



## 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 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.<sup>1-3</sup> 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.<sup>1,2,3</sup>

**PQI process:** Upon receipt of abemaciclib prescription:

- Screen for appropriate antidiarrheal medication:<sup>4,5,6</sup>
  - Loperamide (OTC)
    - Take two caplets (4 mg) followed by one caplet (2 mg) 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) 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) 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 ( $\geq 7$  stools per day), may require inpatient admission for fluid and electrolyte administration

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## Abemaciclib Dose Modifications

CTCAE Grade of diarrhea	Abemaciclib dose modification
Grade 1	No dose modification required
Grade 2	If toxicity dose not resolve within 24 hours to $\leq$ 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 $\leq$ Grade 1. Resume at next lower dose
Grade 3 or 4 or requires hospitalization	Suspend dose until toxicity resolves to $\leq$ Grade 1. Resume at next lower dose

## Patient Centered Activities:

- Patient Education
  - Explain abemaciclib associated diarrhea's 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 hasn't improved within 24 hours with treatment, consider reducing dose
  - Diet Recommendations:<sup>4,5,6</sup>
    - 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

## 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 (Version 1.2018). [https://www.nccn.org/professionals/physician\\_gls/pdf/palliative.pdf](https://www.nccn.org/professionals/physician_gls/pdf/palliative.pdf). Accessed May 16, 2018.
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.

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