SANDOZ

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Direct Healthcare Professional Communication (DHPC) Letter (November 20th,2024)

Medicines containing 5-fluorouracil i.v. (Fluorouracil Ebewe, FLORYL): In patients with moderate or severe renal impairment, phenotyping for dihydropyrimidine dehydrogenase (DPD) deficiency by measuring blood uracil levels should be interpreted with caution

Dear healthcare professional,

The marketing authorization holders of medicines containing 5-fluorouracil i.v. (5-FU Fluorouracil Ebewe, FLORYL), in agreement with <SFDA> we would like to inform you of the following:

Summary

- **In patients with moderate or severe renal impairment, blood uracil levels used for dihydropyrimidine dehydrogenase (DPD) phenotyping should be interpreted with caution, as impaired kidney function can lead to increased uracil blood levels.**
- **Consequently, there is an increased risk for incorrect diagnosis of DPD deficiency, which may result in underdosing of 5-FU, leading to reduced treatment efficacy.**

Background on the safety concern

Parenteral 5-fluorouracil (5-FU) is part of the standard therapy for various malignancies, including colorectal, pancreatic, gastric, breast, and head and neck cancer. It is mostly used in combination with other anticancer agents.

The rate-limiting enzyme in the catabolism of 5-FU is dihydropyrimidine dehydrogenase (DPD). As a result, patients with impaired DPD enzyme function are at increased risk of severe or life-threatening toxicity when treated with 5-FU or one of its prodrugs, phenotyping and/or genotyping before initiation of treatment is recommended.

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 or fatal toxicity and must not be treated with 5-FU or other fluoropyrimidines (capecitabine, tegafur).

• Patients with partial DPD deficiency are at increased risk of severe and potentially life--threatening toxicity. To limit the risk of severe toxicity, a reduced starting dose should be considered. Subsequent doses may be increased in the absence of serious toxicity, as the efficacy of a reduced dose has not been established.

If blood uracil levels are used to determine the DPD phenotype, the phenotype result must be interpreted with caution in patients with moderate or severe renal impairment, as renal impairment can lead to increased blood uracil levels. This could result in an incorrect diagnosis of DPD deficiency

and consequently underdosing of 5-FU or other fluoropyrimidines in these patients. <National guideline should be considered when choosing the appropriate approach to determine DPD activity. In regards, Saudi product information has been updated accordingly>.

Reporting adverse events

Reporting suspected adverse reactions after approval is of great importance. It enables continuous monitoring of the benefit-risk ratio of the drug. Healthcare professionals are requested to report any suspected adverse reactions to the marketing authorization holder or to the Saudi Food & Drug authority.

Call for reporting, or to report any suspected adverse reactions associated with the use of Medicines containing 5-fluorouracil in accordance with the national requirements via the national spontaneous reporting system to:

The National Pharmacovigilance Center

Unified Contact Center: 19999

Fax: +966112057662

Email: npc.drug@sfda.gov.sa

Website: https://ade.sfda.gov.sa

Product Name	**MAH contacts Information**
Fluorouracil Ebewe	HTTPS://PVI1J.SOLUTIONS.IQVIA.COM/PVI-WE ADVERSE.EVENTS.SAU@SANDOZ.COM
FLORYL	MENA-PV@ACCORD-HEALTHCARE.COM HOME | ACCORD HEALTHCARE, GENERIC & BIOSIMILAR MEDICINES

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