Staying on Verzenio[1]

A GUIDE TO MANAGING DIARRHEA

EXPECT

PLAN

ACT

The established Expect, Plan, Act protocol can help keep patients on treatment.

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

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.

EXPECT

Across Verzenio trials, diarrhea was the most common adverse reaction[1]*

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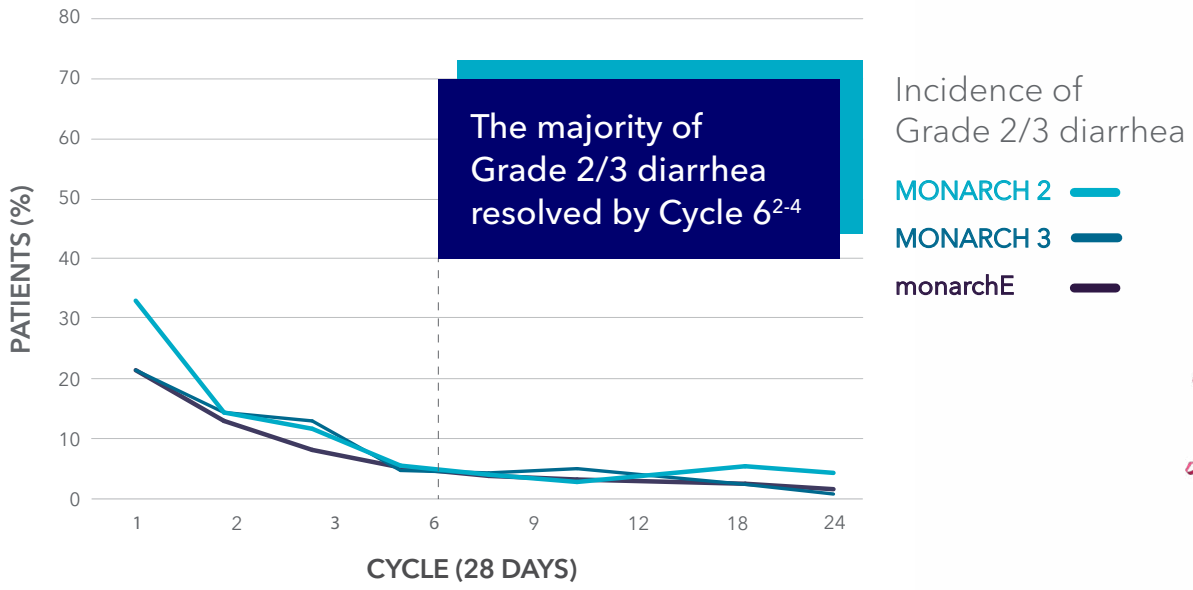
twice a day

DIARRHEA INCIDENCE WAS HIGHEST IN THE FIRST MONTH, WITH REDUCED FREQUENCY THEREAFTER[1-4]



*monarchE, MONARCH 1, MONARCH 2, and MONARCH 3.[1]

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

EXPECT

Most cases of diarrhea were low grade and manageable[1]

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twice a day

NO PATIENTS EXPERIENCED GRADE 4 DIARRHEA[1]

	HR+, HER2– High-Risk EBC	HR+, HER2– MBC		
	Verzenio + ET* (N=2,791)	Verzenio + AI (N=372)	Verzenio + fulvestrant (N=441)	Single-agent Verzenio (N=132)
GRADE 3	8%	9%	13%	20%
ALL GRADES	84%	81%	86%	90%

- Diarrhea occurred in 81-90% of patients (n=3,691)[1]

*The monarchE study included one death associated with diarrhea.[1]

DIARRHEA WAS TRANSIENT WITH A PREDICTABLE TIMELINE FOR ONSET AND RESOLUTION[1]

Week 1 (6-8 days):
Median time to onset (all Grades)[1]

Week 2-3 (5-11 days):
Median time to resolution (Grades 2 and 3)[1]

Most cases of Grades 2/3 diarrhea resolved within 2 weeks[1]

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

PLAN

Established diarrhea management strategies help keep patients on treatment[1]

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Making a plan[1]

- Before starting Verzenio, ensure your patients have an over-the-counter antidiarrheal medicine available
- At the first sign of loose stools, inform patients to start the antidiarrheal medicine and notify their healthcare team
- Discuss any dietary changes with the healthcare team prior to initiating treatment

ACROSS VERZENIO TRIALS, DISCONTINUATION RATES DUE TO DIARRHEA WERE LOW[1]

HR+, HER2– High-Risk EBC	HR+, HER2– MBC		
Verzenio + ET (N=2,791)	Verzenio + AI (N=372)	Verzenio + fulvestrant (N=441)	Single-agent Verzenio (N=132)
5%	**2%**	**1%**	**1%**

VERZENIO (abemaciclib) CONTINUOUS CARE™

Comprehensive support when patients start on Verzenio*

Free loperamide kit

Upon prescriber request, patients can receive a one-time supply of loperamide at no cost.

MyRightDose†

Ensuring patients don't pay for another prescription should a dose reduction be required, this dose-exchange program delivers the appropriate dose to your patient in as little as 48 hours at no extra cost.

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

*The Verzenio Continuous Care™ Program is not a guarantee of coverage. Terms and conditions apply for all programs. See enrollment form for details.

†Additional terms and conditions apply. See the MyRightDose enrollment form for details.

PLAN

Diet may impact your patients' experience with diarrhea[5,6]

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

- Advise your patients to continue eating their normal diet with modifications as needed
- These suggestions serve as a guide and are not specific to Verzenio

WHAT YOU SHOULD RECOMMEND

- Drink plenty of fluids
- More frequent smaller meals
- Soft, bland foods
- Foods high in potassium and sodium

WHAT YOUR PATIENTS SHOULD AVOID

- Dairy or high-fiber products
- Fatty, greasy, or spicy foods
- Caffeinated or alcoholic beverages

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

ACT

Help your patients manage their diarrhea with dose modifications[1]

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

APPROXIMATELY 1 IN 5 PATIENTS* REQUIRED A DOSE MODIFICATION TO HELP MANAGE DIARRHEA WHEN TREATED WITH VERZENIO PLUS ET[1†]

	HR+, HER2– High-Risk EBC	HR+, HER2– MBC		
	Verzenio + ET (N=2,791)	Verzenio + AI (N=372)	Verzenio + fulvestrant (N=441)	Single-agent Verzenio (N=132)
Patients who required a dose interruption*	20%	15%	19%	24%
Patients who required a dose reduction*	17%	13%	19%	20%

*Among all patients studied in the monarchE, MONARCH 1, MONARCH 2, and MONARCH 3 trials.

†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 tablets are available in 50 mg increments, allowing for straightforward dose modifications[1]

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

ACT

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

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

DOSE MODIFICATIONS (ALL GRADES)*

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.[1]

CTCAE GRADE[7]	STOOLS/ DAY OVER BASELINE[1,7]	SUSPEND DOSE UNTIL TOXICITY RESOLVES TO[1]	DOSE MODIFICATION[1]
Grade 1	**<4 stools**	N/A	None
Grade 2 that does not resolve within 24 hours	4-6 stools		None
Grade 2 that persists or recurs after the same dose despite maximal supportive measures	4-6 stools	**<4 stools/day over baseline**	**Resume at** *next lower dose*
Grade 3 or **Grade 4** or requires hospitalization	≥7 stools Life-threatening consequences or urgent intervention and/or hospitalization indicated		**Resume at** *next lower dose*

Across Verzenio trials†, dose reductions were common. Verzenio efficacy was maintained following dose reduction.[1,8,9]

~44% of patients received a dose reduction to help them remain on treatment.[1,8,9]

Please refer to the full Prescribing Information for recommended dose modifications for adverse reactions including hematological toxicities, diarrhea, hepatotoxicity, interstitial lung disease (ILD)/pneumonitis, venous thromboembolic events (VTEs), and other toxicities.[1]

*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.[1]

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

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

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

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

150 mg in combination with ET[1]* | TWICE DAILY[1]

200 mg single agent[1] | TWICE DAILY[1]

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

MBC: Until disease progression or unacceptable toxicity[1]

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

Please refer to the full Prescribing Information for additional guidance.

*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.

For your patients who require dose adjustments

ACROSS VERZENIO TRIALS†, DOSE REDUCTIONS WERE COMMON[1]

Verzenio efficacy was not compromised following dose reduction[1,8,9]

~44% of patients received a dose reduction to help them remain on treatment[1,8,9]

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 recommended dose modifications for adverse reactions including hematological toxicities, diarrhea, hepatotoxicity, interstitial lung disease (ILD)/pneumonitis, venous thromboembolic events (VTEs), and other toxicities.[1]

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

SELECT IMPORTANT SAFETY INFORMATION

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).

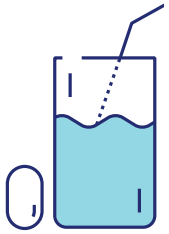
Please see Select Important Safety Information throughout and full Prescribing Information for Verzenio.

Dosing considerations[1]

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

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

SELECT IMPORTANT SAFETY INFORMATION FOR VERZENIO (ABEMACICLIB) (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.

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.

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.

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.

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

SELECT IMPORTANT SAFETY INFORMATION FOR VERZENIO (ABEMACICLIB) (CONT'D)

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.

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 %).

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%).

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%).

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

SELECT IMPORTANT SAFETY INFORMATION FOR VERZENIO (ABEMACICLIB) (CONT'D)

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 (abemaciclib). Prescribing Information. Lilly USA, LLC. **2.** Data on file. Lilly USA, LLC. DOF-AL-US-0096. **3.** Data on file. Lilly USA, LLC. DOF-AL-US-0032. **4.** Data on file. Lilly USA, LLC. DOF-AL-US-0087. **5.** NCI. Eating Hints: Before, During, and After Cancer Treatment. Bethesda, MD: NCI; 2018. **6.** Diarrhea: Cancer Treatment Side Effect. NCI website. https://www.cancer.gov/about-cancer/treatment/side-effects/diarrhea. **7.** National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE). Version 5.0; 2017. **8.** Rugo HS, Huober J, García-Sáenz JA, et al. Management of abemaciclib-associated adverse events in patients with hormone receptor-positive, human epidermal growth factor receptor 2negative advanced breast cancer: safety analysis of MONARCH 2 and MONARCH 3. *Oncologist*. 2021;26:e53-e65. doi:10.1002/onco.13531 **9.** 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.

Managing diarrhea[1]

EXPECT

Diarrhea is a common side effect.[1]

- If diarrhea occurs, your patients will likely experience it in the first month[1]

PLAN

Ensure your patients have an over-the-counter antidiarrheal, such as loperamide, on hand before starting Verzenio[1]

ACT

At the first sign of loose stools, your patient should immediately start an antidiarrheal, increase fluids, and notify your office[1]

- After 24 hours, follow up with your patient. If the diarrhea has not resolved within 24 hours to ≤Grade 1 with antidiarrheal medication, **suspend Verzenio until diarrhea resolves[1]**
- If necessary, reduce the dose[1]
- Across trials, 15-24% of patients required a Verzenio dose interruption, 13-20% of patients required a dose reduction[1]

Verzenio has been shown to be efficacious at reduced doses† so you can find the dose that's right for your patient.[8] Dose modifications for diarrhea are available in the full Prescribing Information.

† Dose interruptions, reductions, or discontinuations.[8]

Remember to follow up within 24 hours to ensure your patients are best supported in their treatment journey.[1]

Click here to learn more about patient support options with Verzenio Continuous Care™

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.

PP-AL-US-4228 02/2024

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