤Grade 1. Resume at *next lower dose*. |
| **Grade 3** or **Grade 4** or requires hospitalization | ≥7 stools/day over baseline Life-threatening consequences or urgent intervention and/or hospitalization indicated | Suspend dose until toxicity resolves to ≤Grade 1. Resume at *next lower dose*. |

*At the first sign of loose stools, start treatment with antidiarrheal agents, such as loperamide, increase intake of oral fluids and contact your provider. Once an antidiarrheal agent is started, advise patients to follow up if symptoms do not improve after the first 24 hours.

### SELECT IMPORTANT SAFETY INFORMATION (CONT'D)

**Grade ≥3 increases in alanine aminotransferase (ALT)** (2 to 6%) and **aspartate aminotransferase (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 4 hepatic transaminase elevation.

**Please see Select Important Safety Information throughout and full Prescribing Information for Verzenio.**

# Dose modifications[1,2]

## 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 | SEVERITY OF HEPATOTOXICITY (ALT/AST) | | | DOSE MODIFICATIONS |
|---|---|---|---|---|
| **Grade 1** or **Grade 2** | **>ULN-3.0 x ULN**<br>>3.0-5.0 x ULN | **without** | T-BIL >2 x ULN | No dose modification required. |
| **Grade 2** persistent or recurrent or **Grade 3** | >3.0-5.0 x ULN<br>>5.0-20.0 x ULN | **without** | T-BIL >2 x ULN | Suspend dose until toxicity resolves to baseline or Grade 1. Resume at *next lower dose*. |
| **Elevations** >3 x ULN in the absence of cholestasis | | **with** | T-BIL >2 x ULN | Discontinue Verzenio. |
| **Grade 4** | >20.0 x ULN | | | Discontinue Verzenio. |

ALT=alanine aminotransferase; AST=aspartate aminotransferase; T-BIL=total bilirubin; ULN=upper limit of normal.

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### SELECT IMPORTANT SAFETY INFORMATION (CONT'D)

**Venous thromboembolic events (VTE)** were reported in 2 to 5% of patients across three clinical trials in 3559 patients treated with Verzenio (monarchE, MONARCH 2, MONARCH 3). VTE 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 VTE have been reported in patients treated with Verzenio.

Verzenio has not been studied in patients with early breast cancer who had a history of VTE. Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism and treat as medically appropriate. Dose interruption is recommended for EBC patients with any grade VTE and for MBC patients with a Grade 3 or 4 VTE.

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# Dose modifications[1,2]

## Venous thromboembolic events (VTEs)

| | CTCAE GRADE | SEVERITY OF VTE | DOSE MODIFICATIONS |
|---|---|---|---|
| **EBC** | **Any grade** | Any event | Suspend dose and treat as clinically indicated. Resume Verzenio when the patient is clinically stable. |
| **MBC** | **Grade 1** or **Grade 2** | Medical intervention not indicated (eg, superficial thrombosis); Medical intervention indicated | No dose modification is required. |
| | **Grade 3** or **Grade 4** | Urgent medical intervention indicated (eg, pulmonary embolism or intracardiac thrombus); Life threatening consequences with hemodynamic or neurologic instability | Suspend dose and treat as clinically indicated. Resume Verzenio when the patient is clinically stable. |

### SELECT IMPORTANT SAFETY INFORMATION (CONT'D)

Verzenio can cause **fetal harm** when administered to a pregnant woman, based on findings from animal studies and the mechanism of action. 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. Based on findings in animals, Verzenio may impair fertility in males of reproductive potential. There are no data on the presence of Verzenio in human milk or its effects on the breastfed child or on milk production. Advise lactating women not to breastfeed during Verzenio treatment and for at least 3 weeks after the last dose because of the potential for serious adverse reactions in breastfed infants.

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# Dose modifications[1,2]

## Interstitial lung disease (ILD)/pneumonitis

| CTCAE GRADE | SEVERITY OF ILD/ PNEUMONITIS | DOSE MODIFICATIONS |
|---|---|---|
| **Grade 1** or **Grade 2** | Asymptomatic<br>Symptomatic | No dose modification required. |
| **Grade 2** that is persistent or recurrent and does not resolve with maximal supportive measures within 7 days | Symptomatic | Suspend dose until toxicity resolves to baseline or ≤Grade 1. Resume at *next lower dose*. |
| **Grade 3** or **Grade 4** | Severe symptoms<br>Life-threatening respiratory compromise | Discontinue Verzenio. |

**SELECT IMPORTANT SAFETY INFORMATION (CONT'D)**

The **most common adverse reactions (all grades, ≥10%)** observed in **monarchE for Verzenio plus tamoxifen or an aromatase inhibitor vs tamoxifen or an aromatase inhibitor, with a difference between arms of ≥2%**, were diarrhea (84% vs 9%), infections (51% vs 39%), neutropenia (46% vs 6%), fatigue (41% vs 18%), leukopenia (38% vs 7%), nausea (30% vs 9%), anemia (24% vs 4%), headache (20% vs 15%), vomiting (18% vs 4.6%), stomatitis (14% vs 5%), lymphopenia (14% vs 3%), thrombocytopenia (13% vs 2%), decreased appetite (12% vs 2.4%), ALT increased (12% vs 6%), AST increased (12% vs 5%), dizziness (11% vs 7%), rash (11% vs 4.5%), and alopecia (11% vs 2.7%).

**Please see Select Important Safety Information throughout and full Prescribing Information for Verzenio.**

# Dose modifications[1]

## Other toxicities*

| CTCAE GRADE | DOSE MODIFICATIONS |
|---|---|
| **Grade 1** or **Grade 2** | No dose modification required. |
| **Grade 2** that persists or recurs and does not resolve with maximal supportive measures within 7 days | Suspend dose until toxicity resolves to baseline or ≤Grade 1. Resume *at next lower dose*. |
| **Grade 3** or **Grade 4** | Suspend dose until toxicity resolves to baseline or ≤Grade 1. Resume *at next lower dose*. |

*Excluding diarrhea, hematologic toxicity, ILD/pneumonitis, hepatotoxicity, and VTEs.

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**SELECT IMPORTANT SAFETY INFORMATION (CONT'D)**

The **most frequently reported ≥5% Grade 3 or 4 adverse reaction** that occurred in the Verzenio arm vs the tamoxifen or an aromatase inhibitor arm of monarchE were neutropenia (19.6% vs 1%), leukopenia (11% vs <1%), diarrhea (8% vs 0.2%), and lymphopenia (5% vs <1%).

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# Dose modifications[1]

## Use with CYP3A inhibitors and inducers

**Avoid concomitant use of the strong CYP3A inhibitor ketoconazole.**

**With other strong CYP3A inhibitors:**

- Reduce the Verzenio dose to 100 mg twice daily
- If strong CYP3A inhibitor is discontinued, increase the Verzenio dose (after 3-5 half-lives of the inhibitor) to the dose that was used before starting the strong inhibitor
- In patients who have had a dose reduction to 100 mg twice daily due to adverse reactions (ARs), further reduce the Verzenio dose to 50 mg twice daily

**With moderate CYP3A inhibitors:**

- Monitor for ARs and consider reducing Verzenio by 50 mg per dose at a time

**With strong and moderate CYP3A inducers:**

- Avoid and consider alternative agents

## For patients with hepatic impairment

| | |
|---|---|
| **Child-Pugh Class A or B** | No dose adjustment necessary. |
| **Child-Pugh Class C** | Reduce dose to once a day. |

## For patients with renal impairment

| | |
|---|---|
| **CLcr ≥30-89 mL/min** | No dose adjustment necessary. |
| **CLcr <30 mL/min, ESRD, or in patients on dialysis** | Pharmacokinetics of Verzenio is not known. |

ESRD=end-stage renal disease.

### SELECT IMPORTANT SAFETY INFORMATION (CONT'D)

**Lab abnormalities (all grades; Grade 3 or 4)** for **monarchE in ≥10% for Verzenio plus tamoxifen or an aromatase inhibitor with a difference between arms of ≥2%** were increased serum creatinine (99% vs 91%; .5% vs <.1%), decreased white blood cells (89% vs 28%; 19.1% vs 1.1%), decreased neutrophil count (84% vs 23%; 18.7% vs 1.9%), anemia (68% vs 17%; 1% vs .1%), decreased lymphocyte count (59% vs 24%; 13.2% vs 2.5%), decreased platelet count (37% vs 10%; .9% vs .2%), increased ALT (37% vs 24%; 2.6% vs 1.2%), increased AST (31% vs 18%; 1.6% vs .9%), and hypokalemia (11% vs 3.8%; 1.3% vs 0.2%).

**Please see Select Important Safety Information throughout and full Prescribing Information for Verzenio.**

## SELECT IMPORTANT SAFETY INFORMATION (CONT'D)

The **most common adverse reactions (all grades, ≥10%)** observed in **MONARCH 3 for Verzenio plus anastrozole or letrozole vs anastrozole or letrozole, with a difference between arms of ≥2%**, were diarrhea (81% vs 30%), fatigue (40% vs 32%), neutropenia (41% vs 2%), infections (39% vs 29%), nausea (39% vs 20%), abdominal pain (29% vs 12%), vomiting (28% vs 12%), anemia (28% vs 5%), alopecia (27% vs 11%), decreased appetite (24% vs 9%), leukopenia (21% vs 2%), creatinine increased (19% vs 4%), constipation (16% vs 12%), ALT increased (16% vs 7%), AST increased (15% vs 7%), rash (14% vs 5%), pruritus (13% vs 9%), cough (13% vs 9%), dyspnea (12% vs 6%), dizziness (11% vs 9%), weight decreased (10% vs 3.1%), influenza-like illness (10% vs 8%), and thrombocytopenia (10% vs 2%).

The **most frequently reported ≥5% Grade 3 or 4 adverse reactions** that occurred in the Verzenio arm vs the placebo arm of **MONARCH 3** were neutropenia (22% vs 1%), diarrhea (9% vs 1.2%), leukopenia (7% vs <1%), increased ALT (6% vs 2%), and anemia (6% vs 1%).

**Lab abnormalities (all grades; Grade 3 or 4)** for **MONARCH 3 in ≥10% for Verzenio plus anastrozole or letrozole with a difference between arms of ≥2%** were increased serum creatinine (98% vs 84%; 2.2% vs 0%), decreased white blood cells (82% vs 27%; 13% vs 0.6%), anemia (82% vs 28%; 1.6% vs 0%), decreased neutrophil count (80% vs 21%; 21.9% vs 2.6%), decreased lymphocyte count (53% vs 26%; 7.6% vs 1.9%), decreased platelet count (36% vs 12%; 1.9% vs 0.6%), increased ALT (48% vs 25%; 6.6% vs 1.9%), and increased AST (37% vs 23%; 3.8% vs 0.6%).

The **most common adverse reactions (all grades, ≥10%)** observed in **MONARCH 2 for Verzenio plus fulvestrant vs fulvestrant, with a difference between arms of ≥2%,** were diarrhea (86% vs 25%), neutropenia (46% vs 4%), fatigue (46% vs 32%), nausea (45% vs 23%), infections (43% vs 25%), abdominal pain (35% vs 16%), anemia (29% vs 4%), leukopenia (28% vs 2%), decreased appetite (27% vs 12%), vomiting (26% vs 10%), headache (20% vs 15%), dysgeusia (18% vs 2.7%), thrombocytopenia (16% vs 3%), alopecia (16% vs 1.8%), stomatitis (15% vs 10%), ALT increased (13% vs 5%), pruritus (13% vs 6%), cough (13% vs 11%), dizziness (12% vs 6%), AST increased (12% vs 7%), peripheral edema (12% vs 7%), creatinine increased (12% vs <1%), rash (11% vs 4.5%), pyrexia (11% vs 6%), and weight decreased (10% vs 2.2%).

The **most frequently reported ≥5% Grade 3 or 4 adverse reactions** that occurred in the Verzenio arm vs the placebo arm of **MONARCH 2** were neutropenia (25% vs 1%), diarrhea (13% vs 0.4%), leukopenia (9% vs 0%), anemia (7% vs 1%), and infections (5.7% vs 3.5%).

**Lab abnormalities (all grades; Grade 3 or 4)** for **MONARCH 2 in ≥10% for Verzenio plus fulvestrant with a difference between arms of ≥2%** were increased serum creatinine (98% vs 74%; 1.2% vs 0%), decreased white blood cells (90% vs 33%; 23.7% vs .9%), decreased neutrophil count (87% vs 30%; 32.5% vs 4.2%), anemia (84% vs 34%; 2.6% vs .5%), decreased lymphocyte count (63% vs 32%; 12.2% vs 1.8%), decreased platelet count (53% vs 15%; 2.1% vs 0%), increased ALT (41% vs 32%; 4.6% vs 1.4%), and increased AST (37% vs 25%; 3.9% vs 4.2%).

The most common adverse reactions (all grades, ≥10%) observed in MONARCH 1 with Verzenio were diarrhea (90%), fatigue (65%), nausea (64%), decreased appetite (45%), abdominal pain (39%), neutropenia (37%), vomiting (35%), infections (31%), anemia (25%), thrombocytopenia (20%), headache (20%), cough (19%), constipation (17%), leukopenia (17%), arthralgia (15%), dry mouth (14%), weight decreased (14%), stomatitis (14%), creatinine increased (13%), alopecia (12%), dysgeusia (12%), pyrexia (11%), dizziness (11%), and dehydration (10%).

The **most frequently reported ≥5% Grade 3 or 4 adverse reactions** from **MONARCH 1** with Verzenio were diarrhea (20%), neutropenia (24%), fatigue (13%), and leukopenia (5%).

**Lab abnormalities (all grades; Grade 3 or 4) for MONARCH 1** with Verzenio were increased serum creatinine (99%; .8%), decreased white blood cells (91%; 28%), decreased neutrophil count (88%; 26.6%), anemia (69%; 0%), decreased lymphocyte count (42%; 13.8%), decreased platelet count (41%; 2.3%), increased ALT (31%; 3.1%), and increased AST (30%; 3.8%).

**Strong and moderate CYP3A inhibitors** increased the exposure of abemaciclib plus its active metabolites to a clinically meaningful extent and may lead to increased toxicity. Avoid concomitant use of ketoconazole. Ketoconazole is predicted to increase the AUC of abemaciclib by up to 16-fold. 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 to 5 half-lives of the inhibitor) to the dose that was used before starting the inhibitor. With concomitant use of moderate CYP3A inhibitors, monitor for adverse reactions and consider reducing the Verzenio dose in 50 mg decrements. Patients should avoid grapefruit products.

**Avoid concomitant use of strong or moderate CYP3A inducers and consider alternative agents.** Coadministration of strong or moderate CYP3A inducers decreased the plasma concentrations of abemaciclib plus its active metabolites and may lead to reduced activity.

**With severe hepatic impairment** (Child-Pugh C), reduce the Verzenio dosing frequency to once daily. The pharmacokinetics of Verzenio in patients with **severe renal impairment** (CLcr <30 mL/min), end stage renal disease, or in patients on dialysis **is unknown**. No dosage adjustments are necessary in patients with mild or moderate hepatic (Child-Pugh A or B) and/or renal impairment (CLcr ≥30-89 mL/min).

**Please see Select Important Safety Information throughout and full Prescribing Information for Verzenio.**

AL HCP ISI 12OCT2021

**References: 1.** Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company. **2.** National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE). Version 5.0; 2017. **3.** Rugo HS, Huober J, García-Saenz JA, et al. Management of abemaciclib-associated adverse events in patients with hormone receptor-positive, human epidermal growth factor receptor 2-negative advanced breast cancer: safety analysis of MONARCH 2 and MONARCH 3. Oncologist. 2021;26:e53-e65. doi:10.1002/onco.13531 **4.** O'Shaughnessy J, Cicin I, Testa L, et al. Impact of dose reductions on efficacy of adjuvant abemaciclib for patients with high-risk early breast cancer (EBC): analyses from the monarchE study. Poster and slides presented at: ESMO Conference; October 20-24, 2023; Madrid, Spain.

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