SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Oxytetracycline 250 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Oxytetracycline 250.0 mg (as dihydrate).

Excipients with known effect:
Each tablet contains lactose 13.44mg, sucrose 180mg and tartrazine (E102) approximately 0.24mg.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Coated tablet.

Round, yellow, sugar coated tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Oxytetracycline is a bacteriostatic broad-spectrum antibiotic, active against a wide variety of Gram-positive and Gram-negative organisms.

Infections caused by oxytetracycline-sensitive organisms include:

1) *Respiratory tract infections:* Pneumonia, whooping cough and other lower respiratory tract infections due to susceptible strains of *Streptococcus pneumoniae, Haemophilus influenzae, Klebsiella pneumoniae* and other organisms. *Mycoplasma pneumoniae* pneumonia. Treatment of chronic bronchitis (including the prophylaxis of acute exacerbations).

2) *Urinary tract infections:* caused by susceptible strains of the Klebsiella species. Enterobacter species, *Escherichia coli, Streptococcus faecalis* and other organisms.

3) *Sexually transmitted diseases:* Infections due to *Chlamydia trachomatis* including uncomplicated urethral, endocervical or rectal infections. Non-gonococcal

urethritis caused by *Ureaplasma urealyticum.* Oxytetracycline is also indicated in chancroid, granuloma inguinale and lymphogranuloma venereum. Oxytetracycline is an alternative drug in the treatment of gonorrhoea and syphilis.

4) *Skin infections:* Acne vulgaris when antibiotic therapy is considered necessary and severe rosacea.

5) *Ophthalmic infections:* Trachoma, although the infectious agent, as judged by immunofluorescence, is not always eliminated. Inclusion conjunctivitis may be treated with oral oxytetracycline alone or in combination with topical agents.

6) *Rickettsial infections:* Rocky Mountain spotted fever, typhus group, Q fever and Coxiella endocarditis and tick fevers.

7) *Other infections:* Stagnant loop syndrome, Psittacosis, brucellosis (in combination with streptomycin), cholera, bubonic plague, louse and tick-borne relapsing fever, tularaemia, glanders, melioidosis and acute intestinal amoebiasis (as an adjunct to amoebicides).

Oxytetracycline is an alternative drug in the treatment of leptospirosis, gas-gangrene and tetanus.

4.2 Posology and method of administration

Posology

The tablets are for oral administration and are best taken on an empty stomach (1 hour before food or 2 hours after). If gastric irritation occurs, tablets should be taken with food. Tablets should be taken well before going to bed. Therapy should be continued up to three days after symptoms have subsided.

The tablets must not be given to children below the age of 12.

All infections due to Group A beta-haemolytic streptococci should be treated for at least 10 days.

Adults (including the elderly) and children over 12 years: The minimum recommended dosage is 250mg every six hours. Therapeutic levels are attained more rapidly by the administration of 500mg initially, followed by 250mg every six hours. For severe infections, the dosage may be increased to 500mg every six hours.

Elderly: Usual adult dose. Caution should be observed as subclinical renal insufficiency may lead to drug accumulation.

Renal impairment: In general, tetracyclines are contraindicated in renal impairment and the dosing recommendations only apply if use of this class of drug is deemed absolutely essential. Total dosage should be decreased by reduction of recommended individual doses and/or by extending time intervals between doses.

Dosage Recommendations in Specific Infections:

Skin infections: 250-500mg daily in single or divided doses should be administered for at least 3 months in the treatment of acne vulgaris and severe rosacea.

Streptococcal infections: A therapeutic dose of oxytetracycline should be administered for at least 10 days.

Brucellosis: 500mg four times daily accompanied by streptomycin.

Sexually transmitted diseases: 500mg four times daily for 7 days is recommended in the following infections:
Uncomplicated gonococcal infections (except anorectal infections in men); uncomplicated urethra; endocervical or rectal infection caused by *Chlamydia trachomatis;* non-gonococcal urethritis caused by *Ureaplasma urealyticum.*

Acute epididymo-orchitis caused by *Chlamydia trachomatis,* or *Neisseria gonorroeae:* 500mg four times daily for 10 days.

Primary and Secondary syphilis: 500mg four times daily for 15 days. Syphilis of more than one year's duration, (latent syphilis of uncertain or more than one year's duration, cardiovascular or late benign syphilis) except neurosyphilis, should be treated with 500mg four times daily for 30 days. Patient compliance with this regimen may be difficult so care should be taken to encourage optimal compliance. Close follow-up including laboratory tests, is recommended.

Method of administration
For oral administration.

4.3 Contraindications

Must not be given to children under 12 years.

Known hypersensitivity to the active substance, to any of the tetracyclines or to any of the excipients listed in section 6.1.

Chronic renal or hepatic dysfunction.

Pregnancy or breastfeeding.

Systemic lupus erythematosus (SLE).

Patients receiving vitamin A or retinoid therapy.

4.4 Special warnings and precautions for use

Tetracycline drugs may cause permanent tooth discoloration (yellow-grey-brown), if administered during tooth development, in the last half of pregnancy and in infancy up to twelve years of age. Enamel hypoplasia has also been reported. This adverse reaction is more common during long-term use of the drug but has been observed following repeated short-term courses.

The anti-anabolic action of tetracyclines may cause an increase in BUN. While this is not a problem in those with normal renal function, in patients with significantly impaired renal function, higher serum levels of oxytetracycline may lead to azotaemia, hyperphosphataemia and acidosis.

Absorption is adversely affected by milk, antacids and aluminium, calcium, iron, magnesium and zinc salts.

Tetracyclines depress plasma prothrombin activity, therefore reduced dosages of concurrent anticoagulants may be required.

When treating venereal disease, where co-existent syphilis is suspected, proper diagnostic procedures should be utilised. In all such cases, monthly serological tests should be made for at least four months.

The use of antibiotics may occasionally result in the overgrowth of non-susceptible organisms including Candida. Constant observation of the patients is essential. If a resistant organism appears, the antibiotic should be discontinued and appropriate therapy instituted.

In long term therapy, periodic laboratory evaluation of organ systems, including haematopoietic, renal and hepatic studies should be performed.

High doses of tetracyclines have been associated with a syndrome involving fatty liver degeneration and pancreatitis.

The use of tetracyclines in general is contraindicated in renal impairment due to excessive systemic accumulation and used with caution in patients with hepatic impairment or those receiving drugs which may have hepatotoxic effects; high doses should be avoided.

Care is advised when administering to patients with myasthenia gravis.

Treatment should cease if symptoms of benign intracranial hypertension (e.g. headache and visual disturbance) develop.

Photosensitivity reactions may occur in hypersensitive persons and such patients should be warned to avoid direct exposure to natural or artificial sunlight and to discontinue therapy at the first sign of skin discomfort.

Use in the elderly: Special care should be taken when treating the elderly.

Patients with rare hereditary problems of fructose or galactose intolerance, total lactase deficiency, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine as it contains lactose and sucrose.

The tablet colouring contains tartrazine (E102). This may cause allergic reactions.

This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially “sodium free”.

4.5 Interaction with other medicinal products and other forms of interaction

The absorption of oxytetracycline may be impaired by antacids and preparations containing aluminium, calcium, iron, magnesium or zinc. Allow two to three hours between doses of oxytetracycline and antacids.

Some foods and dairy products may interfere with absorption.

Anti-diarrhoeal preparations such as kaolin-pectin and bismuth subsalicylate hinder absorption of tetracyclines.

Combination of tetracyclines with diuretics may be detrimental to renal function.

There have been reports of nephrotoxicity (increased blood urea nitrogen and serum creatinine) and death in some cases when oxytetracycline therapy has been combined with methoxyflurane or other drugs known to be nephrotoxic.

Since oxytetracycline has been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require a downward adjustment of their anticoagulant dose. Oxytetracycline may prolong the action of coumarin anticoagulants.

An increased incidence of benign intracranial hypertension has been reported when retinoids, Vitamin A and tetracyclines are used concomitantly and therefore concurrent use is contraindicated.

A few cases of pregnancy or breakthrough bleeding have been attributed to the concurrent use of oxytetracycline with oral contraceptives and alternate contraceptive advice should be sought where necessary.

Oxytetracycline should not be given concurrently with bactericidal drugs such as penicillins as bacteriostatic drugs may interfere with the bactericidal action of penicillin.

Oxytetracycline may increase the hypoglycaemic effects of insulin and sulfonylureas in patients with diabetes mellitus.

4.6 Fertility, pregnancy and lactation

Pregnancy
Should not be used during pregnancy unless considered essential. Tetracyclines cross the placenta and may have toxic effects on foetal tissues, particularly on skeletal development. The use of tetracycline compounds during pregnancy has been associated with reports of maternal liver toxicity. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be appraised of the potential hazard to the foetus.

Breast-feeding
Tetracyclines are excreted in breast milk and are therefore contraindicated in nursing mothers.

Use in newborns, infants and children:
All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in the fibula growth rate has been observed in premature infants given oral tetracycline in doses of 25mg/kg every 6 hours. This reaction was reversed when the drug was discontinued.

4.7 Effects on ability to drive and use machines

No or negligible influence.

4.8 Undesirable effects

Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); frequency not known (cannot be estimated from the available data).

Blood and lymphatic system disorders:
Frequency not known: Haemolytic anaemia, thrombocytopenia, neutropenia, eosinophilia.

Endocrine disorders:
Frequency not known: brown-black microscopic discoloration of thyroid tissue in use over prolonged periods. (No abnormalities of thyroid function are known to occur).

Nervous system disorders:
Frequency not known: Bulging fontanelles in infants, benign intracranial hypertension. If raised intracranial pressure occurs treatment with oxytetracycline should be stopped.

Cardiac disorders:
Frequency not known: Pericarditis.

Gastro-intestinal disorders:
Rare: oesophagitis, oesophageal ulceration (reported in patients taking capsule or tablet forms of drugs in the tetracyclines class. Most of these patients took medication immediately before going to bed).

Frequency not known: Gastrointestinal irritation giving rise to nausea, abdominal discomfort, vomiting, diarrhoea, anorexia, dysphagia (if GI irritation occurs, tablets should be taken with food), Pseudomembranous colitis, intestinal overgrowth of resistant organisms (Candida albicans, in particular), may occur and cause glossitis, rectal and vaginal irritation and inflammatory lesions (with candidial overgrowth) in the anogenital regions. Similarly, resistant staphylococci may cause enterocolitis. Tooth discoloration, pancreatitis.

Hepatobiliary disorders:
Frequency not known: Hepatotoxicity (hepatitis, jaundice, hepatic failure), fatty liver degeneration.

Skin and subcutaneous tissue disorders:
Uncommon: Exfoliative dermatitis.

Frequency not known: Macropapular and erythematous rashes, photo-erythema (Patients exposed to direct sunlight or ultraviolet light should be advised to discontinue treatment if any skin reaction occurs).
Hypersensitivity reactions: urticaria, angioneurotic oedema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus.

Renal and urinary disorders:
Frequency not known: Renal dysfunction.

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 at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

There are no specific overdose problems or symptoms. Gastric lavage and administration of milk or antacids may be employed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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Mechanism of action
Oxytetracycline is a broad spectrum tetracycline antibiotic with activity against a large number of gram positive and gram negative bacteria. It acts by interfering with bacterial protein synthesis.

5.2 Pharmacokinetic properties

Absorption
The tetracyclines are incompletely and irregularly absorbed from the gastrointestinal 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. Plasma concentrations will depend upon the degree of absorption. Peak plasma concentrations occur about 1 to 3 hours after ingestion.

It is recommended that tetracyclines should be given before food.

A dose of 500mg every 6 hours by mouth is reported to produce a steady-state plasma concentrations of 3 to 4µg per ml.

In the circulation, tetracyclines are bound to plasma proteins in varying degrees, but reported values differ considerably: from about 20 to 40% for oxytetracycline.

Distribution
They are widely distributed throughout the body tissues and fluids. Small amounts appear in saliva, and the fluids of the eye and lung.

Tetracyclines appear in the milk of nursing mothers where concentrations may be 60% or more of those in the plasma. They diffuse across the placenta and appear in

the foetal circulation in concentrations of about 25 to 75% of those in the maternal blood. Tetracyclines are retained at sites of new bone formation and recent calcification and in developing teeth.

Elimination
The tetracyclines are excreted in the urine and in the faeces. Renal clearance is by glomerular filtration.

The tetracyclines are excreted in the bile where concentrations 5 to 25 times those in plasma can occur. Since there is some enterohepatic reabsorption complete elimination is slow. Considerable quantities occur in the faeces after administration by mouth.

5.3 Preclinical safety data

No data of relevance which is additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Pregelatinised Maize Starch
Sodium Laurilsulfate
Gelatin
Magnesium Stearate
Talc
Sucrose
Titanium Dioxide E171
Yellow colour containing Dried Aluminium Hydroxide & Tartrazine (E102).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

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

Blister packs: Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container

HDPE tablet containers with LDPE caps of 1000 tablets.

Al/PVC blisters enclosed in an outer carton.

Pack sizes: 28 tablets.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

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