



תאריך: יוני 2022

רופא/ה, רוקח/ת נכבד/ה

חברת טבע מודיעה על העדכונים הבאים בעלון לרופא של התכשיר:

Fluorouracil Teva

50 mg/ml, solution for injection

פלואורואורציל טבע, 50 מ"ג/מ"ל, תמיסה להזרקה

Contains: fluorouracil 50 mg/ml

עדכונים בעלון לרופא

התוויה כפי שאושרה בתעודת הרישום:

Palliative management of carcinoma of the colon, rectum, breast, stomach and pancreas, in selected patients considered incurable by surgery or other means.

As leucovorin-fluorouracil chemotherapy combination for cancer treatment.

ברצוננו להודיע שהעלון לרופא עודכן, בפירוט שלהלן כלולים העדכונים העיקריים בלבד (תוספות מסומנות באדום והסרות מידע כטקסט מחוק):

4.3 Contraindications

Fluorouracil should not be used in:

- During pregnancy and breast-feeding (see section 4.6)

[...]

4.4 Special warnings and precautions for use

Cardiotoxicity

Treatment with fluoropyrimidines has been associated with cardiotoxicity, including myocardial infarction, angina pectoris, arrhythmias, myocarditis, cardiogenic shock, sudden death, **stress cardiomyopathy (Takotsubo syndrome)** and ECG changes (including, in very rare cases, prolongation of the QT interval)

Encephalopathy

During post-marketing surveillance, there have been reports of cases of encephalopathy (including hyperammonemic encephalopathy, leucoencephalopathy and **posterior reversible encephalopathy syndrome [PRES]**) associated with 5-fluorouracil treatment. Signs and symptoms of encephalopathy include mental state changes, confusion, disorientation, coma and ataxia. If any of these symptoms

occur, treatment should be discontinued immediately, and serum ammonia levels should be determined. If serum ammonia levels are elevated, ammonia-lowering treatment should be initiated.

Hyperammonemic encephalopathy often occurs concurrently with lactic acidosis.

Caution should be exercised when administering fluorouracil to patients with impaired renal and/or hepatic function. Patients with impaired renal and/or hepatic function may be at increased risk for hyperammonemia and hyperammonemic encephalopathy.

Tumor lysis syndrome

During post-marketing surveillance, there have been reports of cases of tumor lysis syndrome associated with fluorouracil therapy. Patients at increased risk of tumor lysis syndrome (e.g., patients with renal impairment, hyperuricemia, high tumor burden, rapid disease progression) should be closely monitored. Preventive measures (e.g., hydration, correction of high uric acid levels) should be considered.

[...]

4.6 Fertility, pregnancy and breast-feeding

Pregnancy

~~Fluorouracil may have mutagenic effects and should not be used during pregnancy.~~

There are no adequate and well-controlled studies in pregnant women; however, fetal defects and miscarriages have been reported.

Women of childbearing potential should be advised to avoid pregnancy and to use effective contraception during and up to 6 months after the conclusion of treatment with fluorouracil.

If this drug is used during pregnancy, or if the woman becomes pregnant whilst on therapy with this drug, she should be fully informed of the potential hazard to the fetus, and advised to undergo genetic counseling.

5-fluorouracil should only be used during pregnancy if the potential benefit justifies the potential risk to the fetus.

Fertility

Fluorouracil may have mutagenic effects. Therefore, men treated with fluorouracil are advised not to father a child during treatment and up to 3 months thereafter.

4.8 Undesirable effects

Metabolism and nutrition disorders

Common: Hyperuricemia.

Not known: **Lactic acidosis, tumor lysis syndrome.**

Nervous system disorders

Rare: Nystagmus, headache, dizziness, Parkinson's symptoms, pyramidal signs and euphoria.

Peripheral neuropathy (in combination regimens with radiation therapy).

Very rare: Dysgeusia.

(Leuko-)encephalopathy with symptoms such as ataxia, speech disorders, confusion, disorientation, muscle weakness, aphasia, seizures or coma.

Not known: Hyperammonemic encephalopathy, **posterior reversible encephalopathy syndrome (PRES)**.

Cardiac disorders

Common: Ischemic changes in ECG.

Uncommon: Chest pain resembling angina pectoris.

Rare: Arrhythmias, myocardial infarction, myocarditis, heart failure, dilated cardiomyopathy and cardiogenic shock.

Very rare: Cardiac arrest and sudden cardiac death.

Not known: Pericarditis, **stress cardiomyopathy (Takotsubo syndrome)**.

Gastrointestinal disorders

Common: Mucositis (stomatitis, esophagitis, proctitis), watery diarrhea, nausea and vomiting.

Rare: Dehydration as well as ulcers and bleeding in the gastrointestinal tract.

Not known: **Pneumatosis intestinalis**.

Skin and subcutaneous tissue disorders

The so-called "hand-foot syndrome" with dysesthesia as well as redness, swelling, pain and peeling of the skin on the palms and soles occurs more frequently after administration as a continuous I.V. infusion than after I.V. bolus injections.

Common: Alopecia (usually reversible).

Rare: Exanthema, dry skin with fissures, dermatitis, urticaria, photosensitivity, hyperpigmentation of the skin and streaky hyperpigmentation or pigment loss along the vein course.

Nail changes (e.g., diffuse superficial bluish pigmentation, hyperpigmentation, nail dystrophy, pain and thickening of the nail bed, paronychia) and onycholysis.

Not known: **Cutaneous lupus erythematosus (CLE)**.

[...]

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר האינטרנט של משרד הבריאות
וניתן לקבלו מודפס ע"י פניה לחברת טבע. <https://israeldrugs.health.gov.il>