Summary Product Characteristics

1.

Name of the nonproprietary International Product: Oxytetracycline Capsules BP 250 mg

Route of Administration: Oral

2. Qualitative and Quantitative composition:

Sr. No.	Ingredients	Specification	Qty / capsule (mg)	% Overages	Reason for inclusion
Active					
1	Oxytetracycline Hydrochloride	BP	250.00	-	Active
Excipients					
2	Maize Starch	BP	315.25	-	Diluent
3	Colloidal Anhydrous Silica	BP	0.990	-	Disintegrant
4	Purified Talc	BP	23.760	-	Glidant
5	Empty hard gelatin capsules Yellow / Red size '0'	IH	1 No.	-	Unit dose holder

Where, BP: British Pharmacopoeia; IH: In-House

3. Pharmaceutical Form: Hard Gelatin Capsule.

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:

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

The Capsules 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- gonoccocalurethritis 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 maybe difficult so care should betaken to encourage optimal compliance. Close fllow-up including laboratory tests, is recommended.

Method of Administration

For oral use only. Swallow whole, do not chew.

4.3 Contraindications:

Must not be given to children below 12 years.

Known hypersensitivity to any of the tetracyclines or any of the other ingredients in the formulation, renal or hepatic impairment, systemic lupus erythematosus, pregnancy and breastfeeding women, porphyria, patients receiving vitamin A or retinoid therapy.

4.4 Special warning and precaution for use:

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine as this product contains lactose.

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

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 maybe 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 betaken 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 non susceptible organisms including Candida. If a resistant organism appears, the antibiotic should be discontinued and appropriate therapy instituted.

4.5 Interaction 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 benephrotoxic.

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.

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 Pregnancy and Lactation:

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. 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 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 the ability to drive and use machines:

None known.

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 and dysphagia (If gastric irritation occurs, Capsules 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.

4.9 Overdose

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

5. Pharmacological Particulars:

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Oxytetracycline is abroad spectrum tetracycline antibiotic **ATC code:** D06AA03

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 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 Pre-clinical Safety:

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:

Maize Starch	BP
Colloidal Anhydrous Silica	BP
Purified Talc	BP
Empty hard gelatin capsules Yellow / Red size '0'	IH

6.2 Incompatibilities: Nil.

6.3 Shelf Life: 36 months.

6.4 Special Precautions for storage:

Store at a temperature below 30ºC. Protect from light.

6.5 Nature and contents of container:

Alu-PVC Blister of 12 capsules each, such 10 blisters packed in a primary carton along with the Pack Insert.

6.6 Special precautions for disposal and other handling

None

7. Marketing Authorization Holder: ZMC INTERNATIONAL LTD
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MANUFACTURER: JIANGXI XIERKANGTAI PHARMACEUTICAL CO., LTD, NORTH ZONE, HIGH- NEW TECHNOLOGY INDUSTRIAL ZONE, PINGXIANG, JIANGXI, CHINA

8. Marketing Authorization Number: --

9. Date of first Authorization /renewal of the authorization: --

10. Date of revision of text: September 2022