# ZOLISTAT

( L i n e z o l i d )

TABLETS

INFUSION

**Composition:**
**ZOLISTAT 600mg Tablets:**
Each film coated Tablet contains:
Linezolid .....600mg

**ZOLISTAT 600mg / 300ml Infusion:**
Each 300ml contains:
Linezolid.....600mg

**Description:**
ZOLISTAT (Linezolid) is a synthetic antibacterial agent of oxazolidinone class.

**Mechanism Of Action:**
The oxazolidinones are protein synthesis inhibitors: they stop the growth and reproduction of bacteria by disrupting translation of messenger RNA (mRNA) into proteins in the ribosome. Although its mechanism of action is not fully understood, Linezolid appears to work on the first step of protein synthesis, initiation, unlike most other protein synthesis inhibitors, which inhibit elongation. It does so by preventing the formation of the initiation complex, composed of the 30S and 50S subunits of the ribosome, tRNA and mRNA. Linezolid binds to the 23S portion of the 50S subunit (the center of peptidyltransferase activity). Due to this unique mechanism of action, cross-resistance between Linezolid and other protein synthesis inhibitors is highly infrequent or nonexistent.

**Pharmacokinetics:**
**Absorption:**
Linezolid is rapidly and extensively absorbed after oral administration. Maximum plasma concentrations are reached approximately 1 to 2 hours after dosing, and the absolute bioavailability is approximately 100%. Linezolid may be administered without regard to the timing of meals.

**Distribution:**
Animal and human pharmacokinetic studies have demonstrated that 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 oxidation of the morpholine ring, which results in two inactive ring-opened carboxylic acid metabolites: the aminoethoxyacetic acid metabolite (A), and the hydroxyethyl glycine metabolite (B). Formation of metabolite A is presumed to be formed via an enzymatic pathway whereas metabolite B is mediated by a non-enzymatic chemical oxidation mechanism in vitro.

**Excretion:**
Non-renal clearance accounts for approximately 65% of the total clearance of Linezolid. Under steady-state conditions, approximately 30% of the dose appears in the urine as Linezolid, 40% as metabolite B, and 10% as metabolite A. The renal clearance of Linezolid is low (average 40ml/min) and suggests net tubular reabsorption. Virtually no Linezolid appears in feces.

**Indications:**
Zolistat (Linezolid) is indicated for the treatment of infections caused by susceptible strains of the designated microorganisms in the specific conditions listed below. Linezolid is not indicated for the treatment of Gram-negative infections. It is critical that specific Gram-negative therapy be initiated immediately if a concomitant Gram-negative pathogen is documented or suspected.

**Pneumonia:**
Nosocomial pneumonia caused by Staphylococcus aureus (methicillin-susceptible and -resistant isolates) or Streptococcus pneumoniae.
Community-acquired pneumonia caused by Streptococcus pneumoniae, including cases with concurrent bacteremia, or Staphylococcus aureus (methicillin-susceptible isolates only).

**Skin and Skin Structure Infections:**
Complicated skin and skin structure infections, including diabetic foot infections, without concomitant osteomyelitis, caused by Staphylococcus aureus, Streptococcus pyogenes, or Streptococcus agalactiae.
Uncomplicated skin and skin structure infections caused by Staphylococcus aureus or Streptococcus pyogenes.

**Vancomycin-resistant Enterococcus faecium Infections:**
Vancomycin-resistant Enterococcus faecium infections, including cases with concurrent bacteremia.

**Contraindications:**
Linezolid formulations are contraindicated for use in patients who have known hypersensitivity to Linezolid or any of the other product components, and contraindicated to patients taking any monoamine oxidase inhibitors (MAOI) or within two weeks of taking any MAOI.

**Dosage and Administration:**
**General Dosage and Administration:**
The recommended dosage for Zolistat (Linezolid) formulations for the treatment of infections is described in the Table below.

| Infections | Dosage and Route 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<br>Community-acquired pneumonia, including concurrent bacteremia<br>Complicated skin and skin structure infection | 10 mg/kg intravenously or oral after every 8 hours | 600 mg intravenously or oral after every 12 hours | 10 to 14 |
| Vancomycin-resistant Enterococcus faecium infections, including concurrent bacteremia | 10 mg/kg intravenously or oral after every 8 hours | 600 mg intravenously or oral after every 12 hours | 14 to 28 |

| | | | |
|---|---|---|---|
| Uncomplicated skin and skin structure infections | Less than 5 yrs: 10 mg/kg oral after 8 hours<br>5-11 yrs: 10 mg/kg oral every 12 hours | Adults: 400 mg oral after every 12 hours<br>Adolescents: 600 mg oral after every 12 hours | 10 to 14 |

**Adverse Effect:**
Adverse reactions in adult and/or pediatric patients treated with Linezolid include diarrhea, vomiting, headache, nausea, anemia, dizziness, rash, taste alteration, vaginal moniliasis, oral moniliasis, abnormal liver function tests, fungal infection, tongue discoloration, localized and generalized abdominal pain.

**Overdose:**
In the event of over-dosage, supportive care is advised, with maintenance of glomerular filtration. Haemodialysis may facilitate more rapid elimination of Linezolid. In a Phase 1 clinical trial, approximately 30% of a dose of Linezolid was removed during a 3-hour haemodialysis session beginning 3 hours after the dose of Linezolid was administered. Data are not available for removal of Linezolid with peritoneal dialysis or hemoperfusion. Clinical signs of acute toxicity in animals were decreased activity and ataxia in rats and vomiting and tremors in dogs treated with 3000 mg/kg/day and 2000 mg/kg/day, respectively.

**Special Population:**
**Pregnancy:**
There are no adequate and well-controlled studies in pregnant women. Linezolid should be used during pregnancy only if the potential benefit justifies the potential risk to fetus.

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

**Pediatric:**
The safety and effectiveness of Linezolid for the treatment of pediatric patients are supported by evidence from adequate and well-controlled studies in adults, pharmacokinetic data in pediatric patients, and additional data from a comparator-controlled studies in pediatric patients ranging in age from birth through 11 years in all infections mentioned in indication except uncomplicated skin and skin structure infection which is supported by evidence from a comparator-controlled study in pediatric patients ranging in age from 5 through 17 years.

**Nursing Mother:**
Linezolid and its metabolites are excreted in the milk of lactating rats. Concentrations in milk were similar to those in maternal plasma. 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 nursing mother.

**Presentation:**
Zolistat 600mg Tablet, Alu-Alu pack of 2x6 Tablets.
Zolistat 600mg/300ml Infusion in pack of 1's.

**Storage & Administration:**
Protect from heat, light and moisture.
To be sold on the prescription of a registered medical practitioner only.
Keep all medicines out of the reach of children.

**Tablet:**
Store below 30°C.
For oral use only.
**Infusion:**
Store at 15-30°C.
For IV infusion use only.
Do not refrigerate or freeze.
Keep infusion in unit carton until ready to use, infusion may exhibit a yellow color that can intensify over time without adversely effecting product.

**Instructions:**
Do not use if vial is leaking, solution is cloudy or contains undissolved particles. To be administered by I.V. Infusion over a period of 30 to 120 minutes.

## زولِسٹیٹ (لِنَیزولِڈ)

ٹیبلیٹس 600 ملی گرام / 2 x 6's | انفیوژن 600 ملی گرام/300 ملی لیٹر

ہدایات:

برائے ٹیبلیٹس:

دوا کو 30 ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔

صرف کھانے کے لئے استعمال کریں۔

برائے اِنفیوژن:

دوا کو 15 سے 30 ڈگری سینٹی گریڈ درجہ حرارت پر رکھیں۔ گرمی اور روشنی سے بچائیں۔

منجمد ہونے سے بچائیں۔

اِنفیوژن کو استعمال کے وقت ہی کارٹن سے نکالیں، محلول کا رنگ وقت گزرنے کے ساتھ پیلا ہوسکتا ہے، جس کا اِنفیوژن کی افادیت پر کوئی اثر نہیں ہوتا۔

تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔ صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

نوٹ: وائل کے لیک ہونے، دھندلا ہونے، یا اُس میں غیر حل پذیر ذرات نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔

آئی وی اِنفیوژن مریض کے جسم میں 30 سے 120 منٹ کے دوران داخل کیا جائے۔

Manufactured by:
**STANDPHARM PAKISTAN (PVT) LTD**
20 Km Ferozepur Road Lahore, Pakistan.