Important Drug Safety Notice

TO ALL PARTICIPATING PHARMACIES

Circular Letter MC26-004-CG
February 13, 2026

FDA announced that is providing a communication to increase awareness of recent updates to the product labeling of capecitabine (Xeloda) and fluorouracil (5-FU) related to risks associated with dihydropyrimidine dehydrogenase (DPD) deficiency.

RECOMMENDATIONS

1. All healthcare providers should be aware of the risks of DPD deficiency, inform patients prior to treatment about the potential for serious and life-threatening toxicities due to DPD deficiency, and test patients for genetic variants of DPYD prior to initiating treatment with capecitabine or 5-FU unless immediate treatment is necessary.

2. See the full prescribing information for Xeloda (capecitabine) and 5-FU for additional information on DPD deficiency, located in the Boxed Warning and Sections 2, 5, 12, and 17.

3. Expect patients to visit your pharmacy asking for information on this safety issue and prepare your pharmacy staff on how to handle the situation.

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Safety labeling update for capecitabine and fluorouracil (5-FU) on risks associated with dihydropyrimidine dehydrogenase (DPD) deficiency

The U.S. Food and Drug Administration (FDA) is providing this communication to increase awareness of recent updates to the product labeling of capecitabine (Xeloda) and fluorouracil (5-FU) related to risks associated with dihydropyrimidine dehydrogenase (DPD) deficiency. All healthcare providers should be aware of the risks of DPD deficiency, inform patients prior to treatment about the potential for serious and life-threatening toxicities due to DPD deficiency, and test patients for genetic variants of *DPYD* prior to initiating treatment with capecitabine or 5-FU unless immediate treatment is necessary.

The *DPYD* gene encodes the enzyme DPD, which breaks down >80% of fluorouracil. Patients with certain homozygous or compound heterozygous variants in the *DPYD* gene, known to result in complete or near complete absence of DPD activity (complete DPD deficiency), are at increased risk for acute early-onset toxicity and serious, including fatal, adverse reactions (e.g., mucositis, diarrhea, neutropenia, and neurotoxicity) when exposed to capecitabine or fluorouracil. Patients with partial DPD activity (partial DPD deficiency) may also have an increased risk of serious, including fatal, adverse reactions.

The FDA recently approved revisions to the Xeloda (capecitabine) and 5-FU product labeling to provide further information on DPD deficiency. The following summarizes the key changes that were made to the labeling of both drugs:

- **Boxed Warning:** The Boxed Warning now highlights the risk of serious adverse reactions or death in patients with complete DPD deficiency. It also advises *DPYD* testing prior to initiating capecitabine or 5-FU, unless immediate treatment is necessary, and recommends avoiding use in patients with certain homozygous or compound heterozygous *DYPD* variants that result in complete DPD deficiency.

- **Dosage and Administration:** A new subsection, 2.1 Evaluation and Testing for DPD Deficiency Before Initiating capecitabine or 5-FU, has been added and instructs to avoid use of these drugs in patients known to have certain homozygous or compound heterozygous *DYPD* variants that result in complete DPD deficiency. For patients with partial DPD deficiency, dosing should be individualized.

- **Warnings and Precautions:** Reiterates that prior to initiating capecitabine or 5-FU, patients should be tested for genetic variants of the *DPYD* gene unless immediate treatment is necessary.

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- See the full prescribing information for Xeloda (capecitabine) and 5-FU for additional information on DPD deficiency, located in the Boxed Warning and Sections 2, 5, 12, and 17.

- The FDA will continue to monitor this safety issue and evaluate the evolving landscape and impact of DPD deficiency on the safety of capecitabine and fluorouracil; additional regulatory actions may be considered. The FDA urges patients and healthcare providers to report side effects to the FDA MedWatch program.

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