Size: 125 x 155 mm *FRONT*

TISHU

(L i n e z o l i d)

600mg | 400mg

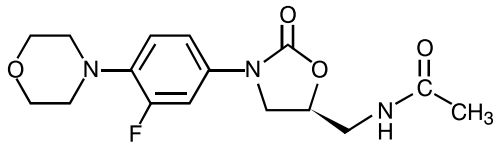
ٹشو ٹیبلیٹس

۶۰۰ ملی گرام | ۴۰۰ ملی گرام

DESCRIPTION

TISHU Tablets contain linezolid, which is a synthetic antibacterial agent of the oxazolidinone class.The chemical name for linezolid is (S)-N-[[3-[3-Fluoro-4-(4-morpholinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide.

The empirical formula is $C_{16}H_{20}FN_3O_4$. Its molecular weight is 337.35, and its chemical structure is represented below:



COMPOSITION

Each TISHU 600mg tablet

Each film-coated tablet contains: Linezolid 600mg

Each TISHU 400mg tablet

Each film-coated tablet contains: Linezolid 400mg

CLINICAL PHARMACOLOGY

Mechanism of Action:

Linezolid is a synthetic antibacterial agent of the oxazolidinone class, which has clinical utility in the treatment of infections caused by aerobic Gram-positive bacteria. The in vitro spectrum of activity of linezolid also includes certain Gram-negative bacteria and anaerobic bacteria. Linezolid binds to a site on the bacterial 23S ribosomal RNA of the 50S subunit and prevents the formation of a functional 70S initiation complex, which is essential for bacterial reproduction. The result of time-kill studies have shown linezolid to be bacteriostatic against enterococci and staphylococci. For streptococci, linezolid was found to be bactericidal for the majority of isolates.

Microbiology

Linezolid has been shown to be active against most isolates of the following microorganism, both in-vitro and in clinical infections:

Gram positive aerobes: Enterococcus faecalis, Enterococcus faecium, Staphylococcus aureus
Coagulase negative staphylococci, Streptococcus agalactiae, Streptococcus pneumonia, Streptococcus pyogenes, Group C streptococci, Group G streptococci.
Gram positive anaerobes: Clostridium perfringens, Peptostreptococcus anaerobius, Peptostreptococcus species.
Gram-negative aerobes: Pasteurella canis, Pasteurella multocida.
Resistant organisms: Haemophilus influenzae, Moraxella catarrhalis, Neisseria species, Enterobacteriaceae
Pseudomonas aeruginosa.

Pharmacokinetics:

Absorption: Linezolid is 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:*** Linezolid is primarily metabolized by hepatic via oxidation of the morpholine ring, resulting in two inactive metabolites (aminoethoxyacetic acid, hydroxyethyl glycine); does not involve CYP. ***Elimination:*** Nonrenal clearance accounts for approximately 65% of the total clearance of Linezolid.

INDICATIONS

TISHU (Linezolid) is an oxazolidinone class antibacterial indicated in adults and children for the treatment of the following infections caused by susceptible Gram-positive bacteria

- **Nosocomial Pneumonia** (Caused by Staphylococcus aureus (methicillin-susceptible and -resistant isolates) or Streptococcus pneumonia).
- **Community-acquired Pneumonia** (Caused by Streptococcus pneumoniae, including cases with concurrent bacteremia, or Staphylococcus aureus (methicillin-susceptible isolates only).
- **Complicated Skin and Skin Structure Infections, including diabetic foot infections, without concomitant osteomyelitis** (Caused by Staphylococcus aureus (methicillin-susceptible and -resistant isolates), Streptococcus pyogenes, or Streptococcus agalactiae).
- **Uncomplicated Skin and Skin Structure Infections** (Caused by Staphylococcus aureus (methicillin-susceptible isolates only) or Streptococcus pyogenes).
- **Vancomycin-resistant Enterococcus faecium Infections** (Vancomycin-resistant Enterococcus faecium infections, including cases with concurrent bacteremia).

DOSAGE & ADMINISTRATION:

Infections	Dosage, Route and Frequency of Administration		Recommended Duration of Treatment (consecutive days)
	Pediatric Patients (Birth through 11 Years of Age)	Adults and Adolescents (12 Years and Older)	
Nosocomial pneumonia	10mg/kg intravenously or oral every 8 hours	600mg intravenously or oral every 12 hours	10-14
Community-acquired pneumonia, including concurrent bacteremia			
Complicated skin and skin structure infections			
Vancomycin-resistant Enterococcus faecium infections, including concurrent bacteremia	10mg/kg intravenously or oral every 8 hours	600mg intravenously or oral every 12 hours	14-28
Uncomplicated skin and skin structure infections	Less than 5 Yrs: 10mg/kg oral every 8 hours 5-11 Yrs: 10mg/kg oral every 12 hours	**Adults:** 400mg oral every 12 hours **Adolescents:** 600mg oral every 12 hours	10-14

Neonates less than 7 days: Most pre-term neonates less than 7 days of age (gestational age less than 34 weeks) have lower systemic linezolid clearance values and larger AUC values than many full-term neonates and older infants. These neonates should be initiated with a dosing regimen of 10 mg/kg every 12 hours. Consideration may be given to the use of 10 mg/kg every 8 hours regimen in neonates with a sub-optimal clinical response. All neonatal patients should receive 10 mg/kg every 8 hours by 7 days of life.

BACK

Size: 125 x 155 mm

CONTRAINDICATIONS
• Known hypersensitivity to linezolid or any of the other product components.
• Patients taking any monoamine oxidase inhibitors (MAOI) or within two weeks of taking an MAO

WARNINGS AND PRECAUTIONS
Myelosuppression: Monitor complete blood counts weekly. Thrombocytopenia has been reported more often in patients with severe renal and in patients with moderate to severe hepatic impairment. Consider discontinuation in patients who develop or have worsening myelosuppression.
Peripheral and Optic Neuropathy: Reported primarily in patients treated for longer than 28 days. If patients experience symptoms of visual impairment, prompt ophthalmic evaluation is recommended.
Serotonin Syndrome: Monitor patients taking serotonergic agents, including antidepressants and opioids, for signs of serotonin syndrome. Patients taking serotonergic antidepressants should receive Linezolid only if no other therapies are available. Discontinue serotonergic antidepressants and monitor patients for signs and symptoms of both serotonin syndrome and antidepressant discontinuation.
A mortality imbalance was seen in an investigational study in linezolid treated patients with catheter-related bloodstream infections.
Clostridioides difficile-Associated Diarrhea: Evaluate if diarrhea occurs. Potential interactions producing elevation of blood pressure: monitor blood pressure.
Hypoglycemia: Postmarketing cases of symptomatic hypoglycemia have been reported in patients with diabetes mellitus receiving insulin or oral hypoglycemic agents.
Hyponatremia and/or Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH): Monitor serum sodium levels regularly in patients at risk of hyponatremia and/or SIADH.

INTERACTIONS:
Linezolid is a reversible, nonselective inhibitor of MAO. Serotonergic 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:
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.

OVERDOSAGE:
No specific antidote is known. No cases of overdose have been reported. However, in case of overdose supportive care is advised together with maintenance of glomerular filtration. Approximately 30% of a Linezolid dose is removed during 3 hours of haemodialysis, but no data are available for the removal of Linezolid by peritoneal dialysis or haemoperfusion. The two primary metabolites of Linezolid are also removed to some extent by haemodialysis.

STORAGE
Do not store above 30°C.
Protect from light and moisture.

HOW SUPPLIED
TISHU (Linezolid) Tablets 600mg are available in alu alu blister pack of 10's.
TISHU (Linezolid) Tablets 400mg are available in alu alu blister pack of 10's.

خوراک اور ترکیب استعمال: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
دھوپ، گرمی اور نمی سے محفوظ رکھیں۔ تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔
صرف رجسٹرڈ میڈیکل پریکٹیشنر کے نسخے پر فروخت کے لئے۔

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