Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Tetracycline 250 mg Hard Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains Tetracycline Hydrochloride 250 mg.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Hard Capsule
Size ‘1’, hard gelatin capsules with scarlet caps and yellow bodies, containing a yellow powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the treatment of infections due to micro-organisms sensitive to tetracycline.

4.2 Posology and method of administration

Adults:

The usual total daily dosage is 1000 to 2000 mg in divided doses.

Children:

The usual total daily dosage is 20 to 40 mg/kg in divided doses.

Route of administration

Oral.

4.3 Contraindications

(i) Use in patients with advanced renal insufficiency.

(ii) Use in patients with hypersensitivity to tetracyclines.

4.4 Special warnings and precautions for use

(i) Tetracycline should only be administered with great caution in patients with hepatic insufficiency. Careful monitoring of dosage by serum levels is necessary.

(ii) Prolonged use of an anti-infective may result in the development of infection due to organisms resistant to the anti-infective.

(iii) Tetracyclines are absorbed to some extent by developing bones and teeth and may produce staining and enamel hypoplasia. For this reason during the second half of pregnancy, lactation and breast feeding, and in children up to the age of eight years, tetracycline should only be administered if considered essential by the physician and for as short a treatment period as is feasible. Repeated courses should be avoided. The effect appears to be related to *total dosage given,* and not only to duration of treatment.

(iv) Tetracyclines should only be administered with great caution in patients with renal insufficiency and dosage may require reduction.

(v) Cross resistance between tetracyclines may develop in micro-organisms, and cross-sensitisation in patients.

(vi) Phototoxicity and photosensitivity may occur.

(vii) Patients taking an oral contraceptive pill should be advised that there is a possibility of an interaction with tetracyclines, and they should be advised to use additional contraceptive measures (such as a condom).

4.5 Interaction with other medicinal products and other forms of interaction

(i) Administration of tetracycline with milk, antacids, calcium or iron preparations may affect absorption.

(ii) Tetracycline may prolong the action of coumarin anticoagulants and per se delay coagulation.

(iii) Tetracycline should only be used with great caution in conjunction with other potentially hepatotoxic drugs.

(iv) Tetracycline therapy should not be used in conjunction with penicillins.

4.6 Pregnancy and lactation

This product should only be used during pregnancy if considered essential by the physician as tetracycline is deposited in the bone-forming tissues in the form of a calcium complex and may cause irreversible discoloration of the teeth and defects in dental enamel.

Tetracycline is not recommended for use in women breast feeding infants.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Gastrointestinal disturbances including nausea, vomiting diarrhoea and rarely dysphagia have been reported. There have been a few cases of oesophagitis and oesophageal ulceration in patients taking oral tetracyclines in solid dose form, usually where medication was taken immediately before retiring or with inadequate fluid.

Oral candidiasis, vulvovaginitis and pruritis can occur due to overgrowth with *Candida albicans* and there may be overgrowth of resistant coliform organisms, such as Pseudomembranous spp. and Proteus spp., causing diarrhoea.

In common with other tetracyclines, transient increases in liver function test values, hepatitis, jaundice and hepatic failure have been reported rarely. A few cases of pancreatitis have been reported.

Erythematous and maculopapular rashes, photosensitivity, pruritis, bullous dermatoses, exfoliative dermatitis and skin discoloration have occurred occasionally, but serious skin reactions are rare.

Bulging fontalles in infants and benign intracranial hypertension in juveniles and adults have been reported. Treatment should cease if evidence of raised intracranial pressure such as severe or persistent headache or blurred vision are

noted. While the condition and symptoms usually resolve soon after discontinuation of the tetracycline, the possibility of permanent sequelae exists.

There have been isolated cases of myasthenia. Hypersensitivity reactions, including exacerbation of systemic lupus erythematous, may occur.
Serum-sickness like reaction and single organ dysfunction may also occur.

Renal dysfunction, especially in patients with pre-existing renal impairment, and rarely, acute renal failure or nephritis, have been reported with tetracyclines.

4.9 Overdose

After oral ingestion the toxicity of tetracyclines is generally low. Symptoms and signs that may occur after an acute overdose include: transient fever, vomiting, malaena, jaundice and haematoma formation; transaminases may be elevated and prothrombin time prolonged. In cases of overdose, treatment should be instituted as soon as possible, especially in young children. The stomach should be washed out by gastric lavage, followed by appropriate symptomatic and supportive measures. Antacids may be used to reduce tetracycline absorption. In severe cases of poisoning, peritoneal haemodialysis should be performed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The group of tetracycline antibiotics have a broad spectrum of antimicrobial activity and act by interfering with bacterial protein synthesis. They are active against a large number of gram-positive and gram-negative pathogenic bacteria, including some which are resistant to penicillin, and are mainly bacteriostatic.

5.2 Pharmacokinetic properties

The tetracyclines are incompletely and irregularly absorbed from the gastro-intestinal tract. The degree of absorption is diminished by the soluble salts of divalent and trivalent metals, with which tetracyclines form stable complexes and to a variable degree by milk or food. It has been recommended that tetracycline should be taken before food. Sodium metaphosphate may enhance the absorption of tetracycline. The biological half-life of tetracycline has been reported to be 8.5 hours. The tetracyclines are excreted in the urine and in the faeces. Renal clearance is by glomerular filtration and concentrations in the urine of up to 300 microgram per ml of tetracycline may be reached 2 hours after a dose is taken and be maintained for 6 to 12 hours.

5.3 Preclinical safety data

No further information provided.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Starch Maize
Magnesium stearate

Capsule shell

Erythrosin (E127)
Titanium dioxide (E171)
Gelatin
Quinoline yellow (E104)
Indigo carmine (E132)

6.2 Incompatibilities

None applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.
Keep the container tightly closed.

6.5 Nature and contents of container

Polypropylene tubes with low density polyethylene caps.
Pack size: 40, 50, 100, 250, 500 and 1000 capsules.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Clonmel Healthcare Limited
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8 MARKETING AUTHORISATION NUMBER

PA 126/51/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

December 2005