SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Leucovorin Teva Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Calcium folinate 16.2mg (equivalent to 15mg folinic acid)

Excipient with known effect: Lactose 194.3 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

A standard convex tablet, almost white to cream with slight speckling.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

To diminish the toxicity and counteract the action of folic acid antagonists such as methotrexate in cytotoxic therapy. Known as leucovorin rescue.

Amelioration of the blood picture in some megaloblastic anaemias due to folate deficiency.

4.2 Posology and method of administration

For oral administration.

Calcium Folinate Rescue:

Adults and Children: In general up to 120mg in divided doses over 12 - 24 hours by intramuscular injection, bolus intravenous injection, or intravenous infusion in 0.9% w/v sodium chloride solution followed by 12 - 15mg intramuscularly or 15mg orally, every six hours for the next 48 hours.

Leucovorin Teva should not be given simultaneously with methotrexate as it may reduce or suppress its anti-neoplastic activity. It is recommended that administration should commence within the first 24 hours following methotrexate.

In overdose situations or when the half-life of methotrexate is increased (e.g. renal function impairment or pleural or peritoneal effusions) it is important that Leucovorin Teva be given until the blood concentration of methotrexate declines to non-toxic concentrations. In these cases, doses of Leucovorin Teva equal to or greater than those of methotrexate should be given.

Folinate deficiency:
Adults: 15mg (one tablet) per day.

Children up to 12 years: 0.25mg/kg/day.

4.3 Contraindications

Hypersensitivity to the preparation or active substance or to any of the excipient listed in section 6.1.
Pernicious anaemia or other megaloblastic anaemia where vitamin B_{12} is deficient.

4.4 Special warnings and precautions for use

High dose methotrexate therapy together with leucovorin rescue should only be carried out under the direction of physicians experienced in antitumour chemotherapy.

Leucovorin Teva should not be used in the treatment of pernicious anaemia or megaloblastic anaemias due to the lack of where vitamin B_{12} is deficient.

Lactose
Leucovorin Teva Tablets contains the ingredient, lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Calcium Folinate should not be given simultaneously with folic acid antagonist, for the purpose of reducing or preventing clinical toxicity, as the therapeutic effect of the antagonist may be nullified.

Potential interactions between folinic acid and anti-epileptics may occur; the plasma concentrations of phenobarbital, phenytoin and primidone may possibly be reduced, increasing the frequency of seizures in susceptible patients.

Concurrent administration of chloramphenicol and Calcium Folinate in folate-deficient patients may result in antagonism of the haematopoietic response to folic acid.

Calcium Folinate may enhance the toxicity of flurouracil.

4.6 Pregnancy and lactation

Caution should be exercised in pregnancy and lactation

Pregnancy
Should treatment with methotrexate or other folate antagonists take place despite pregnancy or lactation, there are no limitations as to the use of Calcium Folinate to diminish toxicity or counteract the effects.
Nevertheless, during pregnancy, methotrexate should only be administered on strict indications, where the benefits of the drug to the mother should be weighed against possible hazards to the foetus

5-fluorouracil use is generally contraindicated during pregnancy and contraindicated during breastfeeding; this applies also to the combined use of Calcium Folinate with 5- fluorouracil.

Breast-feeding
It is not known whether Calcium Folinate is excreted into human breast milk. Calcium Folinate can be used during breast-feeding when considered necessary according to the therapeutic indications.

4.7 Effects on ability to drive and use machines

None known

4.8 Undesirable effects

Adverse reactions to calcium folinate are rare, but following intravenous or intramuscular administration, occasional pyrexial reactions have been reported.

The most common dose-limiting adverse reaction occurring in patients receiving combination of Calcium Folinate and 5-fluorouracil are stomatitis and diarrhoea. In addition, haematological adverse reactions, such as leukocytopenia and thrombocytopenia, may occur. These adverse reactions are dose-dependent and their occurrence can usually be decreased by reducing the dosage of cytotoxic drugs. These adverse reactions can be controlled by close monitoring of haematological values, e.g. blood leucocyte and thrombocyte levels, serum electrolyte (e.g. Na, K, Ca) and creatinine levels.

Anaphylactoid and urticaria allergic reactions have also been reported with the use of Calcium Folinate.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form:
https://sideeffects.health.gov.il

4.9 Overdose

No special instructions

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: V03A F03 Detoxifying agents for antineoplastic treatment
Calcium Folinate is used in conjunction with methotrexate, after methotrexate therapy is stopped to reduce the toxicity of the methotrexate, it is also administered in some megaloblastic anaemia.

Methotrexate rescue: Calcium Folinate acts partly by providing a fresh supply of tetrahydrofolate and also by competitively displacing methotrexate from dihydrofolate reductase so that its excretion is accelerated (methotrexate binds to the enzyme dihydrofolate reductase, which is responsible for reducing dietary folic acid

to dihydrofolate and tetrahydrofolate thus inhibiting its action).

Megaloblastic anaemia: Calcium Folinate is an active folic acid derivative and it can therefore relieve pathological conditions associated with folic acid deficiency e.g. megaloblastic anaemia.

5.2 Pharmacokinetic properties

Calcium Folinate is readily soluble; folinic acid is absorbed by the proximal portion of the small intestine. It is rapidly distributed in tissues.

5.3 Preclinical safety data

Preclinical information has not been included because the safety profile of calcium folinate has been established after many years of clinical use. Please refer to section 4.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Starch
Pregelatinized starch
Magnesium stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store in a dark place, below 25°C

6.5 Nature and contents of container

PVC/Aluminium blister strips in packs of 10 or 12 tablets.

6.6 Special precautions for disposal

Not applicable

7. Manufacturer & License Holder

Teva Israel Ltd.
124 Dvora HaNevi'a St., Tel Aviv 6944020

8. MARKETING AUTHORISATION NUMBER

032-83-22115

This leaflet was revised on June 2022 according to MOH guidelines