Composing a Letter of Medical Necessity (LMN)

The following information is presented for informational purposes only and is not intended to provide reimbursement or legal advice. Laws, regulations, and policies concerning reimbursement are complex and are updated frequently. While we have made an effort to be current as of the issue date of this document, the information may not be as current or comprehensive when you view it. Providers are encouraged to contact third-party payers for specific information on their coverage policies. For questions, please call Verzenio Continuous Care™ at 1-844-VERZENIO. Verzenio Continuous Care may provide information but not assistance in drafting the letter.

Many health plans require that an LMN accompanies a Coverage Authorization Appeals Letter.* The purpose of an LMN is to explain the prescribing healthcare provider's (HCP's) rationale and clinical decision making when choosing a treatment.

This resource, **Composing a Letter of Medical Necessity (LMN)**, provides information on the process of drafting an LMN. Included on pages 3 and 4 is a list of considerations, which can be followed when creating an LMN.

- **Patients who are continuing therapy:** There are three common scenarios in which this denial of coverage can occur:
  - The patient initiated therapy with a patient assistance program
  - The patient has switched insurance companies
  - The patient's insurance no longer covers Verzenio
- **Patients who are new to therapy:** Some plans have specific Coverage Authorization Forms that must be used to document an LMN

Follow the patient's plan requirements when requesting Verzenio; otherwise, treatment may be delayed.

* For Medicare beneficiaries, specific requirements must be met for the HCP to be considered a legal representative of the patient in an appeal. For additional information, please visit https://www.cms.gov/Medicare/CMS-Forms/CMS-Forms/downloads/cms1696.pdf.

Indications

Verzenio is indicated for the treatment of hormone receptor–positive (HR+), human epidermal growth factor receptor 2–negative (HER2–) advanced or metastatic breast cancer (MBC):

- In combination with fulvestrant for women with disease progression following endocrine therapy
- In combination with an aromatase inhibitor (AI) for postmenopausal women as initial endocrine-based therapy
- As a single agent for adult patients with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting

Select Important Safety Information

Diarrhea occurred in 81% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 86% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and 90% of patients receiving Verzenio alone in MONARCH 1. Grade 3 diarrhea occurred in 9% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 13% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and in 20% of patients receiving Verzenio alone in MONARCH 1. Episodes of diarrhea have been associated with dehydration and infection.

Diarrhea incidence was greatest during the first month of Verzenio dosing. In MONARCH 3, the median time to onset of the first diarrhea event was 8 days, and the median duration of diarrhea for Grades 2 and 3 were 11 and 8 days, respectively. In MONARCH 2, the median time to onset of the first diarrhea event was 6 days, and the median duration of diarrhea for Grades 2 and 3 were 9 days and 6 days, respectively. In MONARCH 3, 19% of patients with diarrhea required a dose omission and 13% required a dose reduction. In MONARCH 2, 22% of patients with diarrhea required a dose omission and 22% required a dose reduction. The time to onset and resolution for diarrhea were similar across MONARCH 3, MONARCH 2, and MONARCH 1.

Instruct patients that at the first sign of loose stools, they should start antidiarrheal therapy such as loperamide, 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 Important Safety Information on pages 5 and 6 and click to access the full Prescribing Information for Verzenio.

Composing a Letter of Medical Necessity (LMN)

Recommended components of an LMN

1. Include the patient's full name, date of birth, plan identification number, and case identification number if a decision has already been rendered.
2. Provide a copy of the patient's records with the following details: patient's history, diagnosis with specific International Classification of Diseases (ICD) code, and condition.
3. Note the severity of the patient's condition.
4. Document prior treatments, the duration of each, and the rationale for discontinuation. It may be beneficial to include CPT-4 and/or J-codes to define prior services/treatments, so that the health plan can conduct research and make a timely determination.
5. Attach clinical documentation that supports your recommendation; this information may be found in the Verzenio prescribing information and/or clinical peer-reviewed literature.

Example LMN

Patients who are currently receiving treatment

[Date]
[Medical Director]
[Name of Health Plan]
[Mailing Address]

Re: **[Patient's Name]**
[Plan Identification Number]
1 **[Date of Birth]**
[Case Identification]

To whom it may concern:

2 I am writing to provide additional information to support my claim for **[patient's name]**'s continued treatment of **[advanced or metastatic]** breast cancer with Verzenio® (abemaciclib 50, 100, 150, 200 mg tablets). In brief, continued treatment with Verzenio **[dose, frequency]** is medically appropriate and necessary for this patient. This letter outlines the patient's medical history and previous treatments to support my recommendation for treatment with Verzenio.

3 **[In this section, describe the severity of advanced or metastatic breast cancer at the time when the patient was first prescribed Verzenio. In addition, include a summary of the patient's clinical response to Verzenio and list improvements (if any) in clinical presentation since treatment began. It may be necessary to review past medical records to gather this information.]**

Patient's history, diagnosis, condition, and symptoms*:
Patient must have a diagnosis of HR+, HER2– advanced or metastatic breast cancer†

Patient must also have one of the following:
- ☐ For Verzenio in combination with an aromatase inhibitor, no prior systemic therapy in the advanced or metastatic setting
- ☐ For Verzenio in combination with fulvestrant, disease progression following endocrine therapy
- ☐ For Verzenio taken as a single agent, disease progression following endocrine therapy and prior chemotherapy in the metastatic setting

4

Past Treatments‡	Start/Stop Dates	Reason(s) for Discontinuing
[Insert text]	[Insert text]	[Insert text]
[Insert text]	[Insert text]	[Insert text]

5 **[Provide clinical rationale for this treatment; your treatment decisions may be enhanced by this information, which may be found in the Verzenio prescribing information and/or clinical peer-reviewed literature.]**

[Insert your recommendation summary here, including your professional opinion of the patient's likely prognosis or disease progression without treatment with Verzenio.]

Please feel free to contact me, **[HCP's name]**, at **[office phone number]** for any additional information you may require. I look forward to receiving your timely response and approval of this claim.

Sincerely,

[Physician's name and signature]
[Physician's medical specialty]
[Physician's NPI]
[Physician's practice name]
[Phone #]
[Fax #]

[Patient's name and signature]

Encl: Medical records
Clinical trial information

* Include patient's medical records and supporting documentation.
† Hormone receptor–positive (HR+) and human epidermal growth factor receptor 2–negative (HER2–).
‡ Identify drug name, strength, dosage form, and therapeutic outcome.

Please see Important Safety Information on the following page and click to access full Prescribing Information for Verzenio.

Considerations for Why Verzenio May Be Medically Necessary

Based on the patient's medical need and history, some considerations may be, but are not limited to the following.

Medical Necessity is based on a specific patient's individual need for treatment of their medical condition. Only include information in the LMN that accurately reflects the particular patient's need and medical history. Based on the patient's medical need and history, the journal articles listed on page 4 may be relevant.

- **Verzernio + fulvestrant provided statistically significant OS improvement in HR+, HER2– MBC patients, with consistent results even in women likely to do worse[1-7]***

  * Visceral disease and primary resistance were studied in the clinical trial and have been associated with a worse prognosis.[1-8]

  – OS was a secondary endpoint of MONARCH 2

  – Demonstrated a **9.4-month statistically significant survival advantage** in combination with fulvestrant[1,2]

  - Median PFS in the ITT population[1]: 16.4 months with Verzenio + fulvestrant (n=446) (95% CI: 14.4-19.3) vs 9.3 months with placebo + fulvestrant (n=223) (95% CI: 7.4-12.7); HR=0.553 (95% CI: 0.449-0.681) *P*<.0001. The percentage of PFS events at the time of analysis was 49.8% (n=222) and 70.4% (n=157) in the Verzenio + fulvestrant and placebo + fulvestrant arms, respectively[1]

  - Median OS in the ITT population[2]: 46.7 months with Verzenio + fulvestrant (n=446) (95% CI: 39.2-52.2) vs 37.3 months with placebo + fulvestrant (n=223) (95% CI: 34.4-43.2); HR=0.757 (95% CI: 0.606-0.945) *P*=.0137. Results are based on a preplanned interim analysis and considered to be definitive. The percentage of deaths at the time of analysis was 47.3% (n=211) and 57.0% (n=127) in the Verzenio + fulvestrant and placebo + fulvestrant arms, respectively[2]

  – Demonstrated an **8.1-month numerical increase** in median OS (mOS) in women with visceral disease†

  – Demonstrated a **7.2-month numerical increase** in mOS in women with primary endocrine therapy resistance‡

  - Preplanned subgroup analyses of PFS and OS were performed for stratification factors of disease site (including visceral disease) and endocrine resistance (including primary ET resistance). Analyses were not adjusted for multiplicity, and the study was not powered to test the effect of Verzenio + fulvestrant among subgroups[9]

- **Verzenio + fulvestrant delayed time to chemotherapy[8]**

  – 50.2-month median time to chemotherapy with Verzenio + fulvestrant (n/N=200/446) vs 22.1 months with placebo + fulvestrant (n/N=135/223); HR=0.625 (95% CI: 0.501-0.779)

  – Time to chemotherapy is defined as time from randomization to initiation of first post-discontinuation chemotherapy. Patients who died prior to receiving chemotherapy (n=111) did not contribute an event to this analysis

  – This exploratory analysis was not controlled for type 1 error, and the study was not powered to test this endpoint

MONARCH 2 study design

MONARCH 2 was a phase III, randomized, double-blind, placebo-controlled trial that enrolled 669 patients with HR+, HER2– MBC who progressed on or after ET. Pre/perimenopausal women (17%) were rendered postmenopausal prior to the study. Patients had received no chemotherapy and no more than 1 prior ET in the metastatic setting. Patients were randomized 2:1 to Verzenio + fulvestrant (n=446) or placebo + fulvestrant (n=223). Verzenio and placebo were dosed PO BID on a continuous dosing schedule until disease progression or unacceptable toxicity. 500 mg fulvestrant was administered by IM injection on days 1, 15, and 29 of the first month and once monthly thereafter. The primary endpoint was PFS. Key secondary endpoints were ORR, OS, and DoR.[1,8]

† Visceral disease = ≥1 lesion on an internal organ on, or in, the third space (eg, lung, liver, pleural, or peritoneal metastatic involvement).[10]
‡ Primary resistance = relapse within 2 years of adjuvant ET or progressive disease within 6 months of first-line ET for MBC.[1]

BID=twice a day; CI=confidence interval; DoR=duration of response; ET=endocrine therapy; HR=hazard ratio; IM=intramuscular; ITT=intention to treat; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; PO=orally.

Select Important Safety Information

Neutropenia occurred in 41% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 46% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and 37% of patients receiving Verzenio alone in MONARCH 1. A Grade ≥3 decrease in neutrophil count (based on laboratory findings) occurred in 22% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 32% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and in 27% of patients receiving Verzenio alone in MONARCH 1. In MONARCH 3, the median time to first episode of Grade ≥3 neutropenia was 33 days, and in MONARCH 2 and MONARCH 1, was 29 days. In MONARCH 3, median duration of Grade ≥3 neutropenia was 11 days, and for MONARCH 2 and MONARCH 1 was 15 days.

See additional information about neutropenia on the following page.

Please see Important Safety Information on pages 5 and 6 and click to access the full Prescribing Information for Verzenio.

Considerations for Why Verzenio May Be Medically Necessary (cont'd)

- Verzenio is the only CDK4 & 6 inhibitor to receive single-agent approval[1]
  - 19.7% ORR (n=26) (95% CI: 13.3-27.5) per investigator assessment[1,11]*
  - 17.4% ORR (n=23) (95% CI: 11.4-25.0) per independent review[1,11]*

MONARCH 1 study design

MONARCH 1 was a single-arm, open-label, multicenter study in 132 women with measurable HR+, HER2− MBC whose disease progressed during or after ET, had received a taxane in any setting, and who received 1 or 2 prior chemotherapy regimens in the metastatic setting. Patients had an Eastern Cooperative Oncology Group Performance Status of 0 or 1. Patients took 200 mg of Verzenio orally, twice daily, on a continuous schedule, unless disease progression or unacceptable toxicity occurred. The primary endpoint was ORR. A key secondary endpoint was DoR.[1,11]

* ORR was defined as the proportion of patients with CR + PR and does not include stable disease. PR defined as ≥30% reduction in target lesion size per RECIST 1.1.[7,11]
CDK=cyclin-dependent kinase; CR=complete response; PR=partial response; RECIST=Response Evaluation Criteria in Solid Tumors.

References

1. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2019.
2. Data on file, Lilly USA, LLC. DOF-AL-US-0088.
3. Imkampe A, et al. *Eur J Surg Oncol.* 2007;33:420-423.
4. Largillier R, et al. *Ann Oncol.* 2008;19:2012-2019.
5. Solomayer EF, et al. *Breast Cancer Res Treat.* 2000;59:271-278.
6. Cardoso F, et al. *Breast.* 2017;31:244-259.
7. Eisenhauer EA, et al. *Eur J Cancer.* 2009;45(2):228-247.
8. Sledge GW Jr, et al. *J Clin Oncol.* 2017;35:2875-2884.
9. Data on file, Lilly USA, LLC. ONC20180103a.
10. Data on file, Lilly USA, LLC. ONC20171128a.
11. Dickler MN, et al. *Clin Cancer Res.* 2017;23:5218-5224.

Relevant Journal Articles for Review and Consideration in Support of Verzenio's Use:

- Sledge GW Jr, Toi M, Neven P, et al. The effect of abemaciclib plus fulvestrant on overall survival in hormone receptor-positive, ERBB2-negative breast cancer that progressed on endocrine therapy—MONARCH 2: a randomized clinical trial. *JAMA Oncol*. https://www.jamanetwork.com/journals/jamaoncology/fullarticle/2752266. Published September 29, 2019. Accessed October 23, 2019.
- Di Leo A, O'Shaughnessy J, Sledge GW Jr, et al. Prognostic characteristics in hormone receptor-positive advanced breast cancer and characterization of abemaciclib efficacy. *NPJ Breast Cancer.* 2018;4:41. https://www.nature.com/articles/s41523-018-0094-2. Published December 18, 2018. Accessed October 23, 2019.

Medical Necessity is based on a specific patient's individual need for treatment of their medical condition. Only include information in the LMN that accurately reflects the particular patient's need and medical history. Based on the patient's medical need and history, the journal articles listed above may be relevant.

Select Important Safety Information

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.

Febrile neutropenia has been reported in <1% of patients exposed to Verzenio in the MONARCH studies. 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 additional information about neutropenia on the previous page.

Please see Important Safety Information on pages 5 and 6 and click to access the full Prescribing Information for Verzenio.

Important Safety Information

Diarrhea occurred in 81% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 86% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and 90% of patients receiving Verzenio alone in MONARCH 1. Grade 3 diarrhea occurred in 9% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 13% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and in 20% of patients receiving Verzenio alone in MONARCH 1. Episodes of diarrhea have been associated with dehydration and infection.

Diarrhea incidence was greatest during the first month of Verzenio dosing. In MONARCH 3, the median time to onset of the first diarrhea event was 8 days, and the median duration of diarrhea for Grades 2 and 3 were 11 and 8 days, respectively. In MONARCH 2, the median time to onset of the first diarrhea event was 6 days, and the median duration of diarrhea for Grades 2 and 3 were 9 days and 6 days, respectively. In MONARCH 3, 19% of patients with diarrhea required a dose omission and 13% required a dose reduction. In MONARCH 2, 22% of patients with diarrhea required a dose omission and 22% required a dose reduction. The time to onset and resolution for diarrhea were similar across MONARCH 3, MONARCH 2, and MONARCH 1.

Instruct patients that at the first sign of loose stools, they should start antidiarrheal therapy such as loperamide, 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.

Neutropenia occurred in 41% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 46% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and 37% of patients receiving Verzenio alone in MONARCH 1. A Grade ≥3 decrease in neutrophil count (based on laboratory findings) occurred in 22% of patients receiving Verzenio plus an aromatase inhibitor in MONARCH 3, 32% of patients receiving Verzenio plus fulvestrant in MONARCH 2 and in 27% of patients receiving Verzenio alone in MONARCH 1. In MONARCH 3, the median time to first episode of Grade ≥3 neutropenia was 33 days, and in MONARCH 2 and MONARCH 1, was 29 days. In MONARCH 3, median duration of Grade ≥3 neutropenia was 11 days, and for MONARCH 2 and MONARCH 1 was 15 days.

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.

Febrile neutropenia has been reported in <1% of patients exposed to Verzenio in the MONARCH studies. Two deaths due to neutropenic sepsis were observed in MONARCH 2. Inform patients to promptly report any episodes of fever to their healthcare provider.

Severe, life-threatening, or fatal **interstitial lung disease (ILD) and/or pneumonitis** can occur in patients treated with Verzenio and other CDK4/6 inhibitors. Across clinical trials (MONARCH 1, MONARCH 2, MONARCH 3), 3.3% of Verzenio-treated patients had ILD/pneumonitis of any grade, 0.6% had Grade 3 or 4, and 0.4% had fatal outcomes. Additional cases of ILD/pneumonitis have been observed in the post-marketing setting, with fatalities reported.

Monitor patients for pulmonary symptoms indicative of ILD/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/pneumonitis. Permanently discontinue Verzenio in all patients with grade 3 or 4 ILD/pneumonitis.

Grade ≥3 increases in **alanine aminotransferase (ALT)** (6% versus 2%) and **aspartate aminotransferase (AST)** (3% versus 1%) were reported in the Verzenio and placebo arms, respectively, in MONARCH 3. Grade ≥3 increases in ALT (4% versus 2%) and AST (2% versus 3%) were reported in the Verzenio and placebo arms respectively, in MONARCH 2.

In MONARCH 3, for patients receiving Verzenio plus an aromatase inhibitor with Grade ≥3 increases in ALT or AST, median time to onset was 61 and 71 days, respectively, and median time to resolution to Grade <3 was 14 and 15 days, respectively. In MONARCH 2, for patients receiving Verzenio plus fulvestrant with Grade ≥3 increases in ALT or AST, median time to onset was 57 and 185 days, respectively, and median time to resolution to Grade <3 was 14 and 13 days, respectively.

For assessment of potential **hepatotoxicity,** 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 Grade 3 or 4, hepatic transaminase elevation.

Venous thromboembolic events were reported in 5% of patients treated with Verzenio plus an aromatase inhibitor as compared to 0.6% of patients treated with an aromatase inhibitor plus placebo in MONARCH 3. Venous thromboembolic events were reported in 5% of patients treated with Verzenio plus fulvestrant in MONARCH 2 as compared to 0.9% of patients treated with fulvestrant plus placebo. 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. Across the clinical development program, deaths due to venous thromboembolism have been reported. Monitor patients for signs and symptoms of venous thrombosis and pulmonary embolism and treat as medically appropriate.

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.

Please see additional Important Safety Information on page 6 and click to access the full Prescribing Information for Verzenio.

Verzenio® abemaciclib
50 | 100 | 150 | 200 mg tablets

Important Safety Information (cont'd)

Advise females of reproductive potential to use effective contraception during treatment with Verzenio and for at least 3 weeks after the last dose. 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. Based on findings in animals, Verzenio may impair fertility in males of reproductive potential.

The **most common adverse reactions (all grades, ≥10%)** observed in **MONARCH 3 for Verzenio plus anastrozole or letrozole** and **≥2% higher than placebo plus anastrozole or letrozole vs placebo plus anastrozole or letrozole** were diarrhea (81% vs 30%), neutropenia (41% vs 2%), fatigue (40% vs 32%), 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%), influenza-like illness (10% vs 8%), and thrombocytopenia (10% vs 2%).

The **most common adverse reactions (all grades, ≥10%)** observed in **MONARCH 2 for Verzenio plus fulvestrant and ≥2% higher than placebo plus fulvestrant vs placebo plus fulvestrant** 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 3%), thrombocytopenia (16% vs 3%), alopecia (16% vs 2%), 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%), pyrexia (11% vs 6%), and weight decreased (10% vs 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%), leukopenia (17%), constipation (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** that occurred in the Verzenio arm vs the placebo arm of **MONARCH 3** were neutropenia (22% vs 2%), diarrhea (9% vs 1%), leukopenia (8% vs <1%), ALT increased (7% vs 2%), and anemia (6% vs 1%).

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 (27% vs 2%), diarrhea (13% vs <1%), leukopenia (9% vs 0%), anemia (7% vs 1%), and infections (6% vs 3%).

The **most frequently reported ≥5% Grade 3 or 4 adverse reactions** from **MONARCH 1** with Verzenio were neutropenia (24%), diarrhea (20%), fatigue (13%), infections (7%), leukopenia (6%), anemia (5%), and nausea (5%).

Lab abnormalities (all grades; Grade 3 or 4) for **MONARCH 3 in ≥10% for Verzenio plus anastrozole or letrozole and ≥2% higher than placebo plus anastrozole or letrozole vs placebo plus anastrozole or letrozole** were increased serum creatinine (98% vs 84%; 2% vs 0%), decreased white blood cells (82% vs 27%; 13% vs <1%), anemia (82% vs 28%; 2% vs 0%), decreased neutrophil count (80% vs 21%; 22% vs 3%), decreased lymphocyte count (53% vs 26%; 8% vs 2%), decreased platelet count (36% vs 12%; 2% vs <1%), increased ALT (48% vs 25%; 7% vs 2%), and increased AST (37% vs 23%; 4% vs <1%).

Lab abnormalities (all grades; Grade 3 or 4) for MONARCH 2 in ≥10% for Verzenio plus fulvestrant and ≥2% higher than placebo plus fulvestrant vs placebo plus fulvestrant were increased serum creatinine (98% vs 74%; 1% vs 0%), decreased white blood cells (90% vs 33%; 23% vs 1%), decreased neutrophil count (87% vs 30%; 33% vs 4%), anemia (84% vs 33%; 3% vs <1%), decreased lymphocyte count (63% vs 32%; 12% vs 2%), decreased platelet count (53% vs 15%; 2% vs 0%), increased ALT (41% vs 32%; 5% vs 1%), and increased AST (37% vs 25%; 4% vs 4%).

Lab abnormalities (all grades; Grade 3 or 4) for MONARCH 1 with Verzenio were increased serum creatinine (98%; <1%), decreased white blood cells (91%; 28%), decreased neutrophil count (88%; 27%), anemia (68%; 0%), decreased lymphocyte count (42%; 14%), decreased platelet count (41%; 2%), increased ALT (31%; 3%), and increased AST (30%; 4%).

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 the strong CYP3A inhibitor 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 Class 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 full Prescribing Information for Verzenio.

AL HCP ISI 17SEP2019

Verzenio® abemaciclib
50 | 100 | 150 | 200 mg tablets

Lilly