Bosch

For Medical Professional Only

Zolrest

(Linezolid)

زولریسٹ

CLASSIFICATION:
Antibiotic, Oxazolidinone.

COMPOSITION:
Zolrest 600 mg Film-Coated Tablets.
Each tablet contains 600 mg linezolid.
Zolrest 200 mg, 400 mg & 600 mg Solution for Infusion.
1 ml contains 2 mg linezolid.

PHARMACOLOGY:
Linezolid is a synthetic antibacterial agent. It inhibits bacterial protein synthesis by binding to bacterial 23S ribosomal RNA of the 50S subunit. Linezolid is bacteriostatic against enterococci and staphylococci and bactericidal against most strains of streptococci.

PHARMACOKINETICS:
Absorption: Rapidly and extensively absorbed after oral dosing. Maximum plasma concentrations are reached approximately 1 to 2 hours after dosing, and the absolute **bioavailability is approximately 100%**. Therefore, linezolid may be given orally or intravenously without dose adjustment.

Distribution: Linezolid readily distributes to well-perfused tissues. The plasma protein binding of linezolid is approximately 31% and is concentration-independent. The volume of distribution of linezolid at steady-state averaged 40 to 50 liters in healthy adult volunteers.

Metabolism: Hepatic via oxidation of the morpholine ring, resulting in two inactive metabolites (aminoethoxyacetic acid, hydroxyethyl glycine); does not involve CYP.

Elimination: Non renal clearance accounts for approximately 65% of the total clearance of Linezolid.

INDICATIONS:
Vancomycin-Resistant *Enterococcus faecium* infections, including cases with concurrent bacteremia. Nosocomial pneumonia, complicated skin and skin structure infections, community acquired pneumonia including concurrent bacteremia.

Non-FDA approved indication: Treatment of mycobacterial infections. Linezolid has been used as a third-line regimen for the treatment of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB).

DOSAGE & ADMINISTRATION:

Dosage guidelines for Linezolid

Infection	Dosage and Route of Administration Adults & Adolescents (12 Years and Older)	Recommended Duration of Treatment (consecutive days)
Complicated skin and skin structure infections	600 mg IV or oral q 12h	10 to 14
Community-acquired pneumonia, including concurrent bacteremia		
Nosocomial pneumonia		
Vancomycin-resistant Enterococcus faecium infections, including concurrent bacteremia	600 mg IV or oral q 12h	14 to 28
Uncomplicated skin and skin structure infections	Adults: 400mg oral q12h Adolescents: 600mg oral q12h	10 to 14
Tuberculosis (MDR-TB or XDR-TB)	600 mg IV or oral daily	Up to 2 yrs until sputum culture conversion if tolerated

Indications	Children (>7 days to 11 years old)	Teenagers and adults (> 12 years old)
- Complicated skin & soft tissue infections - Pneumonia - Bacteremia	10 mg/kg intravenously or orally every 8 hours	600 mg intravenously or orally every 12 hours
- Simple skin & soft tissue infections	< 5 years: 10 mg/kg intravenously or orally every 8 hours 5-11 years: 10 mg/kg intravenously or orally every 12 hours	600 mg intravenously or orally every 12 hours

The dosage in newborns <7 days old is 10 mg/kg intravenously every 12 hours.

Take with or without food. Avoid tyramine-containing foods/beverages.

CONTRAINDICATIONS:
Linezolid formulations are contraindicated for use in patients who have known hypersensitivity to linezolid or any of the other product components.

Monoamine Oxidase Inhibitors
Linezolid should not be used in patients taking any medicinal product which inhibits monoamine oxidases A or B (e.g. phenelzine, isocarboxazid) or within two weeks of taking any such medicinal product.

Potential Interactions Producing Elevation of Blood Pressure
Unless patients are monitored for potential increases in blood pressure, linezolid should not be administered to patients with uncontrolled, pheochromocytoma, thyrotoxicosis and/or patients taking any of the following types of medications: directly and indirectly acting sympathomimetic agents (e.g. pseudoephedrine), vasopressive agents (e.g., norepinephrine), dopaminergic agents (e.g. , dobutamine).

Potential Serotonergic Interactions
Unless patients are carefully observed for signs and/or symptoms of serotonin syndrome, linezolid should not be administered to patients with carcinoid syndrome and/or patients taking any of the following medications: serotonin re-uptake inhibitors, tricyclic antidepressants, serotonin 5-HT1 receptor agonists (triptans), meperidine or buspirone.

WARNINGS/PRECAUTIONS:
Myelosuppression has been reported and may be dependent on duration of therapy (generally >2 weeks of treatment); use with caution in patients with pre-existing myelosuppression, in patients receiving other drugs which may cause bone marrow suppression, or in chronic infection (previous or concurrent antibiotic therapy). Weekly CBC monitoring is recommended. Discontinue linezolid in patients developing myelosuppression. Lactic acidosis had been reported with use. **Unnecessary use may lead to the development of resistance to linezolid; consider alternatives before initiating outpatient treatment.** Peripheral and optic neuropathy has been reported in patients treated with linezolid, primarily those patients treated for longer than the maximum recommended duration of 28 days. Visual function should be monitored in all patients taking linezolid for extended periods (≥ 3 months) and in all patients reporting new visual symptoms regardless of length of therapy with linezolid.
Seizures have been reported; use with caution in patients with a history of seizures. Prolonged use may result in fungal or bacterial superinfection, including *C. difficile* associated diarrhea (CDAD) and pseudomembranous colitis; CDAD has been observed >2 months after antibiotic treatment.

INTERACTIONS:
Linezolid is a reversible, nonselective inhibitor of MAO. Serotenergic agents (e.g., TCA's, venlafaxine, trazodone, sibutramine, meperidine, dextromethorphan, and SSRIs) may cause a serotonin syndrome (eg, agitation, confusion, hallucinations, hyper-reflexia, myoclonus, shivering, tachycardia, hyperpyrexia, cognitive dysfunction) when used concomitantly. Adrenergic agents (eg, phenylpropanolamine, pseudoephedrine, sympathomimetic agents, vasopressor or dopaminergic agents) may cause hypertension. Tramadol may increase the risk of seizures when used concurrently with linezolid. Myelosuppressive medications may increase risk of myelosuppression when used concurrently with linezolid.

HEPATIC INSUFFICIENCY:
No dose adjustment is recommended for patients with mild-to-moderate hepatic insufficiency.

RENAL INSUFFICIENCY:
The pharmacokinetics of the parent drug, linezolid, are not altered in patients with any degree of renal insufficiency;

PREGNANCY CATEGORY C:
There are no adequate and well-controlled studies in pregnant women, Therefore linezolid should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

NURSING MOTHERS:
It is not known whether linezolid is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when linezolid is administered to a nursing woman.

GERIATRIC USE:
The pharmacokinetics of linezolid are not significantly altered in elderly patients (65 years or older). Therefore, dose adjustment for geriatric patients is not necessary.

ADVERSE REACTIONS:
The most common adverse events in patients treated with linezolid were diarrhea (incidence across studies: 2.8% to 11.0%), headache (incidence across studies: 0.5% to 11.3%), and nausea (incidence across studies: 3.4% to 9.6%). Other adverse events reported in Phase 2 and Phase 3 studies included oral moniliasis, vaginal moniliasis, hypertension, dyspepsia, localized abdominal pain, pruritis, and tongue discoloration.

EFFICACY:
Linezolid formulations are indicated in the treatment of the following infections caused by susceptible strains of the designated microorganisms: Vancomycin-resistant *Enterococcus faecium* (VRE) infections, including cases with concurrent bacteremia; nosocomial pneumonia caused by *Staphylococcus aureus* (methicillin-susceptible and –resistant strains) or *Streptococcus pneumoniae* (including multi-drug resistant strains, which refers to isolates resistant to 2 or more of the following antibiotics: penicillin, second-generation cephalosporins, macrolides, tetracycline, and trimethoprim/sulfamethoxazole); community-acquired pneumonia caused by *S. pneumoniae* (including multi-drug resistant strains), including cases with concurrent bacteremia, or *S. aureus* (methicillin-susceptible strains only); complicated skin and skin structure infections, including diabetic foot infections, without concomitant osteomyelitis, caused by S. Aureus (methicillin-susceptible and-resistant strains), *Streptococcus pyogenes*, or *Streptococcus agalactiae*; and uncomplicated skin and skin structure infections caused by *S. Aureus* (methicillin-susceptible strains only) or *S. pyogenes*.
Linezolid has significant in vitro acitivity against *M. tuberculosis*, and has occasionally been used to treat TB.

STORAGE:
- Protect from light, store below 30°C.
- Keep infusion in unit carton until ready to use, infusion may exhibit a yellow colour that can intensify over time without adversely affecting product.
- Do not freeze.
- Do not use solution contains visible foreign particle.
- Keep out of the reach of children.

WARNING: To be sold on prescription of a registered medical practitioner only.

PRESENTATION:
Zolrest 600mg Film Coated Tablet:
Blister pack of 12's tablet.
Zolrest 200mg/100ml Infusion:
1 vial of 100ml infusion solution containing 200mg linezolid.
Zolrest 400mg/200ml Infusion:
1 vial of 200ml infusion solution containing 400mg linezolid.
Zolrest 600mg/300ml Infusion:
1 vial of 300ml infusion solution containing 600mg linezolid.

ہدایات:
- 30°C سے کم درجہ حرارت پر روشنی سے محفوظ رکھیں۔
- انفیوژن کو استعمال کے دوران ہی کارٹن سے نکالیں، محلول کا رنگ وقت گزرنے کے ساتھ ساتھ تیز پیلا ہوسکتا ہے، جسکا انفیوژن کی افادیت پر کوئی اثر نہیں ہوتا۔
- منجمد ہونے سے محفوظ رکھیں۔
- محلول میں غیر حل پذیر ذرات نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔
- بچوں کی پہنچ سے دور رکھیں۔

انتباہ: صرف رجسٹرڈ میڈیکل پریکٹیشنر کے نسخے پر فروخت کے لئے۔

Manufactured by:
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