Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Clonfolic 0.4 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 0.40 mg (400 micrograms) folic acid.

Excipient(s) with known effect
Contains 50 mg lactose monohydrate per tablet.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet
Pale yellow, circular, biconvex tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Clonfolic is indicated for the prevention of first occurrence neural tube defects (including Spina Bifida) in the foetus. For use by women who are planning a pregnancy.

4.2 Posology and method of administration

Adult females

One tablet (0.4mg) daily.

Supplementation should begin at least 14 weeks before the woman conceives and be continued for at least the first 12 weeks of pregnancy.

Method of administration

Oral.

The tablets should be swallowed with water.

4.3 Contraindications

1. Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
2. Vitamin B_{12} deficiency.

4.4 Special warnings and precautions for use

Caution is advised for patients under therapy for folate-dependent tumours when taking folic acid.
Women with pre-existing diabetes, obesity, family history of neural tube defects, or previous pregnancy affected by neural tube defect have an increased risk of having a pregnancy affected by a neural tube defect and higher doses should be considered.

For women taking anti-seizure medication the requirement for folic acid may be different and they should be under the supervision of a physician while taking folic acid supplements.

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

Folic acid status may be affected by a number of drugs:

- Antiepileptics: Folic acid can reduce plasma concentrations of anticonvulsants, particularly phenytoin, phenobarbital and primidone and therefore patients on anti- epileptic therapy may need to have their dose adjusted at regular intervals and should be under the supervision of a physician while taking folic acid supplements
- Antibacterials: chloramphenicol and co-trimoxazole may interfere with folate metabolism
- Sulfasalazine: can reduce the absorption of folic acid
- Preparations containing folic acid or its derivatives may decrease the effectiveness of methotrexate.

Patients with hypersensitivity to folic acid have been demonstrated to have antibodies that cross react with other folic acid analogues, including methotrexate, folinic acid (leucovorin) and aminopterin.

4.6 Fertility, pregnancy and lactation

Folic acid is indicated for use during pregnancy and lactation.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Folic acid is generally well tolerated. Gastro-intestinal disturbances may occur. Hypersensitivity reactions have been reported rarely.

Immune system disorders
Anaphylactic reaction: frequency not known.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

No cases of this kind have been reported, but even extremely high doses are unlikely to cause harm to the patient.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Folic acid is a member of the vitamin B group. Folic acid is reduced in the body to tetrahydrofolate, which is a coenzyme for various metabolic processes including the synthesis of purine and pyrimidine nucleotides, and hence in the synthesis of DNA; it is also involved in some amino-acid conversions, and in the formation and utilisation of formate.

Periconceptional use of folic acid can reduce a woman's risk of having an infant with a neural tube defect. A population-based intervention study confirmed the effectiveness of a daily dose of 400 µg folic acid in a community based setting. Outcomes of pregnancy were evaluated in women taking a daily dose of 400 µg folic acid from the time of premarital examination to the first trimester of pregnancy. The reduction in risk of neural tube defects among the foetuses or infants of women who took folic acid was 79% in a region with a high incidence of neural tube defects and 41% in a region with a lower incidence of neural tube defects.

5.2 Pharmacokinetic properties

Folic acid is absorbed mainly from the proximal part of the small intestine. The naturally occurring folate polyglutamates are largely deconjugated and reduced prior to absorption. It is the 5-methyltetrahydrofolate which appears in the portal circulation, where it is extensively bound to plasma proteins.

Folic acid is rapidly absorbed from normal diets and is distributed in body tissues. The principal storage is the liver; it is also actively concentrated in the cerebrospinal fluid. There is an enterohepatic circulation for folate; about 4 to 5ug is excreted in the urine daily. Administration of larger doses of folic acid leads to proportionately more of the vitamin being excreted in the urine. Folate is distributed into breast milk.

5.3 Preclinical safety data

Folic acid is not mutagenic. Massive doses in rats and in rabbits (100mg/kg upwards) produced precipitation of folate crystals in the neural tubules, particularly the proximal tubules and in the ascending limb of the Loop of Henle. Tubular necrosis is followed by recovery.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose Monohydrate
Maize Starch
Pregelatinised Starch
Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original package in order to protect from moisture.
Keep blister in the outer carton in order to protect from light.

6.5 Nature and contents of container

Blister packs consisting of 250um clear PVC and 20um hard temper aluminium foil contained in a carton.
Pack sizes: 28, 56, 84 and 98 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Clonmel Healthcare Limited
Waterford Road
Clonmel
Co. Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0126/095/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 15th February 1995

Date of last renewal: 15th February 2010

10 DATE OF REVISION OF THE TEXT

July 2018