LORAMYCIN®

Gentamicin

Description

Loramycin® is a systemic antibacterial agent from the aminoglycoside group of antibiotics.

Clinical pharmacology

Loramycin® is actively transported across the bacterial cell membrane, irreversibly binds to one or more specific receptor proteins on the 30s subunit of bacterial ribosomes and interferes with an initiation complex between messenger RNA (mRNA) and the 30s subunit. DNA may be misread, thus producing nonfunctional proteins, polyribosomes are split apart and are unable to synthesize proteins. This results in accelerated aminoglycosides transport, increasing the disruption of bacterial cytoplasmic membranes, and eventual cell death. Loramycin® is bactericidal while most other antibiotics that interfere with protein synthesis are bacteriostatic.

Antibacterial activity

The spectrum of Loramycin® covers aerobic gram negative bacilli and some gram-positive organisms. It is not active against anaerobic organisms.

The antibacterial activity of aminoglycosides against different strains of organisms varies among institutions and regions. However Loramycin® is generally active against most Enterobacteriaceae, including Escherichia coli, Proteus mirabilis, Indole-positive proteus, Citrobacter, Enterobacter, Klebsiella, Providencia and Serratia species. Acinetobacter and Pseudomonas species are also usually susceptible. Loramycin® is active against staphylococcus aureus, but is rarely used as sole therapy since other, less toxic antibiotics are available. Loramycin® administered concurrently with a penicillin, is synergistic against certain susceptible strains of Enterococcus faecalis.

Pharmacokinetics

Oral absorption	poor
Presystemic metabolism	nil
Plasma half – life	
range	1-4 h
Volume of distribution	0.21 $1.kg^{-1}$
Plasma protein binding	low (0-10%)

Indication

1- Biliary tract infections
2- Bone and joint infections
3- Central nervous system infections (including meningitis and ventriculitis)
4- Intraabdominal infections (including peritonitis)
5- Bacterial, gram-negative pneumonia
6- Bacterial septicemia
7- Skin and soft tissue infections (including burn wound infections)
8- Recurrent complicated urinary tract infections

Contraindication

Loramycin® is contraindicated in patients who have shown hypersensitivity to Gentamicin or any other aminoglycosides group of antibiotics.

Precaution

• Before Loramycin® administration, previous hypersensitivity reactions to aminoglycosides must be determined because of cross-hypersensitivity among aminoglycosides.
• Loramycin® may cause neuromuscular blockade. In case of existing infant botulism, myasthenia gravis and parkinsonism, it may result in further skeletal muscle weakness.
• In the patients with renal function impairment or dehydrated, possibly the risk of toxicity increase because of elevated serum concentrations.

It is recommended that Loramycin® be administered in a reduced dosage at a fixed interval, or in normal doses at prolong intervals to patients with impaired renal function.

• Risk – benefit should be considered when eighth-cranial-nerve impairment exists because Loramycin® may cause auditory and vestibular toxicity.
• Surgical, obstetrical, gynecological, or burn patients receiving Loramycin® doses, adjusted on the basis of serum concentrations, may require less than the minimum recommended dose or greater than the maximum recommended dose of Loramycin® because of wide interpatient variability.
• Loramycin® should be used with caution in premature infants and neonates because of their immature renal capability, which may result in prolonged elimination half-life and aminoglycoside induced toxicity.
• Geriatric patients may require smaller daily doses of Loramycin® in accordance with their increased age, decreased renal function and possibly decreased weight.

Pregnancy

Pregnancy category C.

Adequate and well-controlled studies in humans have not been done. Since other aminoglycosides have been reported to cause deafness in the fetus, risk-benefit must be carefully considered when this medication is required in life threatening situations or in serious diseases for which other medications cannot be used or are ineffective.

Breast feeding

Loramycin® is excreted in breast milk in small amounts. However, Loramycin® is poorly absorbed from gastrointestinal tract and problems in nursing infants have not been documented.

Dosage

The dosing and dosage forms available are expressed in terms of Gentamicin base.

Usual adult and adolescent dose

• Systemic antibacterial: intramuscular or intravenous infusion- 1 to 1.7mg (base)per kg of body weight every eight hours for 7 to 10 days or more.

Note: uncomplicated bacterial urinary tract infections: intramuscular or intravenous infusion- Adults less than 60 kg of body weight: 3mg (base) per kg of body weight once a day, or 1.5 mg per kg of body weight every twelve hours. Adults 60 kg of body weight and over: 160 mg (base) once a day, or 80 mg every twelve hours.

• Following hemodialysis, a supplemental dose of 1 to 1.7 mg (base) per kg of body weight may be administered, depending on the severity of the infection.

Usual adult prescribing limits

Up to 8 mg (base) per kg of body weight daily in severe, life-threatening infections.

Note: Doses up to 15mg (base) per kg of body weight daily have been used in the treatment of intraocular infections.

Usual pediatric dose

• Systemic antibacterial: intramuscular or intravenous infusion- premature or full-term neonates up to 1 week of age: 2.5mg (base) per kg of body weight every twelve to twenty-four hours for 7 to 10 days or more.

Older neonates and infants: 2.5 mg (base) per kg of body weight every eight to sixteen hours for 7 to 10 days or more.

Children: 2 to 2.5 mg (base) per kg of body weight every eight hours for 7 to 10 days or more.

Note: The dosing interval of Loramycin® in pediatric patients may vary from every four hours to every twenty-four hours, depending on the medical condition of the patient (cystic fibrosis, burns, renal dysfunction); serum levels must be monitored.

• Following hemodialysis, a supplemental dose of 2 to 2.5 mg (base) per kg of body weight may be administered, depending on the severity of the infection.

Note: Doses up to 8mg (base) daily have been used in infants with functioning ventricular shunts.

Administration

There is no need to prepare a dilution for intramuscular use.

To prepare initial dilution for intravenous infusion

• Add each dose to 50-200 mL of 0.9% sodium chloride injection or 5% dextrose injection to provide a concentration not exceeding 1mg (base) per mL (0.1%).

The resulting solution should be administered slowly over a 30 to 60 minutes period to help decrease the chance of neuromuscular blockade. Pediatric patients may require a proportionately smaller volume of diluent.

• Subcutaneous administration is not recommended and may be painful.
• Loramycin® sulfate injection may also be administered as an aerosol nebulization.

Patient consultation

• Continue receiving Loramycin® for full course of therapy on regular schedule.
• Use the proper dose.

Patient monitoring

• Audiograms, renal and vestibular function determinations may be required prior to, periodically during and following treatment in patients with pre-existing renal or eighth-cranial nerve impairment. If renal, vestibular, or auditory function impairment occurs, reduction in dose or discontinuation of the Loramycin® may be required.
• Urinalyses may be required prior or during treatment to detect albumin, casts and cells in the urine.

Warning

• The safety and efficacy of Loramycin® administration in pregnant women has not been established.
• Loramycin® may cause significant nephrotoxicity or ototoxicity.

Toxicity may develop even with conventional doses particularly in patints with renal function or eighth-cranial-nerve impairment.

• Loramycin® should be monitored in all patients, specially neonates and the elderly, even without renal function impairment, to avoid potentially toxic concentrations from accumulation of the drug.
• If renal toxicity or ototoxicity occurs, drug discontinuation or appropriate dosage adjustment is required.
• Concomitant use with other ototoxic or nephrotoxic drug should be avoided.

Interaction

• Concurrent or sequential use of 2 or more aminoglycosides by any route or concurrent use of capreomycin with Loramycin® should be avoided since the potential for ototoxicity, nephrotoxicity and neuromuscular blockade may be increased. Also concurrent use of 2 or more aminoglycosides may result in reduced bacterial uptake of each one since the medications compete for the same uptake mechanism.
• Extemporaneous admixture of beta-lactam antibacterials (penicillins and cephalosporins) and Loramycin® may result in substantial mutual inactivation. If they are administered concurrently they should be administered in separate sites. Do not mix them in the same intravenous bag or bottle.
• When Loramycin® is administered concurrently with intravenous indomethacin in the premature neonates, plasma concentrations and risk of toxicity increase.
• Concurrent or sequential use of methoxyflurane , parenteral polymyxins, other nephrotoxic or ototoxic medications with Loramycin® may increase the potential for ototoxicity or nephrotoxicity.

• Medications with neuromuscular blocking activity, including halogenated hydrocarbon inhalation anesthetics, opioid analgesics and massive transfusions with citrate anticoagulated blood, should be carefully monitored when used concurrently with Loramycin® since neuromuscular blockade may be inhanced.

Also their concurrent use may antagonize the effect of antimyasthenics on skeletal muscle.

Laboratory value alteration

• Administration of Loramycin® may change the following physiology/laboratory test values: Serum alanin aminotransferase (ALT[SGPT]), Alkaline Phosphatase, Aspartate aminotransferase (AST[SGOT]), bilirubin, Lactate dehydrogenase (LDH), Blood urea nitrogen (BUN), creatinine, calcium, magnesium, potassium, sodium.

Adverse reactions

• Leg cramps, skin rash, fever and seizures have been reported when Loramycin® is administered concurrently by systemic and intrathecal routes.
• Endotoxin-like reactions have been reported with once-daily dosing regiemens of Loramycin®.

Those indicating need for medical attention

• Incidence more frequent

Nephrotoxicity (greatly increased or decreased frequency of urination or amount of urine, increased thirst, loss of appetite, nausea, vomiting), neurotoxicity (muscle twitching, numbness, seizures, tingling), auditory ototoxicity(any loss of hearing, ringing or buzzing, or a feeling of fullness in the ears), vestibular ototoxicity(clumsiness, dizziness, nausea, vomiting, unsteadiness).

• Incidence less frequent

Hypersensitivity

• Incidence rare

Endotoxin-like reaction (shaking, chills, fever), neuromuscular blockade (difficulty in breathing, drawsiness, weakness).

Those indicating possible ototoxicity

vestibular toxicity, or nephrotoxicity and the need for medical attention if they occur or progress after medication is discontinued.

Any loss of hearing, clumsiness or unsteadiness, dizziness, greatly increased or decreased frequency of urination or amount of urine, increased thirst, loss of appetite, nausea or vomiting, ringing or buzzing or a feeling of fullness in the ears.

Overdose

• Loramycin® can be removed by hemodialysis or peritoneal dialysis from the blood of patients with impaired renal funciton.
• Neuromuscular blockade and respiratory depression or paralysis (apnea), that may occur when two or more aminoglycosides are given concurrently, is treated by the administration of anticholinesterase agents or calcium salts and also mechanical respiratory assistance.

Since there is no specific antidote, treatment of Loramycin® overdose should be symptomatic and supportive. Patients in whom intentional overdose is known or suspected, should be referred for psychiatric consultation.

Storage and stability condition

• Store below 30°C.
• Protect form light and freezing.
• Keep out of the reach of children.
• Don't use if injection is discolored or contains percipitate.

Packaging

• Ampoules of 2mL containing 20mg or 80 mg Gentamicin as sulfate.
• Ampoules of 1mL containing 40mg Gentamicin as sulfate.
• Boxes of 10 ampoules.

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