1. NAME OF THE MEDICINAL PRODUCT

PRODUCT NAME: Tetracycline 250mg

BRAND NAME: Salmycin

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

PRODUCT NAME:

Each filled capsule contains:
Tetracycline …….250 mg
Excipients……..q.s

For complete list of excipients refer section 6.1.

3. *PHARMACEUTICAL FORM:*

Capsule
Red cap and yellow body with 'SVNL' logo inscribed on it with yellow powder content

4. *CLINICAL PARTICULARS*

4.1 Therapeutic Indication:

Treatment of infections caused by susceptible strains of Gram-positive and Gram-negative bacteria.

Types of infections include:

Respiratory tract infections:

Pneumonia and other lower respiratory tract infections due to susceptible strains of Streptococcuspneumoniae , Haemophilus influenzae , Klebsiella pneumoniae and other organisms, Mycoplasma pneumoniae , treatment of chronic bronchitis, and prophylaxis of acute exacerbations of chronic bronchitis, treatment of whooping cough.

Urinary tract infections:
Due to susceptible strains of Klebsiella species, Enterobacter species, Escherichia coli, Streptococcus faecalis and other organisms

Sexually transmitted infections:

Due to chlamydia trachomatis including uncomplicated urethral, endocervical or rectal infections. Non-gonococcal urethritis caused by ureaplasma urealyticum . Chancroid granuloma inguinale and lymphogranuloma venereum and as an alternative drug in the treatment of penicillin resistant gonorrhoea and syphilis.

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

Ophthalmic infections:

Trachoma (although the infectious agent is not eliminated). Inclusion conjunctivitis.

Rickettsial infections:

Rocky mountain spotted fever, typhus, Q fever, Coxiella endocarditis and tick fevers.

Other infections:
Stagnant loop syndrome, Psittacosis, brucellosis (in combination with streptomycin), cholera, bubonic plague, louse and tick-borne relapsing fever, tularaemia, glanders, melioidosis, acute intestinal amoebiasis (as an adjunct to amoebicides), leptospirosis, gas gangrene and tetanus.

Unlicensed Uses:

Management of diabetic diarrhoea in autonomic neuropathy.

4.2 Posology and method of administration:

The capsules 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-gonoccocal urethritis 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 may be difficult so care should be taken to encourage optimal compliance. Close follow-up including laboratory tests, is recommended

4.3 Contraindications:

Must not be given to children under 12 years.

If tetracycline administration is considered absolutely essential in these patients, dosages should be reduced and/or the interval between doses should be extended.

Tetracycline may cause an increase in blood urea nitrogen. In patients with severe renal impairment, higher serum levels of tetracycline may lead to azotaemia, hyperphosphataemia and acidosis.

Contraindicated in chronic hepatic impairment.

Use with caution and avoid high doses in patients with acute hepatic impairment.

4.4 Special warning and precautions for use

In the treatment of syphilis, optimal compliance should be encouraged and close follow up, including laboratory tests, is recommended.

Patients should be advised not to self medicate due to the potential of some drugs to interact with tetracycline. This includes anti-diarrhoeal products and vitamin A supplements. Concurrent administration of tetracycline and vitamin A may cause benign intracranial hypertension.

Tetracyclines may cause permanent tooth discolouration if administered during tooth development in children under 12 or during the last half of pregnancy. Enamel hypoplasia has also been reported. This reaction is more common during prolonged use of tetracycline but has also been observed following repeated short term courses.

Patients with renal impairment - See Dosage; Renal impairment. Use with caution in elderly patients as renal impairment in these patients may cause drug accumulation.

Patients with hepatic impairment - See Dosage; Hepatic impairment

In long-term therapy, laboratory evaluation of organ systems, including haematopoietic, renal and hepatic function, should be monitored periodically.

In patients with a venereal disease where syphilis is also suspected, proper diagnostic procedures should be followed. This includes monthly serological tests for at least 4 months.

The use of tetracycline may result in the overgrowth of non-susceptible organisms, such as candida. The patients should be observed closely and if this effect occurs, tetracycline should be discontinued and appropriate therapy initiated.

Use with caution and avoid high doses in patients with acute hepatic impairment.

High doses of tetracycline have been associated with a syndrome involving fatty liver degeneration and pancreatitis.

If patients present with severe and persistent diarrhoea after treatment with tetracycline, consider pseudomembranous colitis. If clostridium difficile is suspected or confirmed tetracycline should be discontinued and appropriate treatment initiated. Anti-peristaltic drugs are contraindicated in this situation.

Photosensitivity reactions may occur in hypersensitive persons. Patients should be warned to avoid direct exposure to natural or artificial sunlight and to discontinue therapy at the first sign of skin discomfort.

Bulging fontanelles in infants and benign intracranial hypertension in juveniles and adults has been reported. Symptoms include headache, visual disturbances, blurred vision, scotomata, and diplopia. Permanent loss of vision has been reported. If evidence of raised intracranial pressure develops, tetracycline should be discontinued.

Systemic lupus erythematosus can be exacerbated by the use of tetracyclines.

Use with caution in patients with myasthenia gravis. Tetracyclines may increase muscle weakness in these patients.

Absorption of tetracyclines is impaired by milk, antacids containing calcium, magnesium, aluminium, and products containing iron or zinc.

If gastric irritation occurs, the capsules should be taken with food.

4.5 Drug Interactions

- Medicines containing iron, calcium, aluminium, magnesium, bismuth and zinc salts, can affect the activity of this medicine, so it should be given between a gap of 2-3 hours.
- It can prolong the action of anticoagulants like coumarin.
- Concomitant use of tetracyclines and retinoids (acitretin, isotretinoin, tretinoin) can increase the risk of high blood pressure inside the brain.

- If you take this medicine along with methoxyflurane which is used as an anaesthetic, can cause adverse effects to kidney like you may find the presence of nitrogen in urine reports.
- Antidiarrhoeal medicines like kaolin-pectin and bismuth subsalicylate can affect the absorption of this medicine
- Water pills like furosemide can impair with kidney function.
- Antibiotics like penicillin can oppose the action of this medicine.
- You are diabetic then it can increase the effect of antidiabetic medicines like insulin, glimepiride.
- Other medicines are atovaquone to treat pneumonia, antacids like sucralfate, lithium to treat the mental condition, digoxin to treat a heart condition, colestipol and cholestyramine, oral contraceptives, strontium ranelate for osteoporosis, ergotamine and methysergide to treat migraine can affect the absorption of this medicine.
- It can cause adverse effects if used along with methotrexate to treat rheumatoid arthritis.

Interactions with food items

- Avoid dairy products during the treatment.

4.6 Fertility, Pregnancy &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. (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 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 ability to drive and use machines:

Tetracycline Capsule does not affect your ability to drive or to use machinery; however, if you experience side effects like dizziness, you should avoid driving or using machines.

4.8 Adverse 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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization 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.

4.9 Overdose

Symptoms of an overdose may include nausea, vomiting, cloudy urine or blood in the urine. If you think you have taken too much of this medicine contact your doctor immediately or visit the nearest hospital.

5. *PHARMACOLOGICAL PROPERTIES:*

5.1 Pharmacodynamic properties

Salmycin 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.

Mode of Action

Tetracycline acts by inhibiting the synthesis of protein which is essential for bacterial growth. Hence helps in stopping the growth and prevents them from increasing in numbers.

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:

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

6. *PHARMACEUTICAL PARTICULARS*

6.1 List of excipients

Magnesium Stearate, Sodium Lauryl Sulphate, Colloidal Anhydrous Silica

6.2 Incompatibilities

No major incompatibilities are known.

6.3 Shelf Life

36 Months, as packaged for sale.

6.4 Special precautions for storage:

Store in a cool dry place at a temperature not exceeding 25°C.

Protect from light

6.5 Nature and contents of container

The capsules are available in Al/PVC blister packs of 30 capsules enclosed in a carton.
10 capsules per blister.

6.6 Special precautions for disposal and other handling

No precaution required.

7. *APPLICANT*

Name of the Applicant:

SAGAR VITACEUTICALS NIGERIA LIMITED

Business Address:
Plot 6, New Makun City,
Along Lagos/Ibadan expressway,
K/m 53/55 Sagamu.
Ogun State,
NIGERIA

Manufactured by:

SAGAR VITACEUTICALS NIGERIA LIMITED.
Plot 6, New Makun City,
Along Lagos/Ibadan expressway,
K/m 53/55 Sagamu.
Ogun State,
NIGERIA

8. *WHO PREQUALIFICATION REFERENCE NUMBER*
Not applicable

9. *DATE OF PREQUALIFICATION / RENEWAL OF PREQUALIFICATION*
Not applicable

10. *DATE OF REVISION OF THE TEXT*
Not applicable