ecpn essentials

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Guiding Patients Through Diarrhea Management on Abemaciclib (Verzenio)

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What is abemaciclib?

Abemaciclib (Verzenio) is a cyclin-dependent kinases 4 and 6 (CDK4/6) inhibitor approved in Canada for the treatment of Hormone Receptor (HR) positive, Human Epidermal growth factor Receptor 2 (HER2) negative breast cancer in the following settings:[1,2]

1 Advanced or Metastatic

- In combination with an aromatase inhibitor as initial endocrine-based therapy.
- In combination with fulvestrant in adults whose disease has progressed following endocrine therapy.
- Monotherapy in adults with disease progression after both endocrine therapy and chemotherapy in the metastatic setting.

2 Early Breast Cancer (High Risk)

- In combination with endocrine therapy (e.g., aromatase inhibitor or tamoxifen) as adjuvant treatment for node-positive, high-risk early breast cancer.

The #1 Side Effect

Diarrhea is the most common and expected adverse effect of abemaciclib. The incidence of diarrhea is higher during the first month of treatment with a median onset of 6–8 days. Studies demonstrated a median duration of 9-11 days for grade 2 diarrhea and 6-8 days for grade 3 diarrhea.[1] Uncontrolled diarrhea is concerning as it can lead to dehydration, fatigue, poor nutrition, and treatment interruptions. This may impact both patient adherence and treatment outcomes. As healthcare providers, our effective and early management of diarrhea has the potential to reduce emergency visits, hospital admissions and the need for dose reductions or discontinuation of abemaciclib, ultimately improving patient outcomes and quality of life. Community pharmacists are often the first point of contact for patients and play a key role in education, monitoring and early identification of serious adverse events.

Mechanism Leading to Diarrhea

There are a few hypothesized mechanisms as to how abemaciclib causes diarrhea:

~81% of abemaciclib and its metabolites are eliminated via the feces,
leading to direct mucosal irritation and inflammation in the gastrointestinal (GI) tract.[3]

Abemaciclib causes histopathologic changes in the small intestine,
suggesting a direct toxic effect on the intestinal mucosa leading to diarrhea.[4]

Abemaciclib uniquely inhibits CDK9, which is crucial for transcription and regeneration of the intestinal epithelial cells.
Therefore, off-target effects may impair enterocyte turnover and mucosal repair, causing diarrhea.[5]

Patient Education & Non-Pharmacologic Measures

Patient education and non-pharmacologic strategies are essential in preventing and managing abemaciclib-induced diarrhea. They help reduce the risk of complications, minimize the need for dose reductions or treatment interruptions, and empower patients to take an active role in managing their symptoms.

Prevention

- Counsel patients proactively and emphasize early onset of diarrhea within the first month of treatment so that they are prepared for what to expect.[2] Below are a few examples of how to address this to patients:
  - "Diarrhea is expected with this medication. It typically happens in most patients, often within the first month of starting treatment. The severity can vary from mild to severe. That's why it's important to know what to watch for and to start managing it right away to prevent it from getting worse."
  - "You will almost certainly experience diarrhea during treatment, typically within the first month. The severity can vary from mild to severe. It's important to recognize it early and begin treatment as soon as possible to stay comfortable and avoid complications."

Management:[1,6]

- Recommend patients stay hydrated and drink at least 6-8 cups of clear, non-caffeinated fluids per day (e.g., water, clear broths, diluted juice, herbal teas). Encourage patients to sip fluids throughout the day rather than drinking large amounts at once to improve tolerance.
- Recommend foods with soluble fiber such as white rice, toast, applesauce, bananas (BRAT Diet), eggs, plain pasta, and skinless poultry, which help to absorb water and bulk up stool, slowing down bowel movements.
- Advise avoiding foods high insoluble fiber (such as whole grains, raw fruits/vegetables, legumes), dairy, spicy or greasy foods, and artificial sweeteners, which speed up transit time and can worsen diarrhea by stimulating bowel movements.
- Encourage 4–5 small meals/snacks per day to ease digestion and reduce gut stimulation.

Pharmacologic Measures

In most patients, diarrhea can be well controlled using supportive medications leading to low rates of treatment discontinuation (<3%) and no negative impact on progression-free survival.[3]

1. First Line Management: Loperamide (Imodium)

- Initiate after the first loose stool: 4 mg, then 2 mg after each loose stool, up to 16 mg/day.[1,2,7]
- Advise patients to follow the above recommendation if they purchase loperamide over the counter.

2. Second Line: Add Lomotil (Diphenoxylate/Atropine)[8,9]

- 2 tablets (2.5 mg diphenoxylate/0.025 mg atropine per tab)
- Take four times daily (QID), space evenly (e.g., 8 AM, 12 PM, 4 PM, 8 PM)
- Maximum: 8 tablets per day (20 mg diphenoxylate total)
- Patients can take loperamide as needed between Lomotil doses if diarrhea continues.

Clinical Approach to adding Lomotil on top of Loperamide[7]

1. Start loperamide at first loose stool
2. Maintain hydration and dietary adjustment
3. If not improving within 24 hours or if reaching the maximum loperamide dose
   – Direct patient to MD for prescription for Lomotil.

Dose adjustments, including temporary treatment holds or reducing the dose of abemaciclib are commonly used to manage diarrhea when supportive medications alone are not sufficient. Recent evidence suggests that dose modifications do not compromise the progression-free or disease-free survival, and allow patients to continue therapy safely and effectively.[10]

Table 1: Dose Modifications of Abemaciclib based on the number of bowel movements.

CTCAE Grade[8]	Action[7]
Grade 1 *(< 4 stools/day)*	Continue therapy + support
Grade 2 *(4–6 stools/day)*	If > 24 h without improvement → hold until ≤ Grade 1; resume same dose, or reduce if recurrent
Grade 3–4 *(≥ 7 stools/day or hospitalization)*	Discontinue until ≤ Grade 1, then resume at lower dose

Red Flags[1,7,12]

Refer patients to the emergency department if they present with any of the following signs and symptoms:

- No improvement after 24 hours of using antidiarrheal medication
- Persistent diarrhea after 48 hours, or > 7 loose stools in one day
- Signs of dehydration (e.g., dizziness, reduced urine output), or symptoms of serious complications such as fever or blood in stool (hydration and infection risk)

Patient Support & Coverage in Canada

- With The Verzenio Continuous Care Program, patients can receive a free one-time supply of loperamide at no cost. Patients can enroll in the program through their oncology team or by contacting Lilly Support Services at 1-888-545-5972.[13]

Clinical Pearls

- Start loperamide with the first loose stool.
- Schedule proactive check-ins with patient during the first 1–2 weeks of treatment to reinforce guidance.
- Educate patients on early signs of dehydration and when to seek medical attention
- Implementing guideline-based diarrhea management has significantly reduced treatment discontinuation in real-world cohorts.[14]
- Recommend patients keep a daily diary of bowel movements and food intake to help identify triggers and track the number and consistency of bowel movements each day.

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