

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Oxytetracycline Tablets BP 250 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 269.57 mg of oxytetracycline dihydrate equivalent to 250mg of oxytetracycline.

Excipients with known effect: Also contains sucrose, glucose and tartrazine aluminium lake (E102).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

A yellow sugar-coated tablet with a smooth polished surface

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:

Therapy should be continued for at least 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 250 mg every six hours. Therapeutic levels are attained more rapidly by the administration of 500 mg initially, followed by 250 mg every six hours. For severe infections, the dosage may be increased to 500 mg 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: Oxytetracycline 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: Oxytetracycline 500mg, four times daily in combination with streptomycin.

Sexually transmitted diseases: Oxytetracycline 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 gonorrhoeae*, Oxytetracycline 500mg four times daily for 10 days.

Primary and secondary syphilis: Oxytetracycline 500mg, four times daily for 15 days. Syphilis of more than a year's duration, (latent syphilis of uncertain or more than a year's duration, cardiovascular or late benign syphilis) except neurosyphilis, should be treated with Oxytetracycline 500mg, four times daily for 30days. 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

Oxytetracycline should be taken on an empty stomach i.e. one hour before or two hours after meals, since food, milk and some dairy products interfere with the absorption. If gastric irritation occurs, tablets should be taken with food. Tablets should be taken well before going to bed.

4.3 Contraindications

- Hypersensitivity to the active substance, any of the tetracycline or any of the excipients listed in section 6.1
- Renal or hepatic impairment
- Systemic lupus erythematosus
- Children under 12 years
- Pregnancy and breastfeeding women
- Porphyria
- 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 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.

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.

Special care should be taken when treating the elderly.

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.

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 4 months.

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.

The use of antibiotics may occasionally result in the overgrowth of nonsusceptible organisms including *Candida*. If a resistant organism appears, the antibiotic should be discontinued and appropriate therapy instituted.

Important information regarding the ingredients of this medicine

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

This medicine also contains tartrazine aluminum lake (E102) which may cause allergic reactions.

4.5 Interactions with other medicinal products and other forms of interaction

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

Since Oxytetracycline has been shown to depress plasma prothrombin activity, patients who are on anticoagulant therapy may require a downward adjustment of their anticoagulant dosage.

Antacids containing aluminium, calcium, iron, magnesium or zinc may impair absorption of oxytetracycline. Allow two to three hours between doses of oxytetracycline and antacids.

Oxytetracycline may potentiate action of some anti-coagulants.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, it is advisable to avoid giving Oxytetracycline in conjunction with penicillin.

The nephrotoxic effects of tetracyclines may be exacerbated by co-administration of diuretics, methoxyflurane or other drugs known to be nephrotoxic.

Dairy products and food may interfere with absorption.

Oxytetracycline may increase hypoglycaemic effects of insulin and sulphonylureas in patients with diabetes mellitus. (See section 4.8)

Benign intracranial hypertension has been reported following the concomitant use of tetracyclines and vitamin A or retinoid and therefore concurrent use is contraindicated.

There is a slight risk of adverse effect on oral contraception. A few cases of pregnancy or breakthrough bleeding have been attributed to the concurrent use of Oxytetracycline with oral contraceptives and alternative contraceptive advice should be sought where necessary.

Oxytetracycline may cause an increase in serum lithium levels when taken concomitantly with lithium-containing medications (e.g. anti-depressants/medicines to treat bi-polar disorder). The lithium dosage should either be adjusted or concomitant treatment stopped, as appropriate.

4.6 Fertility, Pregnancy and lactation

Pregnancy

The product should not be used in pregnancy unless absolutely essential.

Tetracyclines cross the placenta and may have toxic effects on foetal tissues, particularly on skeletal development (see section 4.4).

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 apprised of the potential hazard to the foetus. Tetracyclines are also excreted in breast milk and are therefore contraindicated in nursing mothers.

Use in newborns, infants & Children: All tetracyclines form stable calcium complex in any bone forming tissue.

A decrease in fibula growth rate has been observed in premature infants given oral tetracycline in doses of 25 mg/kg every 6 hours. This reaction was reversed when drug was discontinued.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable Effects

Very common (1/10); common (1/100 to <1/10); uncommon (\geq 1/1,000 to <1/100); rare (\geq 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 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.
(Treatment should cease if evidence of raised intracranial pressure develops.)

Cardiac disorders:

Frequency not known: Pericarditis.

Gastrointestinal disorders:

Rare: oesophagitis, oesophageal ulceration
(Reported in patients receiving capsule and tablet forms of drugs in the tetracycline class. Most of these patients took medication immediately before going to bed.)

Frequency not known: Gastrointestinal irritations giving rise to nausea, abdominal discomfort, vomiting, diarrhoea, anorexia, dysphagia (If gastric 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 discolouration, pancreatitis.

Hepatobiliary system disorders:

Frequency not known: Hepatotoxicity (hepatitis, jaundice and 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

No specific overdose problems or symptoms. Gastric lavage and administration of milk or antacids.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Oxytetracycline is a broad spectrum tetracycline antibiotic with activity against a large number of gram positive and gram negative bacteria.

The product acts by interfering with bacterial protein synthesis.

5.2 Pharmacokinetic properties

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 and 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 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.

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.

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

There is no pre-clinical data of relevance to a prescriber which is additional to that already included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Tablet core:

Cellulose microcrystalline

Alginic acid

Povidone

Magnesium Stearate

Stearic acid

Maize starch

Tablet coat:

Sandarac

Sucrose

Glucose

Purified talc

Tartrazine aluminium lake (E102)

Titanium dioxide (E171)

Povidone

Sodium benzoate

Carnauba wax

6.2. Incompatibilities

Not applicable.

6.3. Shelf Life

36 months.

6.4. Special Precautions for Storage

Glass bottle: Store in a cool dry place.

Blister packs: Store in a cool dry place. Store in the original package.

6.5 Nature and Contents of Container

Amber glass bottle and tin plate screw cap with aluminium faced pulpboard.

The ullage is filled with cotton wool.

Pack sizes: 1000, 112, 56, 28

Blister packs comprising of 250 micron PVC and 20 micron Aluminium foil
Pack sizes: 10, 14, 28, 30, 56, 84, 100
(Not all pack sizes may be marketed)

6.6. Instruction for Use/Handling

Not applicable.

7. MARKETING AUTHORISATION HOLDER

Bristol Laboratories Ltd
Unit3, Canalside,
Northbridge Road
Berkhamsted Herts
HP4 1EG
United Kingdom

8. MARKETING AUTHORIZATION NUMBER(S)

PL 17907/0174

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first Authorisation: 16 February 2005
Date of Renewal: 18 Aug 2009

10 DATE OF REVISION OF THE TEXT

29/07/2020