# 1 NAME OF THE MEDICINAL PRODUCT

Oxytetracycline 250 mg tablets

# 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 250 mg Oxytetracycline Dihydrate.

Excipients with known effect

Sunset yellow (E110)

For a full list of excipients, see section 6.1.

# 3 PHARMACEUTICAL FORM

Film coated tablet

Pale yellow film coated biconvex tablets marked MP10 on one side

# 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. Nongonococcal 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, gasgangrene and tetanus.

## 4.2 Posology and method of administration

*Posology:*

Oxytetracycline Tablets are for oral administration and are best taken on an empty stomach (one hour before food or two hours after), with a glass of water. If gastric irritation occurs, tablets should be taken with food. Food and some dairy products may interfere with absorption. Tablets should be swallowed when standing or sitting down and do not take immediately before going to bed. Therapy should be continued for up to three days after symptoms have subsided.

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. In severe infections; the dosage may be increased to 500 mg every six hours.

*Children under 12 years:* Not to be given.

*Elderly:*
May be given at the usual adult dosage. 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:* 250-500 mg 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:* 500 mg four times daily accompanied by streptomycin.

*Sexually transmitted diseases*: 500 mg 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-gonoccocal urethritis caused by *Ureaplasma urealyticum*.

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

*Primary and Secondary syphilis:* 500 mg 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 500 mg 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:
Oral

## 4.3 Contraindications

- Known hypersensitivity to Oxytetracycline (or any other tetracycline), or to any of the excipients listed in section 6.1
- Children under 12 years of age
- Pregnant or breast-feeding women
- Chronic renal/hepatic dysfunction
- Patients receiving vitamin A or retinoid therapy
- Systemic lupus erythematosus
- Porphyria

## 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.

Tetracycline 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 nonsusceptible organisms including candida. Constant observation of the patient 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.

Special care should be taken when treating the elderly.

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.

This medicine contains sunset yellow (E110) which may cause allergic reactions.

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially “sodium-free”.

## 4.5 Interaction with other medicinal products and other forms of interaction

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

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. Oxytetracycline may prolong the action of coumarin anticoagulants.

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.

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

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.

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.

Dairy products and food may interfere with absorption.

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

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

Oxytetracycline may cause an increase in serum lithium levels when taken concomitantly with lithium-containing medications (e.g. antidepressants/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:

This medicine should not be used in pregnancy unless absolutely essential to the patient's welfare.

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.

Breast-feeding:

Tetracyclines are also 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 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 the drug was discontinued.

## 4.7 Effects on ability to drive and use machines

Oxytetracycline Tablets may have a minor influence on the ability to drive and use machines. Vision disorder may occur following administration of Oxytetracycline Tablets.

## 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 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, photoerythema (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 is no specific antidote. Gastric lavage in the first hours after ingestion along with oral administration of milk or antacids is recommended.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Tetracyclines, ATC code: J01AA06
Oxytetracycline is primarily a bacteriostatic antibiotic with a broad spectrum of activity against gram poistive bacteria and gram negative bacteria, and also some antiprotozoal properties.

### 5.2 Pharmacokinetic properties

The tetracyclines are incompletely and irregularly absorbed from the gastrointestinal tract. Absorption may be affetcted by food, drink and other medicines. It should preferably be given before food and milk drinks and antacids and iron containing medicines should be avoided.

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 500 mg every 6 hours by mouth is reported to produce steady-state plasma concentrations of 3 to 4 μg 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. The biological half-life is in the order of nine and half hour.

### 5.3 Preclinical safety data

Not applicable

# 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Maize starch

Pregelatinised maize starch

Povidone

Sodium starch glycollate

Sodium lauryl sulphate

Magnesium stearate

Opaspray PB-620004 Yellow:

- Titanium dioxide E171
- Quinoline yellow lake E104
- Hydroxypropyl Cellulose E463
- FD&C Yellow #6/Sunset yellow FCF Lake E110

Hypromellose

Ethylcellulose

Diethylphthalate

### 6.2 Incompatibilities

Not known

### 6.3 Shelf life

Container: 36 months

Blister pack: 48 months

### 6.4 Special precautions for storage

Container: Do not store above 25°C. Keep the container tightly closed.
Blister pack: Do not store above 25°C. Store in the original package.

### 6.5 Nature and contents of container

Conatainer: High density polystyrene or polypropylene containers with polypropylene or polythene lids and polyurethane/polythene inserts.
Blister pack: 250µm PVC and 20µm Aluminium foil coated with heat resistant print primer on one side and heat-seal lacquer on the other.

Pack sizes: 28, 30, 50, 56, 60, 84, 100, 250, 500, 1000 tablets.

### 6.6 Special precautions for disposal

Not Applicable

## 7 MARKETING AUTHORISATION HOLDER

Genethics Europe Limited

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Cyprus

## 8 MARKETING AUTHORISATION NUMBER(S)

PL 42976/0007

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

8 January 2001

## 10 DATE OF REVISION OF THE TEXT

24/09/2024