SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Maxcyclin Capsules (Tetracycline BP 250 mg Capsules)

2. Qualitative and quantitative composition

Each Capsule contains

Tetracycline Hydrochloride BP……..250.0 mg.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Capsule.

Yellow/Red capsule printed Tetra/250 on it in Alu-Pvc Blister

4. Clinical particulars

4.1 Therapeutic indications

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

Infections caused by tetracycline-sensitive organisms include:

1) Respiratory tract infections: Pneumonia 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) and whooping cough.

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. Tetracycline is also indicated in chancroid, granuloma inguinale and lymphogranuloma venereum.

4) Tetracycline is an alternative drug in the treatment of penicillin resistant gonorrhoea and syphilis.

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

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

7) Rickettsial infections: Rocky mountain spotted fever, typhus group, Q fever and Coxiella endocarditis and tick fevers.

8) 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).

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

4.2 Posology and method of administration

Posology

Tetracycline should be given one hour before or two hours after meals, since food and some dairy products interfere with absorption. 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, 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 of age: 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 three months in the treatment of acne vulgaris and severe rosacea.

Brucellosis: 500mg tetracycline four times daily accompanied by streptomycin.

Sexually transmitted diseases: 500mg four times daily for seven days is recommended in the following infections: Uncomplicated gonoccal infections (except anorectal infections in man); uncomplicated urethral, endocervical or rectal infection caused by Chlamydia trachomatis; non-gonoccal urethritis caused by Ureaplasma urealyticum. Acute epididymo-orchitis caused by Chlamydia trachomatis, or Neisseria gonorrhoea, 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 constituents in the formulation; chronic renal or hepatic dysfunction, renal impairment, particularly if severe, pregnancy, lactation, systemic lupus erythematosus, children under 12 years (see sections 4.4, 4.6 and 4.8) ; pregnancy and breastfeeding women.

Benign intracranial hypertension has been reported following the concomitant use of tetracyclines and Vitamin A or retinoids and therefore concurrent use should be contraindicated (see section 4.5 and 4.8).

4.4 Special warnings and precautions for use

The use of tetracyclines if administered during tooth development, in the last half of pregnancy and in children under the age of 12 years may cause permanent tooth discolouration (yellow-grey-brown) (see sections 4.3, 4.6 and 4.8) 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 use of tetracycline 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. High doses

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

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 tetracycline may lead to azotaemia, hyperphosphataemia and acidosis.

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

Tetracycline is probably porphyrinogenic. Advice of a porphyria specialist should be sought for tetracycline use in patients with acute porphyria.

Photosensitivity manifested by an exaggerated sunburn reaction has been observed in some individuals taking tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be advised that this reaction can occur with tetracycline drugs, patients should be warned to avoid direct exposure to natural or artificial sunlight and that treatment should be discontinued at the first evidence of skin erythema or skin discomfort.

SLE (systemic lupus erythematosus) can be exacerbated by the use of tetracyclines.

Diarrhoea, particularly if severe, persistent and/or bloody, during or after treatment (including several weeks after treatment) with Tetracycline Capsules, may be symptomatic of Clostridium difficile-associated disease (CDAD). CDAD may range in severity from mild to life threatening, the most severe form of which is pseudomembranous colitis (see section 4.8). It is therefore important to consider this diagnosis in patients who develop serious diarrhoea during or after treatment with Tetracycline Capsules. If CDAD is suspected or confirmed Tetracycline Capsules should be stopped immediately and appropriate therapy initiated without delay. Anti-peristaltic drugs are contraindicated in this clinical situation.

Cross resistance between tetracyclines may develop in micro-organisms and cross- sensitisation patients. The use of antibiotics may occasionally result in the overgrowth of nonsusceptible organisms including Candida (see section 4.8). Constant observation of the patient is essential. Tetracycline should be discontinued and appropriate therapy instituted if there are signs/symptoms of overgrowth of resistant organisms including candida, enteritis, glossitis, stomatitis, vaginitis, pruritis ani or staphylococcal enterocolitis.

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

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.

Care is advised when administered to patients with myasthenia gravis. Tetracycline may increase muscle weakness in patients with myasthenia gravis.

4.5 Interaction with other medicinal products and other forms of interaction

Tetracycline should not be used with penicillins.

Tetracyclines depress plasma prothrombin activity and reduced doses of concomitant anticoagulants such as coumarins and phenindione may be required. Tetracycline may prolong the action of coumarin anticoagulants.

Absorption of tetracycline from the gastrointestinal tract is impaired by the concomitant administration of di and trivalent cations such as iron, calcium, zinc salts, bismuth, magnesium and aluminium salts. Absorption of zinc and oral iron is impaired by tetracycline. Administration of medicinal products containing these cations and tetracycline should be maximally separated by at least two to three hours. The following should be avoided when taking tetracycline: antacids, bismuth containing ulcer-healing drugs, drugs such as quinapril Capsules which contain magnesium carbonate and didanosine which contains calcium and magnesium excipients.

Absorption of tetracycline is impaired by food, milk and dairy products, sucralfate, tripotassium dicitratobismuthate and strontium ranelate (manufacturer of strontium ranelate advises avoid concomitant use).

There have been reports of nephrotoxicity (increased blood urea nitrogen and serum creatinine) and death in some cases when tetracycline therapy has been combined with methoxyflurane.

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

The absorption of tetracycline may be reduced by the concomitant administration of sucralfate. Separating administration should be considered.

Absorption of tetracycline is possibly reduced by colestipol, colestyramine and antidiarrhoeal preparations such as kaolin-pectin and bismuth subsalicylate

Combination of tetracyclines with diuretics may be detrimental to renal function and may aggravate nephrotoxicity by volume depletion.

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

Tetracycline may cause an increase in serum lithium levels. Tetracycline may cause an increase in serum digoxin levels.

Tetracycline may cause an increase in the risk of methotrexate toxicity. Regular monitoring of toxicity is necessary when taken concurrently.

Increased risk of ergotism when tetracycline given with ergotamine and methysergide.

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

Tetracycline reduces plasma concentration of atovaquone.

There is a possible increased risk of benign intracranial hypertension with tetracyclines and retinoids (acitretin, isotretinoin, tretinoin). Concomitant use should be avoided.

Antibacterials inactivate oral typhoid vaccine. Vaccination should not commence within 3 days after completing treatment with any antibacterial agents. Also, it is preferable that antibacterial therapy should not commence within 3 days after the last dose of vaccine.

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 sections 4.3, 4.4 and 4.8). Tetracycline may be deposited in deciduous and permanent teeth giving permanent discolouration.

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.

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.

Breast-feeding

Tetracyclines are also excreted in breast milk and are therefore contraindicated in nursing mothers.

4.7 Effects on ability to drive and use machines

No significant effect.

4.8 Undesirable effects

There are no modern clinical studies available that can be used to determine the frequency of undesirable effects.

The following convention has been utilised for the classification of frequency. Very common ≥ 1/10; common ≥ 1/100 and < 1/10; uncommon ≥ 1/1000 and < 1/100; rare ≥ 1/10,000 and < 1/1000; very rare < 1/10,000; not known (cannot be estimated from the available data).

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

Symptoms:

1. There may be nausea and vomiting.
2. Crystalluria and haematuria may occur following very large doses.
3. Hypersensitivity reactions may occur.

Treatment:

1. There is no specific antidote.
2. Gastric decontamination is not necessary.
3. Give oral fluids for severe vomiting and diarrhoea if required.
4. Manage anaphylaxis reactions conventionally.
5. Single brief convulsions do not require treatment. If frequent or prolonged control with intravenous diazepam or lorazepam.
   General symptomatic therapy as indicated by the patient's clinical condition.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antibacterials for systemic use, tetracyclines ATC code: J01A A07

Mechanism of action

Tetracycline is a broad spectrum antibiotic. It is mainly bacteriostatic and acts by interfering with bacterial protein synthesis.

Tetracyclines are taken up into sensitive bacterial cells by an active transport process. Once within the cell they bind reversibly to the 30S subunit of the ribosome, preventing the binding of aminoacyl transfer RNA and inhibiting protein synthesis and hence cell growth. Although tetracyclines also inhibit protein synthesis in mammalian cells they are not actively taken up, permitting selective effects on the infecting organism.

The deposition of tetracycline in and discolouration of teeth is a problem if given to children or during pregnancy.

Hepatotoxicity may be a problem in patients with impaired liver function.

5.2 Pharmacokinetic properties

Absorption

Most tetracyclines are incompletely absorbed from the gastrointestinal tract, about 60-80% of a dose of tetracycline usually being available. The degree of absorption is diminished by the presence of divalent and trivalent metal ions with which tetracyclines form stable insoluble complexes and to a variable degree by milk or food. Formulation with phosphate may enhance the absorption of tetracycline.

Plasma concentrations will depend upon the degree of absorption. Administration of tetracycline 500mg every 6 hours generally produces steady-state concentrations of 4-5μ g/ml. Peak plasma concentrations occur about 1-3 hours after ingestion. Higher concentrations can be achieved after intravenous administration; concentrations may be higher in women than in men.

Distribution

They are widely distributed throughout the body tissues and fluids. Concentrations in cerebrospinal fluid are relatively low, but may be raised if the meninges are inflamed. 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.

Biotransformation

In the circulation 20-65% of tetracycline is bound to plasma proteins.

The tetracyclines have been classified in terms of their duration of action in the body, although the divisions appear to overlap somewhat.

Elimination

The tetracyclines are excreted in the urine and faeces. Renal clearance is by glomerular filtration. Up to 55% of a dose is eliminated unchanged in the urine; concentrations in the urine of up to 300μ g/ml of tetracycline may be reached two hours after a usual dose is taken and be maintained for up to 12 hours. Urinary excretion is increased if urine is alkalinised. The tetracyclines are excreted in the bile where concentrations 5-25 times those in plasma can occur. Since there is some enterohepatic reabsorption complete elimination is slow.

Considerable quantities occur in the faeces after administration.

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

Talcum

Aerosol

E.H.G sell size 1, color; light yellow/red

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in a cool dry place not above 30° C. Keep the container tightly closed.

Keep this medicine out of the sight and reach of children.

6.5 Nature and contents of container

10 Capsules in blisters x 10 in a mono package (PVC /Aluminum foil).

6.6 Special precautions for disposal and other handling

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

7. MARKETING AUTHORISATION HOLDER

Richygold International Limited (Pharmaceutical formulations)

103C Amuwo-Odofin Industrial Scheme Off Oshodi Apapa Express Way, Lagos Nigeria.

8. MANUFACTURER

Richygold International Limited (Pharmaceutical formulations)

103C Amuwo-Odofin Industrial Scheme Off Oshodi Apapa Express Way, Lagos Nigeria.