

Positive Quality Intervention: Management of Abemaciclib (Verzenio®) Associated Diarrhea

Description: Abemaciclib is FDA-approved in combination with an aromatase inhibitor, fulvestrant, and as a single agent in early high-risk, advanced, or metastatic breast cancer. This PQI will address effective practices for the management of abemaciclib associated diarrhea, a common toxicity with this therapy.

Background: Abemaciclib is an FDA approved Cyclin Dependent Kinase (CDK) 4 and 6 Inhibitor approved for use in hormone receptor (HR) positive and human epidermal growth factor 2 (HER2) negative metastatic breast cancer.¹⁻³ Although the mechanism of abemaciclib-induced diarrhea is not fully understood, management of diet along with drug therapy remains the standard of care in patients with abemaciclib-associated diarrhea. In clinical trials, abemaciclib associated diarrhea most frequently occurred in the first cycle of treatment, with a median onset between 6 and 8 days. Diarrhea was often managed in the clinical trials using anti-diarrheal agents sparing the need for dosage reductions or interruptions in the majority of the population.¹⁻³

PQI Process: Upon receipt of abemaciclib prescription:

- Screen for appropriate antidiarrheal medication:⁴⁻⁶
 - Loperamide (OTC)
 - Take two caplets (4 mg) followed by one caplet (2 mg) by mouth every four hours until diarrhea-free for 12 hours
 - Do not exceed 8 caplets (16 mg) per day
 - If diarrhea does not improve during the first 24 hours of taking loperamide, the patient should contact their health care provider
 - May take up to 12 caplets per day for chemotherapy-induced diarrhea under medical supervision
 - May schedule loperamide around the clock before adding another agent
 - Diphenoxylate/atropine (Rx)
 - Take 2 tablets (5 mg) by mouth three to four times daily (max of 8 tablets per day)
 - May alternate with loperamide to achieve around the clock coverage
 - Common side effects: dry skin and mucous membranes, tachycardia, urinary retention, hyperthermia
 - Although uncommon, respiratory depression can occur due to the diphenoxylate
 - Tincture of opium (Rx)
 - Deodorized tincture of opium 10 mg/mL of morphine - Take 0.6 mL (6 mg) by mouth in water every 3- 4 hours
 - Common side effects: CNS depression, drowsiness, urinary retention, constipation, nausea, headache
 - Although uncommon, respiratory depression can occur
- Follow-up with patient by phone after the first week of therapy
 - If severe diarrhea (≥ 7 stools per day), may require inpatient admission for fluid and electrolyte administration

Abemaciclib Dose Modifications⁷

CTCAE Grade of diarrhea	Abemaciclib dose modification
Grade 1	No dose modification required
Grade 2	If toxicity dose not resolve within 24 hours to ≤Grade 1, suspend dose until resolution. No dose reduction required.
Grade 2 that persists or recurs after resuming the same dose	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.

Patient-Centered Activities:

- Patient Education⁷
 - Provide [Oral Chemotherapy Education \(OCE\)](#) sheet for abemaciclib and [Oral Chemotherapy Education Supplemental Sheet](#) for diarrhea
 - Provide [Treatment Support Kit \(TSK\)](#)
 - Explain abemaciclib associated diarrheas median time to onset in the trials was 6-8 days
 - Instruct patient to call their provider at the first sign of diarrhea
 - Encourage patients to take loperamide at the onset of a loose, watery stool and every two hours until resolution of diarrhea
 - If diarrhea has not improved within 24 hours with treatment, consider reducing dose
 - Diet Recommendations:⁴⁻⁶
 - Avoid greasy, spicy, or fried food
 - Avoid milk, caffeine, alcohol, and high fiber vegetables
 - Eat small frequent meals
 - B.R.A.T Diet - Bananas, Rice, Apple Sauce, Toast
 - Drink three or more liters of clear fluid per day
 - Water, clear liquids, soup, sports drinks
- Schedule patient callback at 7 days to follow-up on medication adherence and monitor for diarrhea

References:

1. Dickler MN, Tolaney SM, Rugo HS et al. MONARCH 1, a phase II study of abemaciclib, a CDK4 and CDK6 inhibitor, as a single agent, in patients with refractory HR+/HER2- metastatic breast cancer. *Clin Cancer Res* 2017; 23(17): 5218-5224.
2. Sledge GW, Toi M, Neven P, et al. MONARCH 2: Abemaciclib in combination with fulvestrant in women with HR+/HER2- advanced breast cancer who had progressed while receiving endocrine therapy. *J Clin Oncol* 2017; 35:2875-2884.
3. Goetz, MP, Toi M, Campone M, et al. MONARCH 3: Abemaciclib as initial therapy for advanced breast cancer. *J Clin Oncol* 2017; 35:3638-3646.
4. National Comprehensive Cancer Network. Palliative Care. https://www.nccn.org/professionals/physician_gls/pdf/palliative.pdf.
5. Rangwala F, Zafar SY, Abernathy AP. Gastrointestinal symptoms in cancer patients with advanced disease: new methodologies, insights, and a proposed approach. *Curr Opin Support Palliat Care* 2012;6:69-76.
6. Richardson G, Dobish R. Chemotherapy induced diarrhea. *J Oncol Pharm Practice* 2007;13:181-198.
7. [Verzenio \[package insert\]](#).