SCHEDULING STATUS:
S4

PROPRIETARY NAME AND DOSAGE FORM:
BETAROXIME T 250 (Tablets)
BETAROXIME T 500 (Tablets)

COMPOSITION:
BETAROXIME T 250 Tablets
Each **BETAROXIME T 250** tablet contains cefuroxime 250 mg (as cefuroxime axetil).
Sugar free.
Excipients:
Hydrogenated Vegetable Oil, Cellulose, Microcrystalline (Avicel pH 102), Colloidal silicon dioxide (Aerosil 200), Croscarmellose Sodium, Sodium Lauryl Sulfate, Hypromellose, Titanium dioxide, Macrogol 400 (Polyglycol 400).

BETAROXIME T 500 Tablets
Each **BETAROXIME T 500** tablet contains cefuroxime 500 mg (as cefuroxime axetil).
Sugar free.
Excipients:
Hydrogenated Vegetable Oil, Cellulose, Microcrystalline (Avicel pH 102), Colloidal silicon dioxide (Aerosil 200), Croscarmellose Sodium, Sodium Lauryl Sulfate, Hypromellose, Titanium dioxide, Macrogol 400 (Polyglycol 400).

PHARMACOLOGICAL CLASSIFICATION:
A 20.1.1 Broad and medium spectrum antibiotics

PHARMACOLOGICAL ACTION:
Cefuroxime is a bactericidal second-generation cephalosporin. The antibacterial action of cefuroxime results from inhibition of bacterial cell wall synthesis by binding to essential target proteins in bacterial cytoplasmic membranes. Cefuroxime has bactericidal activity against a wide range of bacterial organisms, including beta-lactamase producing strains.

Pharmacokinetics:
Cefuroxime axetil is an oral prodrug of cefuroxime. After oral absorption, cefuroxime axetil is hydrolysed in the intestinal mucosa and blood to release cefuroxime into the plasma. Oral absorption is optimal when administered with food. Peak serum levels of cefuroxime occur approximately 2 to 3 hours after oral dosing, when taken with food. Protein binding is approximately 33 % to 50 %. Cefuroxime is not metabolised and is excreted unchanged in the urine by glomerular filtration and tubular secretion. The elimination half-life is between 1 and 1,5 hours after oral dosing. The elimination half-life is prolonged with renal impairment. Serum levels of cefuroxime are reduced by dialysis.

INDICATIONS:
BETAROXIME T is indicated for the treatment of infections caused by susceptible strains of the following organisms in the following infections: -

- Pharyngitis and tonsillitis caused by *Streptococcus pyogenes.*
- Otitis media caused by *Streptococcus pneumoniae, Haemophilus influenzae* (ampicillin-sensitive and resistant strains), *Moraxella (Branhamella) catarrhalis* and *Streptococcus pyogenes.*
- Sinusitis caused by *Streptococcus pneumoniae* and *Haemophilus influenzae.*
- Acute and chronic bronchitis caused by *Streptococcus pneumoniae, Haemophilus influenzae* (ampicillin-sensitive strains) and *Haemophilus parainfluenzae* (ampicillin-sensitive strains).
- Acute uncomplicated cystitis caused by *Escherichia coli* and *Klebsiella pneumoniae.*
- Lyme disease caused by *Borrelia burgdorferi.*

CONTRA-INDICATIONS:
Hypersensitivity to cephalosporin antibiotics or to any components of the formulation.
Hypersensitivity to penicillin and other beta-lactam antibiotics.

WARNINGS:
BETAROXIME T should be used with caution in patients with:

- A history of gastrointestinal disease, especially ulcerative colitis, regional enteritis or pseudomembranous colitis.
- Renal function impairment – A reduced dose may be required.
- Porphyria: Safety has not been established.

Pseudomembranous colitis may occur. Patients who develop abdominal or stomach cramps, abdominal tenderness, severe and watery diarrhoea (which may be bloody) and fever, should be investigated for this diagnosis. If the diagnosis of pseudomembranous colitis is suspected, **BETAROXIME T** should be stopped immediately and appropriate therapy initiated.

INTERACTIONS:
Concurrent administration of probenecid increases the area under the mean serum concentration time-curve by 50 %.
Interactions with Laboratory Tests:
It is recommended that either glucose oxidase or hexokinase methods be used to determine blood/plasma glucose levels in patients receiving **BETAROXIME T**.
This medicine may give false-negative test results with ferricyanide blood glucose test. **BETAROXIME T** does not interfere in the alkaline picrate assay for creatinine. A false-positive Coombs reaction may appear in patients who receive large doses of **BETAROXIME T**.

PREGNANCY AND LACTATION:
Safety and efficacy in pregnancy and lactation have not been established.

DOSAGE AND DIRECTIONS FOR USE:
Adults:
Sinusitis & acute or chronic bronchitis:
250 mg twice daily for seven days (Range 5-10 days)
Acute, uncomplicated cystitis:
125 mg twice daily for seven days (Range 5-10 days)
Lyme disease:
Adults and children over 12 years of age: 500 mg twice daily for 20 days

Children:
There is no experience with **BETAROXIME T** in children under 3 months of age.

- 3 months to 2 years of age: 125 mg twice daily
- Over 2 years of age: 250 mg twice daily

BETAROXIME T should be taken half an hour after food for optimum absorption.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:
Side Effects:
Blood and lymphatic system disorders:
Common (> 1/100 ≤ 1/10): Eosinophilia
Nervous system disorders:
Common (> 1/100 ≤ 1/10): Headache
Respiratory, thoracic and mediastinal disorders:
The following side effect has been reported and the frequency is unknown: Bronchospasm (see hypersensitivity)
Gastrointestinal disorders:
Common (> 1/100 ≤ 1/10): Nausea, diarrhoea, abdominal pain
Uncommon (> 1/1 000 ≤ 1/100): Vomiting
Rare (> 1/10 000 ≤ 1/1 000): Severe and watery diarrhoea, in some cases accompanied by blood in stools, which may be a symptom of enterocolitis. A particular form of enterocolitis is pseudomembranous colitis (see **"Warnings"** and "**Special Precautions"**).
Hepato-biliary disorders:
Common (> 1/100 ≤ 1/10): Transient increases in hepatic enzyme levels
Skin and subcutaneous tissue disorders:
Uncommon (> 1/1 000 ≤ 1/100): Skin rashes (see hypersensitivity)
Rare (> 1/10 000 ≤ 1/1 000): Urticaria, pruritus (see hypersensitivity)
Very rare (≤ 1/10 000): Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis
Reproductive system and breast disorders:
The following side effect has been reported and the frequency is unknown: Vaginal candidiasis
General disorders and administration site conditions:
Hypersensitivity reactions including:
Uncommon (> 1/1 000 ≤ 1/100): Skin rashes
Rare (> 1/10 000 ≤ 1/1 000): Urticaria, pruritus
Very rare (≤ 1/10 000): Drug fever, serum sickness, anaphylaxis
The following side effect has been reported and the frequency is unknown: Bronchospasm
Special precautions:
Prolonged use of **BETAROXIME T** may result in the overgrowth of non-susceptible organisms (e.g. Candida, Enterococci or *Clostridium difficile*). Pseudomembranous colitis has been reported with the use of **BETAROXIME T**. Patients who develop abdominal or stomach cramps, abdominal tenderness, severe and watery diarrhoea (which may be bloody) and fever should be investigated for this diagnosis. The Jarisch-Herxheimer reaction has been reported following treatment with **BETAROXIME T** for Lyme disease. This reaction is a common and usually self-limiting consequence of antibiotic treatment for Lyme disease.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT
(See **"Side Effects And Special Precautions"**)

Symptoms of overdose:
Seizures have been reported.

Treatment of overdose:
Treatment is symptomatic and supportive. Serum levels of **BETAROXIME T** can be reduced by haemodialysis or peritoneal dialysis.

IDENTIFICATION:

BETAROXIME T 250:
A white to off white, film-coated, capsule shaped tablet, with “A33” debossed on one side and plain on the other side.
BETAROXIME T 500:
A white to off white, film-coated, capsule shaped tablet, with “A34” debossed on one side and plain on the other side.

PRESENTATION:
BETAROXIME T 250:
10’s: Printed unit carton containing 1 blister pack (composed of either clear PVC / Aclar and silver coloured aluminium foil backing or silver coloured cold form laminate and silver coloured aluminium foil backing) of 10 tablets each.
BETAROXIME T 500:
10’s: Printed unit carton containing 1 blister pack (composed of either clear PVC / Aclar and silver coloured aluminium foil backing or silver coloured cold form laminate and silver coloured aluminium foil backing) of 10 tablets each.

STORAGE:
Store in a cool (at or below 30°C), dry place. Protect from moisture.
STORE BETAROXIME T TABLETS OUT OF REACH OF CHILDREN.
The blister should not be removed from the carton until required for use.

REGISTRATION NUMBER:
BETAROXIME T 250: 41/20.1.1/0138
BETAROXIME T 500: 41/20.1.1/0139

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION
UNICORN PHARMACEUTICALS (PTY) LTD
CORNER OF SEARLE & PONTAC STREETS
CAPE TOWN
SOUTH AFRICA

DATE OF PUBLICATION OF THIS PACKAGE INSERT.
To be allocated

DATE ON THE REGISTRATION CERTIFICATE OF THE MEDICINE
5 OCTOBER 2007