

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.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:^{4,5,6}
 - 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 (≥ 7 stools per day), may require inpatient admission for fluid and electrolyte administration

Important notice: NCODA has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.



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
 - Provide [Oncology Chemotherapy Education \(OCE\)](#) sheet
 - 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:^{4,5,6}
 - 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

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. 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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