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. 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.

PQI Process: Upon receipt of abemaciclib prescription:
- Screen for appropriate antidiarrheal medication:
  - 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 Modifications

<table>
<thead>
<tr>
<th>CTCAE Grade of diarrhea</th>
<th>Abemaciclib dose modification</th>
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</thead>
<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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Patient-Centered Activities:

- **Patient Education**
  - 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:**
    - 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: