Positive Quality Intervention: Management of Abemaciclib Associated Diarrhea

Description of PQI: Abemaciclib (Verzenio®) 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. 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.1,2,3

PQI process: 
Upon receipt of abemaciclib prescription:
• Screen for appropriate antidiarrheal medication:
  o Loperamide
  o Diphenoxylate/atropine
  o Tincture of opium
• If no antidiarrheal agent present on medication list, encourage patient to pick up over-the-counter loperamide and keep well stocked while taking abemaciclib
• Counsel patient on compliance and anti-diarrheal specific administration and side effects
• Follow-up with patient by phone after the first week of therapy
  o If loperamide alone does not control diarrhea, contact prescriber for diphenoxylate/atropine (or other antidiarrheal agent)
  o If severe diarrhea (≥ 7 stools per day), may require inpatient admission for fluid and electrolyte administration

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**Diet Recommendations**[^5,^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)

### Abemaciclib Dose Modifications

<table>
<thead>
<tr>
<th>CTCAE Grade of diarrhea</th>
<th>Abemaciclib dose modification</th>
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<tbody>
<tr>
<td>Grade 1</td>
<td>No dose modification required</td>
</tr>
<tr>
<td>Grade 2</td>
<td>If toxicity dose not resolve within 24 hours to ≤Grade 1, suspend dose until resolution. No dose reduction required</td>
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<tr>
<td>Grade 2 that persists or recurs after resuming the same dose</td>
<td>Suspend dose until toxicity resolves to ≤Grade 1. Resume at next lower dose</td>
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<tr>
<td>Grade 3 or 4 or requires hospitalization</td>
<td>Suspend dose until toxicity resolves to ≤Grade 1. Resume at next lower dose</td>
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</tbody>
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### Drug Therapy Recommendations[^5,^6]:
- **Loperamide (over-the-counter)**
  - Take two caplets (4 mg) followed by one caplet (2 mg) every four hours until diarrhea-free for 12 hours
  - Stop loperamide after no sign of diarrhea 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 (Prescription Only)**
  - 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 component

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• **Tincture of Opium (Prescription Only)**
  - Deodorized tincture of opium 10 mg/mL of morphine
    - Take 0.6 mL (6 mg) in water every 3 to 4 hours
  - Common side effects: CNS depression, drowsiness, urinary retention, constipation, nausea, headache
    - Although uncommon, respiratory depression can occur

**Patient Centered Activities:**
- **Patient Compliance**
  - Encourage patients to take loperamide at the onset of a loose, watery stool and every two hours until resolution of diarrhea
  - This medication only needs to be taken as needed for loose, watery stools
- **Patient Education**
  - Explain abemaciclib associated diarrhea’s median time to onset in the trials was from 6 to 8 days
  - Drink 6-8 (~3 liters) large glasses (water, clear liquids, soup, sports drinks)
  - Instruct patient to call their provider at the first sign of diarrhea
    - If diarrhea hasn’t improved within 24 hours, your doctor may want to reduce the abemaciclib dose

**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.

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