Summary of Product Characteristics

1. Name of the Medicinal Product

Calcium Folinate 15 mg Tablets

2. Qualitative and Quantitative Composition

Each tablet contains 19.1 mg of calcium folinate (as pentahydrate) equivalent to 15 mg calcium folinate.

Excipients with known effect:
Lactose

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 120 mg 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 - 15 mg intramuscularly or 15 mg orally, every six hours for the next 48 hours.

Calcium Folinate 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 Calcium Folinate be given until the blood concentration of methotrexate declines to non-toxic concentrations. In these cases, doses of Calcium Folinate equal to or greater than those of methotrexate should be given.

Folate deficiency:
Adults: 15 mg (one tablet) per day.
Children up to 12 years: 0.25 mg/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.

Lactose
Calcium Folinate 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. Interactions 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 antiepileptics 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
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. 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.

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 leucocytopenia 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, and 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 authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9. Overdose

There have been no reported sequelae in patients who have received significantly more Calcium Folinate then the recommended dosage. However, excessive amounts of Calcium Folinate may nullify the chemotherapeutic effect of folic acid antagonists.

Should overdosage of the combination of 5-fluorouracil and Calcium Folinate occur, the overdosage instructions for 5-FU should be followed.

5. Pharmacological Properties

5.1 Pharmacodynamic Properties

ATC Code: V03A F03 Detoxifying agents for antineoplastic treatment

Calcium Folinate is used in conjunction with methotrexate to reduce the toxicity of the methotrexate, it is also administered in 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
Maize starch
Pregelatinised maize starch
Magnesium stearate (E572)

6.2. Incompatibilities

Not applicable.

6.3. Shelf Life

36 months.

6.4. Special Precautions for Storage

Do not store above 25°C. Store in original container.

6.5. Nature and Contents of Container

Aluminium blister strips in packs of 10 tablets.

6.6. Instruction for Use/Handling

Not applicable.

Administrative Data

7. Marketing Authorisation Holder

Teva UK Limited,
Ridings Point,
Whistler Drive,
Castleford,
WF10 5HX,
United Kingdom

8. Marketing Authorisation Number

PL 00289/0468

9. Date of First Authorisation/Renewal of Authorisation

18 May 1998

10. Date of (Partial) Revision of the Text

25/05/2022.

POM