

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1 NAME OF THE MEDICINAL PRODUCT

Oxytetracycline Tablets BP 250mg

### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 250mg Oxytetracycline Dihydrate PhEur.

### 3 PHARMACEUTICAL FORM

Yellow film-coated tablets

Yellow, circular, biconvex film-coated tablets, impressed "C" on one face and the identifying letters "OT" on the reverse.

### 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*

Oxytetracycline tablets are for oral administration and are best taken on an empty stomach (1 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 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.

*Children under 12 years*: Contraindicated in this age group.

*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 gonorrhoeae*: 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**

Known hypersensitivity to any of the tetracyclines or any of the other ingredients in the formulation; chronic renal/hepatic dysfunction; systemic lupus erythematosus; children under 12 years; pregnancy and breastfeeding women; 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 nonsusceptible 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.

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.

#### **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.

Antidiarrhoeal 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 oxytetracycline 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 sulfonylureas 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.

#### **4.6 Fertility, pregnancy and lactation**

##### Pregnancy

Not to be used in pregnancy unless 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 25mg/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 ( $\geq 1/10$ ); common ( $\geq 1/100$  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; website:

[www.mhra.gov.uk/yellowcard](http://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**

Oxytetracycline is a bacteriostatic antibiotic with a broad spectrum of activity against bacteria, and also some antiprotozoal properties.

### **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 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 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**

Not applicable

## 6.1. List of Excipients

Also contains: magnesium stearate, maize starch, propylene glycol, colloidal silica, sodium lauryl sulfate, E104, E110, E171, E463, E464, E553

## 6.2. Incompatibilities

None known

## 6.3. Shelf life

*Shelf-life*

Three years from the date of manufacture.

*Shelf-life after dilution/reconstitution*

Not applicable.

*Shelf-life after first opening*

Not applicable.

## 6.4. Special precautions for storage

Keep container tightly closed.

Store below 25°C in a dry place.

## 6.5. Nature and contents of container

The product containers are rigid injection moulded polypropylene or injection blow-moulded polyethylene containers and snap-on polyethylene lids; in case any supply difficulties should arise the alternative is amber glass containers with screw caps.

The product may also be supplied in blister packs in cartons:

a) Carton: Printed carton manufactured from white folding box board. b) Blister pack: (i) 250µm white rigid PVC. (ii) Surface printed 20µm hard temper aluminium foil with 5-7g/M<sup>2</sup> PVC and PVdC compatible heat seal lacquer on the reverse side.

Pack size: 7's, 10's, 14's, 21's, 28's, 30's, 56's, 60's, 84's, 100's, 112's, 250's, 500's, 1000's

Product may also be supplied in bulk packs, for reassembly purposes only, in polybags contained in tins, skillets or polybuckets filled with suitable cushioning material. Bulk packs are included for *temporary* storage of the finished product before final packaging into the proposed marketing containers.

Maximum size of bulk packs: 50,000.

**6.6 Special precautions for disposal**

Not applicable.

**7 MARKETING AUTHORISATION HOLDER**

Accord-UK Ltd

(Trading style: Accord)

Whiddon Valley

Barnstaple

Devon

EX32 8NS

**8 MARKETING AUTHORISATION NUMBER**

PL 00142/0372

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

26/04/1995 / 03/06/2005

**10 DATE OF REVISION OF THE TEXT**

14/11/2019