SWISS PHARMA

Module 1- Administrative information and prescribing information

1.3 Product Information

1.3.1 Summary of Product Characteristics (SmPC)

Enclosed

CLARIMAX 500 (CLARITHROMYCIN TABLETS USP 500 MG)

1.3.1 Summary Product Characteristics (SPC)

1 NAME OF THE MEDICINAL PRODUCT

CLARIMAX 500 (Clarithromycin Tablets USP 500 mg), 500 mg per Tablets, Film coated Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Film coated tablet contains
Clarithromycin USP 500 mg
Excipients Q.S.
Approved colour used

Kindly refer section 6.1 for full list of Excipients.

3 PHARMACEUTICAL FORM

Film coated tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Clarimax is indicated for the treatment of the following mild to moderate severe infections caused by susceptible organisms:

- Lower respiratory tract infections such as bronchitis and pneumonia.
- Upper respiratory tract infections such as pharyngitis and sinusitis.
- Mild to moderately severe acute otitis media due to S. pneumoniae, M. catarrhalis and H. influenza.
- Skin and soft tissue infections such as folliculitis, cellulitis or erysipelas.
- Eradication of helicobacter pylori when used in combination with a proton pump inhibitor and another antibiotic to decrease recurrence of duodenal ulcer.

4.2 Posology and method of administration

Adults: 250 mg twice daily. In more severe infections, the dosage may be increased to 500 mg twice daily.
Renal impairment: Creatinine clearance (<30ml/min): reduce dose by half i.e 250 mg once daily or 250 mg twice daily for severe infections. Limit the duration of treatment to 14 days
Eradication of H.pylori: Adults: 500 mg twice daily, in combination with an appropriate antibiotic and acid lowering agent, for 7 to 10 days. The safety & efficacy of CLARIMAX in combination with proton pump inhibitor other than omeprazole has not been established.
Atypical mycobacterial infections (MAC) in HIV patients:
Adults: 500 mg twice daily treatment of disseminated MAC infections in AIDS patients should continue as long as clinical and microbiological benefit is demonstrated. A decrease in efficacy has been noted in patients taking CLARIMAX for more than 12 weeks. CLARIMAX should be

used in conjunction with other antimycobacterial agents. CLARIMAX may be taken with or without meals.

4.3 Contraindications

Hypersensitivity to macrolide antibiotics or to any component of the formulation.
Concomitant administration of CLARIMAX with astemizole, cisapride, pimozide and terfenadine.

4.4 Special warnings and precautions for use

CLARIMAX should be used with caution:
Liver function impairment- the pharmacokinetics are altered. No dosage adjustment is required in patients with hepatic function impairment, unless there is also concurrent severe renal function impairment.
Renal function impairment (severe)- the elimination of clarimax is reduced in patients with renal function impairment. Especially those with a creatinine clearance of <30ml/min. The dose of CLARIMAX should be halved or the dosing interval doubled in patients with a creatinine clearance of <30ml/min.
Rhabdomyolysis has been reported with concomitant use of CLARIMAX and the HMG-CoA reductase inhibitors e.g. simvastatin.
Rifabutin and rifampicin-may decrease serum concentration of CLARIMAX by >50%. Co-Administration Has Been Reported to Cause A Higher Incidence of Uveitis Compared To Rifabutin alone.
Theophylline- the area under the plasma concentration time curve is increased. Monitoring of theophylline serum concentrations recommended.
Cross-resistance between CLARIMAX and other macrolides, lincomycin and clindamycin have been reported.
SPECIAL PRECUATIONS:
Treatment with clarimax should be discontinued if any signs of hepatic dysfunction develop. Hepatic dysfunction is usually reversible, but may be severe, In rare instances, hepatic failure with fatal out come has been reported, usually associated with other serious underlying diseases and/or concomitant medicines. Isolated cases of increased serum creatinine have been reported, but an associated with clarimax has not been established.
There have been less frequent reports of hypoglycaemia some of which occurred in patients on concomitant oral hypoglycaemics or insulin. Adverse effects in immunocompromised patients treated with higher doses of clarimax over long periods include nausea, vomiting, taste perversion, abdominal pain, diarrhoea, rash, headache, hearing disturbance, AST and ALT elevations, elevated BUN levels and abnormally low white blood cell and platelet counts. Additional low- frequency events included dyspnoea, insomnia and dry mouth.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of clarimax with:

- Astemizole, cisapride, pimozide and terfenadine- has resulted in cardiac arrhythmias, including Qtc- interval prolongation, ventricular arrhythmia, ventricular tachycardia, ventricular fibrillation and torsade de pointes. Fatallities have occurred. The most likely

cause is the inhibition of metabolism of these medicines by clarimax . concurrent use is contra- indicated.

- Anticoagulants such as warfarin- clarimax may result in the potentiation of the effect of warfarin. Prothrombin time should be monitored closely.
- Digoxin- clarimax has been shown to increase serum digoxin concentration. Monitoring of digoxin serum concentration is recommended.
- Carbamazepine or other medicines metabolised by the cytochrome P450 enzymes system for example, alprazolam, cyclosporine, disopyramide, ergot alkaloids, methylprednisolone, midazolam, omeprazole, quinidine, sildenafil, simvastatin, tacrolimus, triazolam, vinblastine, phenytoin and vroate-clarimax may be associated with increased levels of these medicines. Seum concentration of these medicines may require monitoring. Rhabdomyolysis has been reported with concomitant use of clarimax and HMGCoA reductase inhibitors e.g. simvastatin.
- Rifabutin & Rifampicin- May decreases serum concentration of clarimax > 50% Co-administration has been reported to cause a higher incidence of uveitis compared to rifabutin alone.
- Theophylline- the area under the plasma concentration time curve is increased, monitoring of theophylline serum concentration is recommended.
- Zidovudine- A decrease in the steady state concentration of zidovudine may occur. Doses of zidovudine and clarimax should be taken at least 4 hour apart.
- Retonavir- The metabolism of clarimax is inhibited. No dosage reduction of clarimax is needed in patients with normal renal function. Patients with renal function impairment require a reduction in the dosage of clarimax as follows:
- Creatinine clearance 30 to 60 ml/min-reduce dose by 50%
- Creatinine clearance <30 ml/min-reduce dose by 75%
- Do not exceed a dose of 1 g/day during concurrent administration of clarimax with ritonavir.
- Inhibitors and non- nucleosides reverse transcriptase inhibitors may have a similar effect on Clarimax.

4.6 Pregnancy and lactation

Safety and efficacy in pregnancy and lactation have not been established. CLARIMAX is excreted in the breast milk.

4.7 Effects on ability to drive and use machines

There are no data on the effect of clarithromycin on the ability to drive or use machines. The potential for dizziness, vertigo, confusion and disorientation, which may occur with the medication, should be taken into account before patients drive or use machines.

4.8 Undesirable effects

Haematological: less frequent; leucopenia, thrombocytopenia
Endocrine/metabolic: Less frequent: Hypoglycaemia.
Nervous system: headache, anxiety, dizziness, insomnia, hallucinations, bad dreams, vertigo, tinnitus, disorientation, Depersonalization, confusion, hearing loss, convulsions.

Cardiovascular: QT prolongation, ventricular tachycardia, torsadesde pointes.
Gastro- intestinal: frequent: nausea, vomiting, abdominal pain, abnormal taste, diarrhoea.
Less frequent: Glossitis, stomatitis, oral candidiasis, tongue discolouration, tooth discolouration, pseudomembranous colitis.
Liver: less frequent: increase in liver enzymes, hepatocellular and /or cholestatic hepatitis, pancreatitis.
Skin: mild skin eruptions, urticaria, steven's- Johnson syndrome, toxic epidermal necrolysis.
Other: Allergic reactions, anaphylaxis.
Special precautions:
Treatment with CLARIMAX should be discontinued if any signs of hepatic dysfunction develop. Hepatic dysfunction is usually reversible but may be sever. In rare instances, hepatic failure with fatal outcome has been reported, usually associated with other serious underlying diseases and/or concomitant medicines. Isolated cases of increased serum creatinine have been reported, but an association with CLARIMAX has not been established.
There have been less frequent reports of hypoglycaemia, some of which occurred in patients on concomitant oral hypoglycaemics or insulin. Adverse effects in immunocompromised patients treated with higher doses of CLARIMAX over long periods include nausea, vomiting taste perversion, abdominal pain, diarrhoea, rash, flatulence, headache, hearing disturbance, AST and ALT elevations, elevated BUN levels and abnormally low white blood cell and platelet counts. Additional low- frequency events included dyspnoea, insomnia and dry mouth.

4.9 Overdose

Symptoms of overdose

Ingestion of large amounts of CLARIMAX can be expected to produce gastro- intestinal symptoms. Allergic reactions accompanying overdosage should be treated by the prompt elimination of un absorbed medicine and supportive measures.

Treatment of Overdose

Treatment is symptomatic and supportive. CLARIMAX is not expected to be appreciably affected by hemodialysis or dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Macrolides ATC Code: J01FA09
Clarithromycin is a macrolide antibiotic. It exerts its antibacterial action by binding reversibly to the 50S ribosomal sub unit of the 70S ribosome of sensitive microorganisms, there by inhibiting bacterial RNA- dependant protein synthesis. The In vitro antibacterial spectrum of pathogen sensitive to clarithromycin includes:
Streptococcus agalactiae, streptococcus pyogenes, streptococcus pneumoniae, legionella pneumophilla
Mycoplasma pneumoniae
Chiamydia trachomatis
Moraxella catarrhais
Haemophillus influenza
Straphylococcus aureus

Helicobacterpylori
Mycobacterium avium, mycobacterium kansasii, mycobacterium cheionae, mycobacterium intracellular

5.2 Pharmacokinetic properties

Clarithromycin is absorbed rapidly from the gastro-intestinal tract after oral administration, but its bioavailability is reduced to 50% to 55% because of rapid first-pass metabolism. Peak plasma concentration occurs approximately 2 hours after administration. Clarithromycin may be given with or without food. Clarithromycin is metabolised by the liver t othe active metabolite. 14-hydroxyclarithromycin, as well as to several other metabolites. Both clarithromycin and 14- hydroxy-clarithromycin distribute widely throughout the body and achieve high intracellular concentration. Tissue concentration generally exceed serum concentration. Clarithromycin does not achieve significant levels in the cerebrospinal fluid. Protein binding of clarithromycin ranges from 40 to 70% and is concentration dependent. The elimination half lives of clarithromycin and 14 hydroxy clarithromycin are approximately 3 to 7 and 5 to 9 hours respectively. Longer half lives are observed after large doses. Clarithromycin is eliminated by renal and non-Renal routes. The amount of clarithromycin excreted unchanged in the urine ranges from 20% to 40%, depending on the dose administered and the formulation. Between 10 and 15% of the dose is excreted in the urine as the 14- hydroxy metabolite.
Although the pharmacokinetics of clarithromycin are altered in patients with hepatic or renal dysfunction, dosage adjustment is not necessary unless a patient has sever renal dysfunction. At higher doses in HIV infected patient's clarithromycin and 14- hydroxy-clarithromycin concentrations are much higher when compared with doses in non- infected patients. The elimination half-lives also appear to be length ended.

5.3 Preclinical safety data

No inhouse preclinical safety data has been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Starch
Microcrystalline cellulose Phosphate
Polyvinyl pyrrolidone
Magnesium stearate
Purified talc
Cross Carmellose sodium
Colloidal anhydrous silica
Hydroxy propyl methyl cellulose
Polyethylene Glycol 4000
Titanium dioxide

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store in a dark, dry place, Not exceeding 30°C temp.
keep out of the reach and sight of children.

6.5 Nature and contents of container <an special equipment for use, administration or implantation>

10 tablets are packed in one blister pack. Such 1 blister pack is packed in Carton along with Insert.

6.6 Special precautions for disposal and other handling

No special requirements.

7. APPLICANT/ MANUFACTURER

APPLICANT:

M/s. FECCOX PHARMACY & GEN ENT LTD.
No.1A, Airport road, Op. Ahmadiyya junction,
Kano, Nigeria

MANUFACTURED BY:

SWISS PHARMA PVT. LTD.
3709, G.I.D.C. Phase IV, Vatva,
City: Ahmedabad –382445, Dist.: Ahmedabad
Gujarat State, India
www.swisspharma.in
Telephone No. (079) 2584 2852, 2584 1418.
Email: exports@swisspharma.in