SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

RETCIN / Erythromycin 250 mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Erythromycin Ph. Eur. 274.00 mg

3 PHARMACEUTICAL FORM

Enteric-coated tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the prophylaxis and treatment of infections caused by Erythromycin-sensitive organisms.

1. Upper and lower respiratory tract infections.
2. Soft tissue and skin infections.
3. Bone infections.
4. Oral and dental infection.
5. Gastro-intestinal infections.
6. Eye infections.
7. Sexually transmitted diseases.
8. Prophylaxis.
9. Microbiological indications. Erythromycin is active against staphylococci, streptococci, haemophilus influenzae, L-forms, mycoplasma pneumoniae, legionella pneumophila, branhamella catarrhalis, bordetella pertussis, corynebacterium diphtheriae, neisseria, treponema pallidum, chlamydia trachomatis, clostridia, ureaplasma urealytica, campylobacter. In the case of corynebacterium diphtheriae should be used as an adjunct to antitoxin.

4.2 Posology and method of administration

Adults and children over 8 years: 1-2 g daily in divided doses for mild to moderate infection. This dosage may be increased to 4 g daily in divided doses. Tablets should be taken before or with meals.

Elderly: No special dosage recommendations.

Period of dosing with regard to indications:

Upper respiratory tract infections: 5 to 10 days

Lower respiratory tract infections: 7 to 14 days or until the signs and symptoms indicate that the condition is cured. Legionnaire's Disease requires prolonged treatment. It is recommended that initially Erythromycin lactobionate intravenously should be administered.

Skin and soft tissue infections: 5 to 10 days. Acne may require prolonged treatment.

Sexually transmitted diseases - NGU and syphilis: 10 to 21 days. Some conditions may require prolonged treatment.

Oral and dental infections: at least 5 days.

Eye infections - Chlamydia inclusion conjunctivitis: 3 weeks.

Gastro-intestinal infections - Campylobacter: a minimum of 5 days.

RETCIN is taken by mouth.

4.3 Contraindications

RETCIN is contraindicated in patients sensitive to Erythromycin. Use of RETCIN in conjunction with other anti-infection agents except when especially warranted.
Erythromycin is contraindicated with either Astemizole or Terfenadine and is also contra-indicated with ergotamine and di-hydroergotamine.

Concomitant administration of erythromycin and lomitapide is contraindicated (see section 4.5).

4.4 Special warnings and precautions for use

Caution should be exercised when administering RETCIN to patients with impaired hepatic function as the drug is principally excreted by the liver. Super infection caused by non-susceptible bacteria or fungi may occur during prolonged or repeated therapy and this is more likely when other anti-bacterial agents are simultaneously employed.

Hepatic dysfunction including increased liver enzymes and/or cholestatic hepatitis, with or without jaundice, has been infrequently reported with erythromycin.

Renal impairment. Prolongation of QT interval (ventricular tachycardia reported). Porphyria.

As with other macrolides, rare serious allergic reactions, including acute generalised exanthematous pustulosis (AGEP) have been reported. If an allergic reaction occurs, the drug should be discontinued and appropriate therapy should be instituted. Physicians should be aware that reappearance of the allergic symptoms may occur when symptomatic therapy is discontinued.

Carefully consider the balance of benefits and risks before prescribing erythromycin for any patients taking hydroxychloroquine or chloroquine, because of the potential for an increased risk of cardiovascular events and cardiovascular mortality (see section 4.5).

RETCIN contains lactose and is unsuitable for people with lactase insufficiency, galactosaemia or glucose/galactose malabsorption syndrome. The product also contains ponceau 4R (E124) which may cause allergic-type reactions including asthma. Allergy is more common in those people who are allergic to aspirin.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of Erythromycin with terfenadine or astemizole is likely to result in an enhanced risk of cardiotoxicity with these drugs. The concomitant use of Erythromycin with either astemizole or terfenadine is therefore contraindicated. There is also an increased risk of ventricular arrhythmias when erythromycin is given with cisapride, pimozide or sertindole. Concomitant use should be avoided. Note, there is a similar risk with amiodarone, amisulpride, moxifloxacin or quinidine when given with parenteral erythromycin.

Concurrent use of erythromycin with ergotamine or di-hydroergotamine has been associated in some patients with acute ergotoxicity with the rapid development of severe peripheral vasospasm and dysethesia.

The anticoagulant effect of coumarins may be increased by erythromycin.

With the following drugs an increase in serum concentration and/or inhibition of their metabolism may occur when they are administered concurrently with erythromycin: acenocoumarol, alfentanil, astemizole, bromocriptine, buspirone, carbamazepine, cabergoline, ciclosporin, corticosteroids, digoxin, disopyramide, eletriptan, eplerenone, galantamine, immuno-suppressants (e.g.

sirolimus, tacrolimus), methylprednisolone, midazolam, phenytoin, sildenafil, terfenadine, triazolam, valproate, vardenafil, warfarin, zopiclone and possibly clozapine, felodipine, rifabutin, tadalafil and loratidine. Also avoid concomitant use of mizolastine and cilostazol.

Monitoring should be undertaken and dosage adjusted accordingly. Plasma concentration of erythromycin may be increased by ritonavir and amprenavir. Cimetidine increases plasma-erythromycin concentration and increases risk of toxicity including deafness.

Erythromycin increases the toxicity of vinblastine therefore avoid concomitant use.

Concurrent administration of Theophylline with oral erythromycin produces a significant decrease in erythromycin serum concentration, which could result in sub-therapeutic concentrations of erythromycin.

Plasma concentration of rosuvastatin and zafirlukast is reduced by erythromycin.

Increased risk of myopathy with simvastatin and possibly atorvastatin, therefore avoid concomitant use.

Avoid concomitant use with lercanidipine, reboxitine and tolterodine.

Concomitant administration of erythromycin with lomitapide is contraindicated due the potential for markedly increased transaminases (see section 4.3).

Hydroxychloroquine and chloroquine: Erythromycin should be used with caution in patients receiving these medicines known to prolong the QT interval due to the potential to induce cardiac arrhythmia and serious adverse cardiovascular events.
Corticosteroids: Caution should be exercised in concomitant use of erythromycin with systemic and inhaled corticosteroids that are primarily metabolised by CYP3A due to the potential for increased systemic exposure to corticosteroids. If concomitant use occurs, patients should be closely monitored for systemic corticosteroid undesirable effects.

4.6 Pregnancy and lactation

The available epidemiological studies on the risk of major congenital malformations with use of macrolides including erythromycin during pregnancy provide conflicting results. Some observational studies in humans have reported cardiovascular malformations after exposure to medicinal products containing erythromycin during early pregnancy.

It has been in wide use for many years without apparent ill consequence. Animal studies have reported no risk.

There is a large amount of data from observational studies performed in several countries on exposure to erythromycin during pregnancy, compared to no antibiotic use or use of another antibiotic during the same period (>24,000 first trimester exposures). While most studies do not suggest an association with adverse fetal effects such as major congenital malformations, cardiovascular malformations or miscarriage, there is limited epidemiological evidence of a small increased risk of major congenital malformations, specifically cardiovascular malformations following first trimester exposure to erythromycin.

Erythromycin has been reported to cross the placental barrier in humans, but foetal plasma levels are generally low.

There have been reports that maternal macrolide antibiotics exposure within 10 weeks of delivery may be associated with a higher risk of infantile hypertrophic pyloric stenosis (IHPS).

Therefore, erythromycin should only be used during pregnancy if clinically needed and the benefit of treatment is expected to outweigh any small increased risks which may exist.

Erythromycin is excreted in breast milk, therefore caution should be exercised when erythromycin is administered to a breast-feeding patient.

4.7 Effects on ability to drive and use machines

Not applicable

4.8 Undesirable effects

Allergic reactions are rare and mild but anaphylaxis has occurred. Skin reactions ranging from mild eruptions to erythema multiforme, Stevens-Johnson syndrome and

toxic epidermal necrolysis have rarely been reported. Occasionally nausea, abdominal discomfort, diarrhoea and vomiting which subside after a few days without having to discontinue treatment.

As with other broad-spectrum antibiotics, pseudomembranous colitis has been reported rarely with erythromycin.

Reversible hearing loss associated with doses of erythromycin usually greater then 4 g per day has been reported.

Symptoms of hepatitis, hepatic dysfunction and/or abnormal liver function test results may occur.

Cardiac effects (including chest pain and arrhythmias) and myasthenia-like syndrome have also been reported.

Skin and subcutaneous tissue disorders
Not known: acute generalised exanthematous pustulosis (AGEP)

4.9 Overdose

Gastric lavage and supportive measures.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The action of Erythromycin is bacteriostatic or bactericidal, depending on the organism and the concentration achieved. The effects of Erythromycin in combination with other antibiotics are unpredictable. The synthesis of penicillinase is variably affected, resulting in synergy where antagonism with susceptible beta-lactams. The listericidal effects of penicillins, rifampicin and gentamycin are antagonised. Erythromycin is synergistic with sulphonamides against *H.influenzae*.

5.2 Pharmacokinetic properties

Erythromycin binding to plasma is 73% for the base. The drug is distributed within an apparent volume of 0.75 l./kg. and eliminated with a half-time of 1 to 1.5 hours. Erythromycin is inactivated by N-demethylation in the liver, but the concentration of active drug in the bile is high and there is evidence of entero-hepatic circulation.

The drug passes the placental barrier to reach concentrations in foetal plasma of 5-20% of those in the maternal circulation.

Erythromycin is distributed to most sites, except brain and CSF.

Erythromycin base is concentrated within alvolar macrophages by active transport to a concentration of 20-30 times that in the plasma. The drug is also concentrated in polymorphonuclear leucocytes.

Erythromycin is inactivated by N-demethylation in the liver. From 5 to 10% of the dose is excreted unchanged in the urine.

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize starch
Potato starch
Sodium starch glycollate
Magnesium stearate

Cellacephate
Diethylphthalate
Aluminium lake E124,
approx. 20% dye content
Carnauba wax
Beeswax

6.2 Incompatibilities

None known

6.3 Shelf life

36 months

6.4 Special precautions for storage

Keep container tightly closed. Protect from light. Store below 25°C in a dry place.

6.5 Nature and contents of container

High density polystyrene or polypropylene containers with polythene or polypropylene lids and polyurethane/polythene inserts

Pack sizes: 28, 30, 50, 56, 60, 84, 100, 250, 500, 1000.

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Chelonia Healthcare Limited
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8 MARKETING AUTHORISATION NUMBER(S)

PL 33414/0045

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

02/03/2006

10 DATE OF REVISION OF THE TEXT

05/06/2023