Direct Healthcare Professional Communication

May 2025

Capecitabine Caution in interpreting the results of screening for dihydropyrimidine dehydrogenase (DPD) deficiency by measuring blood uracil levels in patients with moderate renal impairment

Dear Healthcare Professional,

The General Administration for Pharmaceutical Vigilance (PVGA) at the Egyptian drug authority (EDA) would like to inform you **about Caution in interpreting the results of screening for dihydropyrimidine dehydrogenase (DPD) deficiency by measuring blood uracil levels in patients with moderate renal impairment**

Summary

- In patients with moderate renal impairment (GFR4 between 59 and 30 ml/min), blood uracil levels used for dihydropyrimidine dehydrogenase (DPD) phenotyping should be interpreted with caution, as decreased renal function may lead to increased blood uracil levels.
- Therefore, there is an increased risk of misdiagnosis of DPD deficiency, which may lead to an underdose of capecitabine and lead to reduced treatment efficacy.
- Capecitabine is contraindicated in patients with severe renal impairment

Background on the safety concern

Capecitabine is indicated for the treatment of colorectal cancer, gastric cancer, and breast cancer. It is primarily used in combination with other anticancer agents. Capecitabine is a non-cytotoxic fluoropyrimidine carbamate and acts as an orally administered precursor to the cytotoxic moiety, 5-fluorouracil (5-FU). Biotransformation Sequential enzymatic conversion of capecitabine to 5-FU leads to higher concentrations in tumor cells. The activity of the enzyme dihydropyrimidine dehydrogenase (DPD) determines the rate of 5-fluorouracil catabolism. Patients with DPD deficiency are therefore at increased risk of severe toxicity when treated with 5-FU or one of its prodrugs, such as capecitabine. To identify these patients, pre-treatment testing for DPD deficiency is recommended, despite uncertainties regarding optimal testing methodology.

- Patients with complete DPD deficiency are at high risk of life-threatening toxicity or fatal outcome and should not be treated with capecitabine.

- Patients with partial DPD deficiency are at increased risk of severe and potentially life-threatening toxicity. A reduction in the initial dose should be considered to limit this toxicity. In the absence of severe toxicity, subsequent doses could be increased under close monitoring, as reducing the initial dose may impact treatment efficacy. If blood uracil levels are used to determine the DPD phenotype, the result should be interpreted with caution in patients with moderate renal impairment, as renal impairment can lead to elevated blood uracil levels. This may lead to an incorrect diagnosis of DPD deficiency and, consequently, underdosing of capecitabine, 5-FU, or other fluoropyrimidines in these patients.

Reference

Luxem : https://santesecu.public.lu/dam-assets/fr/espace-professionnel/domaines/dhpc/dhpc-2025/2025-capcitabine.pdf

Call for reporting

Healthcare professionals are asked to report any suspected adverse reactions via the Egyptian reporting system:

Name: General Administration for Pharmaceutical Vigilance

Email: pv.followup@edaegypt.gov.eg

Online reporting: https://vigiflow-eforms.who-umc.org/eg/med
QR Code:

PO Box: 11451

Hotline: 15301