

FDA-REQUIRED REMS* SAFETY INFORMATION

Boxed Warning: Severe Diarrhea and Cardiac Toxicities With FARYDAK Treatment

Severe Diarrhea

What is the risk?

- Diarrhea occurred in 68% of patients treated with FARYDAK compared with 42% in the control arm
- **Severe diarrhea occurred in 25% of FARYDAK-treated patients.** Severe diarrhea is defined as ≥ 7 stools/day, IV fluids, or hospitalization required
 - Diarrhea can occur at any time
 - Diarrhea was the most common adverse event leading to treatment discontinuation

How can I minimize this risk?

- Ensure patients have **anti-diarrheal medications on hand when they start FARYDAK**
- Inform patients to begin **anti-diarrheal medication** at the first sign of abdominal cramping, loose stools
- **For moderate diarrhea** (4 to 6 stools per day)
 - **Inform patients to interrupt FARYDAK** until resolved and restart at the same dose
 - **Consider interrupting bortezomib** until resolved and restart at the same dose
- **For severe diarrhea** (≥ 7 stools/day)
 - **Interrupt FARYDAK** until resolved and restart at reduced dose
 - AND**
 - **Interrupt bortezomib** also until resolved and restart at reduced dose
- **For life-threatening diarrhea, permanently discontinue** FARYDAK and bortezomib
- **Monitor hydration status and electrolytes** (including potassium, magnesium, and phosphate)
 - At baseline and weekly (or more frequently as clinically indicated) during treatment
 - Correct to prevent dehydration and electrolyte disturbances

Cardiac Toxicities

What is the risk?

- **Severe and fatal cardiac ischemic events**, severe arrhythmias, and ECG changes occurred in patients receiving FARYDAK® (panobinostat) capsules. Electrolyte abnormalities may exacerbate arrhythmias
 - **Cardiac ischemic events** occurred in 4% of patients treated with FARYDAK compared with 1% of patients in the control arm
 - **Arrhythmias** occurred in 12% of patients receiving FARYDAK compared with 5% of patients in the control arm
 - **ECG abnormalities** occurred more frequently in patients receiving FARYDAK compared with control arm
 - ST-segment depression: 22% vs 4% (control arm)
 - T-wave abnormalities: 40% vs 18% (control arm)

How can I minimize this risk?

- **Patient selection and evaluation**
 - **Do not start** FARYDAK if patient has
 - Recent myocardial infarction
 - Unstable angina
 - QTcF >450 msec
 - Clinically significant ST-segment or T-wave abnormalities
- **Monitor ECG**
 - Perform an ECG prior to start of therapy and repeat periodically during treatment as clinically indicated
 - Interrupt treatment if QTcF increases to >480 msec
 - If QT prolongation does not resolve, permanently discontinue FARYDAK
- **Monitor electrolytes**
 - Obtain electrolytes including potassium and magnesium at baseline and during therapy
 - Correct abnormal electrolytes before FARYDAK treatment

Indication

FARYDAK is used in combination with bortezomib and dexamethasone to treat patients with multiple myeloma **who have received at least 2 prior regimens, including bortezomib and an immunomodulatory agent.**

This indication is approved under accelerated approval based on progression-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

***A REMS (Risk Evaluation and Mitigation Strategy)** is a program required by the FDA to manage known or potential serious risks associated with a drug product. FDA has determined that a REMS is necessary to ensure that the benefits of FARYDAK outweigh the risks of severe diarrhea and cardiac toxicity. This factsheet is required by the FDA as part of the FARYDAK REMS program.

You are encouraged to report adverse reactions of FARYDAK to Novartis at 1-888-669-6682 and/or the FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

This factsheet does not contain the complete safety profile for FARYDAK. For complete safety information, please see the full Prescribing Information, including Boxed Warning, available at www.FARYDAK-REMS.com.

