**Winthrop**

**Roxithromycin**

150 mg Tablet

**Antibacterial**

**Formulation:** Each Tablet contains:
Roxithromycin 150 mg

**Indications:**
Roxithromycin is a semisynthetic macrolide antibiotic with the following spectrum of activity:
- Strains usually sensitive (MIC < 1 mg/L):
  - More than 95% of the strains are sensitive ("S")
  - Streptococcus spp., methicillin Staphylococcus, Rhodococcus equi
  - Moraxella spp., Bordetella pertussis, Helicobacter pylori, Campylobacter jejuni
  - Corynebacterium diphtheriae
  - Mycoplasma pneumoniae, Coxiella, Chlamydiae, Legionella
  - Treponema pallidum, Borrelia burgdorferi, Leptospira
  - Propionibacterium acne, Actinomyces, Eubacterium, Porphyromonas, Mobiluncus

**Intermediate sensitive strains:**
- The antibiotic is weakly active in vitro. Some successful clinical results have been recorded if the antibiotic level on the infection site is more than the MIC.
  - Haemophilus influenzae and parainfluenzae, Neisseria, gonorrhoeae, Vibo
  - Ureaplasma urealyticum

**Resistant strains (MIC > 4 mg/L):**
- At least 50% of the strains are resistant ("R")
  - methicillin R staphylococcus, Enterobacteriaceae, Pseudomonas spp.
  - Acinetobacter spp.
  - Mycoplasma hominis, Nocardia
  - Fuebacetrium, Bacteroides fragilis

**Variable sensitive strains:**
- The percentage of acquired resistance is variable and the sensitivity is therefore impossible to forecast. An antibiogram is necessary.
- Streptococcus pneumoniae, Enterococci, Campylobacter coli
- Peptostreptococcus, Clostridium perfringens

Roxithromycin has in vitro and in vivo activity on Toxoplasmia gondii.
Roxithromycin has moderate in vitro activity on Mycobacterium avium.

**N.B.:** Some bacterial species are not listed above in absence of clinical indications. Roxithromycin is indicated in the treatment of infections caused or likely caused by roxithromycin sensitive organisms at the following sites:
- Upper respiratory tract infections, e.g. acute pharyngitis, tonsillitis and sinusitis.
- Lower respiratory tract infections, e.g. pneumonia, bronchitis, bacterial infections of chronic airway disease, atypical pneumonia.
- Skin and soft tissue infections, e.g. boils, abscesses and wound infections.
- Additional indication for adults: Non-gonococcal genito-urinary tract infections, e.g., urethritis and cervico-vaginitis.

**Dosage and Administration:**

**Adults:**
- One 150 mg tablet twice daily at 12-hour interval or two 150 mg tablets once a day. Severe hepatic impairment: The dose should be reduced to one 150 mg tablet per day. Roxithromycin should be preferably taken before meals. Duration of treatment depends on the therapeutic indication, on the causative organism and on the clinical picture.

**Pediatrics:**
- The dosage to be used is 5 to 8 mg/Kg/day by the oral route in 2 divided doses. Thus, depending on the child’s weight:
  - For children 24 to 40 Kg: one 100 mg tablet twice daily at 12-hour interval
  - Above 40 Kg: one 150 mg tablet twice a day at 12-hour interval
- Tablet forms should not be used in children under four (4) years of age.
- Roxithromycin should be preferably taken before meals. Treatment must not be prolonged beyond ten (10) days. Duration of treatment depends on the therapeutic indication, on the causative organism and on the clinical picture.

**Contraindications:**

- Hypersensitivity to macrolide antibiotics
- Concomitant therapy with vasoconstrictive ergot alkaloids (see interactions section)
- Association with cisapide (see interactions section)
- Relative contraindication: Association with bromocriptine (see interactions section)

**Precautions:**

- Roxithromycin is not recommended in patients with severe hepatic insufficiency, e.g., hepatic jaundice and/or ascites. If therapy is necessary, the dose of Roxithromycin should be limited to a single 150 mg tablet per day with concomitant surveillance of hepatic function.
- As renal excretion of roxithromycin and its metabolites is minor (approximately 10% of an oral dose), the dosage regimen should be kept unchanged in case of renal insufficiency.
- Plasma half life in elderly subjects is prolonged. Nevertheless, after repeated doses of 150 mg every 12 hours, plasma concentration and area under the curve are identical in young and elderly subjects. Thus, it is not necessary to modify the dosage regimen.

For pediatrics:
At unbound plasma concentrations 30 to 60 times higher than those seen in clinical use abnormalities of the growth plate were observed in young animals. No abnormalities were observed at unbound plasma concentrations 10 to 15 times higher than those seen in clinical use.

**Interactions:**

**Associations contraindicated:**
- Vasodilatatory ergot alkaloids (oral and nasal route).
- As other macrolides, roxithromycin and josamycine, ergotism with possible necrosis of extremities (decreased hepatic clearance of ergot alkaloids) has been reported.
- Cimetidine
- Macrolides decrease the hepatic metabolism of cisapride which can result in increased risk of ventricular arrhythmias, especially torsades de pointes.

**Associations not recommended:**
- Terfenadine
- Caution should be exercised if Roxithromycin is co-prescribed with terfenadine because certain macrolides can elevate plasma concentrations of the latter, which can result in severe ventricular arrhythmias such as torsades de pointes.
- Bromocriptine
- As with other macrolides, erythromycin and josamycin, the possibility of increased plasma levels of bromocriptine exists and thus increased antiparkinsonian activity or occurrence of signs of overdosage.

**Associations requiring precautions for use:**
- Warfarin
- No interaction with warfarin was found in volunteer studies; however, increased activity of prothrombin time which may be explained by the infectious episode have been reported in patients treated with roxithromycin and vitamin K antagonists.
- Disopyramide
- As in vitro study has shown that Roxithromycin can displace protein bound disopyramide, such an effect in vivo may result in increased serum levels of free disopyramide. Consequently, ECG and, if possible disopyramide serum levels should be monitored.
- Digoxin
- Roxithromycin may increase absorption of digoxin. Consequently, ECG and possible digoxin serum levels should be monitored.
- Ciclosporin
- Possible increased plasma levels of ciclosporine and possible creatinemia may occur due to the inhibition of hepatic metabolism of ciclosporine.

**Associations to be taken into account:**
- Theophylline (base and salts) and aminophylline
- Possible increased plasma levels of theophylline, particularly in children, may occur.
- Midazolam
- The effects of midazolam may be enhanced and prolonged by Roxithromycin.

**Use in pregnancy and lactation:**
Studies in several animal species have not shown any teratogenic or fetal effect of Roxithromycin dosed at up to 40 times the human therapeutic dose. However, the safety of Roxithromycin in human pregnancy has not been established. As with all medicines, use should be avoided in pregnancy, especially during the first trimester, unless considered essential by the physician.
Small amounts of Roxithromycin have been detected in human breast milk. Breast feeding should therefore be avoided.

**Side effects:**
- Gastrointestinal symptoms: nausea, vomiting, epigastric pain, diarrhoea, very rarely bloody
- In isolated cases, symptoms of pancreatitis have been observed, most patients have received other drugs for which pancreatitis is a known adverse reaction
- Hypersensitivity reactions (as with antibiotic macrolides) such as rash, urticaria, angioneurotic edema; exceptionally purpura, bronchospasm, anaphylactic shock
- Diarrhoea, headache, paresthesia
- Moderate increases in transaminases ASAT-ALAT and/or alkaline phosphatase, Cholestatic or more rarely, hepatocellular acute hepatitis.
- Macrolide antibiotics may affect taste and/or smell
- Superinfections; As with other antibiotics, the use of roxithromycin, especially if prolonged, may result in overgrowth of non-susceptible organisms. Repeated, evaluation of the patient’s condition is essential. If superinfection occurs during therapy, appropriate measures should be taken.

**Overdose:**
No specific antidote is known. Carry out gastric lavage and symptomatic treatment if overdose occurs.

**Storage conditions:**
Store at temperatures not exceeding 30°C.

**Presentations:**
- Roxithromycin 150 mg adult tablets: blisters of 10’s, boxes of 30’s.
- Also available: Roxithromycin 300 mg tablets: blisters of 10’s, boxes of 30’s.

**Caution:**
- Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

**Manufactured by:**
- PT Aventis Pharma
- Jl. Jend. A. Yani, Pulo Mas, Jakarta, Indonesia

**Imported by:**
- Sharp Pasteur Inc.
- 4/F Feliiza Bldg., 108 V. A. Rufino St., Legaspi Village, 1229 Makati City
**Roxithromycin**

300 mg Tablet

**Antibacterial**

**FORMULATION:** Each Tablet contains:

Roxithromycin ........................................ 300 mg

**MECHANISM OF ACTION:**

Roxithromycin is a semi-synthetic acid-stable 14-membered macrolide with an extended oxime side-chain which confers improved pharmacokinetic properties on the compound compared to other macrolides. Roxithromycin binds to the 50 S subunit of the bacterial ribosome thus inhibiting protein synthesis. It penetrates intracellularly and is highly concentrated in polymorphonuclear leucocytes and macrophages, achieving intracellular concentrations greater than those outside the cell. Roxithromycin enhances the adhesive and chemotactic function of polymorphonuclear neutrophils. In the presence of infection, this leads to phagocytosis and lysis of bacteria.

**PHARMACOLOGY**

Mean plasma concentrations of 6.6 to 7.9 mg/L and 9.1 to 10.8 mg/L were reached within 2 hours following administration of a single oral dose of 150 mg or 300 mg Roxithromycin, respectively to healthy adults. No drug accumulation was seen following a multiple-dose administration of 150 mg Roxithromycin twice daily for up to 11 days in healthy volunteers. Administration of Roxithromycin 150 mg before a meal had little effect on maximum plasma concentrations and bioavailability.

Roxithromycin is strongly, specifically and saturably bound to alpha 1-acid glycoprotein in plasma. It is extensively distributed throughout tissue and body fluids with high corresponding plasma concentrations and greater than MIC values for susceptible bacteria. In urine and feces, 50% and 55% of recovered drug, respectively, appeared as unchanged Roxithromycin: 25% and 22%, respectively as the desacelalidose derivative, and 5% and 7%, respectively as the demethylated derivative, with only unchanged Roxithromycin detected in plasma. The elimination half-life of Roxithromycin following administration of 150 and 300 mg doses ranged from 8.4 to 15.5 hours.

Dosage adjustment is not required in the elderly or in patients with renal impairment.

**INDICATIONS:**

Roxithromycin is indicated for the treatment of infections of the respiratory tract, genitourinary tract, ear, nose and throat, and skin and soft tissue due to susceptible organisms.

**DOSEAGE AND ADMINISTRATION:**

Adult Dose: Oral 300 mg once daily at least 15 to 30 minutes before meals.

**CONTRAINDICATIONS:**

Allergy to other macrolides.

Concomitant therapy with ergot alkaloid vasocostrictors such as ergotamine and dihydroergotamine.

Concomitant therapy with cisapride and terfenadine. Patients with severe hepatic insufficiency.

**PRECAUTIONS:**

Liver problems

Pregnancy and lactation.

**ADVERSE EFFECTS:**

Clinically significant adverse effects are uncommon with Roxithromycin.

The following have been reported:

Gastrointestinal disturbances such as nausea, abdominal pain and diarrhea may sometimes occur.

Allergic mucocutaneous reactions.

Dizziness, headache and paresthesia.

Moderate increase of liver enzymes.

Rarely, bronchospasm.

**DRUG INTERACTIONS:**

There is no clinical or significant interaction with carbamazepine, ranitidine, aluminum or magnesium hydroxide oral contraceptives containing estrogen and progestagens.

In healthy volunteers, a slight increase in plasma concentrations of cyclosporine and theophylline levels which do not necessitate to alter the usual dosage, has been shown.

An in vitro study has shown that Roxithromycin can displace protein-bound disopyramide; such an effect could result in vivo in increased serum levels of free disopyramide.

Roxithromycin may increase the absorption of digoxin.

Effects of midazolam may be enhanced and prolonged in patients treated with Roxithromycin as with other macrolides. Roxithromycin must not be taken with ergot alkaloid vasocostrictors because of possible occurrence of severe vasocostriction with necrosis of the extremities, and cisapride and terfenadine due to elevation of serum concentrations of these drugs.

**AVAILABILITY:**

Available in boxes of 30 tablets

Also available:

Roxithromycin 150 mg in 30's.

**CAUTION:**

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

Store at temperatures not exceeding 30°C.

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**Imported by:**

Sanofi Pasteur Inc
4F Feliza Blvd., 108 V A. Rufino St.,
Legaspi Village, 1229 Makati City