ORADRO (tablets)

(Clarithromycin)

Content

Film-coated tablets. One tablet contains clarithromycin 250 mg or 500 mg.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMICS

Oradro is a semi-synthetic second generation bacteriostatic broad spectrum antibiotic. It exerts its antibacterial action by binding to the 50s ribosomal sub-unit of susceptible bacteria and suppresses protein synthesis. It is highly potent against a wide variety of aerobic and anaerobic gram-positive and gram-negative organisms in vitro and in vivo:

- aerobic gram-positive microorganisms: Staphylococcus spp. (including methicillin-susceptible Staphylococcus aureus,), Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus agalactiae, Streptococcus viridans, Listeria monocytogenes.

- aerobic gram-negative microorganisms: Haemophilus influenzae, Haemophilus parainfluenzae, Moraxella (Branhamella) catarrhalis, Neisseria gonorrhoeae, Legionella pneumophila, Bordetella pertussis, Helicobacter pylori, Campylobacter jejuni.

- mycobacteria: Mycobacterium leprae, Mycobacterium kansasii, Mycobacterium chelonae, Mycobacterium fortuitum, Mycobacterium marinum, Mycobacterium avium complex (MAC), including Mycobacterium avium, Mycobacterium intracellulare).


Production of β-lactamase has no effect on clarithromycin activity.

Enterobacteriaceae, Pseudomonas spp., as well as other lactose-dissolving gram-negative bacteria are not susceptible to Oradro.

The major part of methicillin- and oxacillin-susceptible Staphylococcus spp. is resistant to clarithromycin. Attention should also be paid to the possibility of cross resistance between clarithromycin and other macrolide drugs, as well as lincomycin and clindamycin.

MIC for H. influenzae the 14-hydroxy metabolite, the main clarithromycin metabolite in human’s body, is two-fold more active than clarithromycin. Parent compound and its main metabolite show additive or synergic effect to H. influenza. for Mycobacterium avium complex (MAC) isolates the 14-
OH metabolite is 4-7 times less active than clarithromycin. The clinical significance of this activity against Mycobacterium avium complex is unknown.

PHARMACOKINETICS

Clarithromycin is rapidly absorbed from the gastrointestinal tract after oral administration. The absolute bioavailability is approximately 55%. Food slightly delays both the onset of clarithromycin absorption, but does not affect the extent of clarithromycin bioavailability. Protein binding is over 90%.

Approximately 20% of clarithromycin is immediately metabolized in liver by CYP3A4, CYP3A5 and CYP3A7 enzymes with the formation of 14-OH clarithromycin, the active metabolite against Haemophilus influenza. Peak plasma concentrations were attained less than 3 hours. The steady-state concentration of parent drug and its major metabolite observed following administration of 250 mg daily is 0.62-0.84 µg/ml, is 0.4-0.7 µg/ml respectively; in case of increased dose up to 500 mg, daily Css of intact drug and its metabolite in plasma is 1.77-1.89 and 0.67-0.8 µg/ml respectively. Clarithromycin is extensively distributed in body tissues (lungs, palatine tonsils, saliva, sputum and eardrum, skin and soft tissues) and fluids and because of high tissue penetration, intracellular concentrations are higher than serum concentrations 10-fold. Elimination halftime following the intake of 250 mg is 3-4 hours, and following 500 mg dose intake – 5-7 hours. 20-30% of clarithromycin (40% of suspension) is excreted intact by kidneys, and the remaining part is excreted as metabolites.

THERAPEUTIC INDICATIONS

- upper respiratory tract infections: pharyngitis, laryngitis, tonsillitis, sinusitis;

- lower respiratory tract infections: bronchitis, pneumonia;

- non-complicated skin and subcutaneous tissue infections: folliculitis, furunculosis, erysipelas, impetigo, wound infection;

- gastric and/or duodenal ulcer (in combination therapy) – for treatment of acute duodenal ulcer, eradication of Helicobacter pylori and for the decrease of peptic ulcer recurrence rate;

- treatment and prophylaxis of generalized or localized mycobacterial infections induced by Mycobacterium avium, Mycobacterium intracellulare; localized infections induced by Mycobacterium fortuitum, Mycobacterium kansasii and Mycobacterium chelonae.

Children aged 12 and older:

- upper respiratory tract infections: pharyngitis, laryngitis, tonsillitis, sinusitis, acute maxillary sinusitis;

- lower respiratory tract infections: bronchitis, pneumonia;

- acute otitis media;
- non-complicated skin and subcutaneous tissue infections: folliculitis, furunculosis, erysipelas, impetigo, wound infection;

- treatment and prophylaxis of generalized mycobacterial infections induced by Mycobacterium avium, Mycobacterium intracellulare.

CONTRAINDICATIONS

- Oradro is contraindicated in patients with a known hypersensitivity to clarithromycin, other components of the drug or any of the macrolide antibiotics;

- porphyria;

- Concomitant administration of clarithromycin and any of the following drugs is contraindicated: astemizole, cisapride, pimozide, terfenadine (as it may lead to QT prolongation, ventricular tachycardia, ventricular fibrillation, and torsades de pointes);

- Concomitant administration of clarithromycin and ergotamine or dihydroergotamine is contraindicated as it may lead to ergot toxicity;

- pregnancy and lactation;

- children under 12.

ADVERSE EFFECTS

Gastrointestinal tract: common - diarrhoea, vomiting, nausea, abdominal pain; rarely - glossitis, stomatitis, oral candidiasis, change of color in tongue and teeth (reversible), hepatic dysfunctions, including transient transaminitis and hepatocellular and/or cholestatic hepatitis, with or without jaundice (hepatic dysfunction may be severe and usually reversible), acute pancreatitis, pseudomembranous colitis (moderately severe to life-threatening). Isolated cases of death from impaired hepatic function, generally observed in case of serious concurrent conditions and/or concomitant administration of other medicinal products have been registered.

Nervous system: uncommon – reversible headaches, dizziness, anxiety, insomnia, nightmares, buzzing in ears; rarely – convulsions; very rarely – myalgia, paresthesia, confused consciousness, disorientation, hallucinations, psychosis, depersonalization.

Cardiovascular system: rarely - ventricular tachycardia, torsade de pointes, ventricular fibrillation, Q-T elongation (as of other macrolides).

Sense organs: very rarely – buzzing in ears, tingling, disturbed sense of smell, taste changes (dysgeusia); in isolated cases – hearing loss, reversible after withdrawal.

Urinoexcretory system: very rarely - interstitial nephritis and renal insufficiency.

Laboratory parameters: uncommon – elevated hepatic transaminase, bilirubin; very rarely – leucocytopenia, thrombocytopenia, elevated prothrombin time, hypercreatininemia, hypoglycaemia (in case of concurrent administration of hypoglycaemic agents).

Other: uncommon hemorrhage, bloodstrokes, myalgia, in case of long-term or repeated administration of Oradro superinfection may develop (developed resistance of microorganisms).

DOSAGE AND ADMINISTRATION

Oradro is administered orally without chewing or dispersing, swallowing whole, washing down with small amount of water, any time of the day (it is desirable to administer at the same time of the day) with no regard to food intake. In case of missing the time of administration, the missing dose should be administered as soon as possible. But if the time of next administration has come, the dose should not be doubled to compensate missed intake.

Adults and children over 12 years old: 250 mg every 12 hours. In case of severe infections the dose should be increased up to 500 mg every 12 hours. The usual duration of treatment is 6-14 days.

For Helicobacter pylori eradication the dose of 250-500 mg twice daily is administered, generally during 7-14 days, in combination with other medicinal products.

For patients with Mycobacterium avium infection the initial dose is 500 mg every 12 hours. If during 3-4 weeks on the basis of clinical and bacterial data there is no improvement, the dose may be increased up to 1000 mg twice daily.

The treatment of disseminated infection induced by Mycobacterium avium complex in AIDS patients should be continued as much as the clinical and microbiological efficacy of the medication lasts. Clarithromycin should be administered concomitantly with other antibacterial drugs.

During the treatment of odontogenic infections the recommended dose is 250 mg every 12 hours during 5 days.

Elderly patients: the same dosages as for adults.

Administration in patients with hepatic insufficiency: the dose adjustment in mild to moderate hepatic insufficiency in patients with normal hepatic function is not required.

Administration in patients with renal insufficiency

In patients with renal insufficiency with creatinine clearance less than 30 ml/min the dose of clarithromycin should be decreased twofold, i.e. to 250 mg once daily or 250 mg twice daily in severe infections. The duration of treatment should not be more than 14 days for such patients as the tablet should not be divided, and the dose should not be decreased from 500 mg daily, that is why clarithromycin of prolonged action should not be administered to such patients.
PACKAGING

Oradro 250 mg

Film-coated tablets

7 or 14 tablets in a blister.

1 or 2 blisters with a leaflet in a carton box.

Oradro 500 mg

7 tablets in a blister.

2 blisters with a leaflet in a carton box.