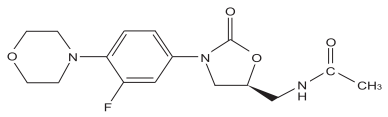
Dyzolid 600 mg
(Linezolid) 12 Tablets

DESCRIPTION:
Linezolid is a synthetic antibacterial agent of the oxazolidinone class. The chemical name for linezolid is (S)-N-[[3-[3-fluoro-4-(4morpholinyl)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:

Dyzolid 600 mg 12 Tablets

Each film coated tablet contains:
Linezolid 600mg

CLINICAL PHARMACOLOGY:
Mechanism of Action
Linezolid is a synthetic antibacterial agent of a new class of antibiotics, the oxazolidinones, with in vitro activity against aerobic gram positive bacteria, certain gram-negative bacteria, and anaerobic microorganisms. Linezolid binds to sites on the bacterial 23S ribosomal RNA of the 50S subunit and prevents the formation of a functional 70S initiation complex, which is an essential component of the bacterial translation process. Linezolid is active against selected gram-positive bacteria that are susceptible or resistant to these antibiotics

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 without dose adjustment

Linezolid may be administered without regard to the timing of meals. The time to reach the maximum concentration is delayed from 1.5 hours to 2.2 hours and Cmax is decreased by about 17% when high fat food is given with linezolid. However, the total exposure measured as $AUC_{0-\infty}$ values is similar under both conditions

Distribution
Linezolid is readily distributed to well-perfused tissues. The plasma protein binding of linezolid is approximately 31% and is concentration-independent. The volume of distribution (Vd) of linezolid at steady-state averaged 40 to 50 liters

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 B is mediated by a non-enzymatic chemical oxidation mechanism in vitro. Linezolid is not detectably metabolized by human cytochrome P450 and it does not inhibit the activities of clinically significant human CYP isoforms (1A2, 2C9, 2C19, 2D6, 2E1, 3A4)

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 the feces, while approximately 6% of the dose appears in the feces as metabolite B, and 3% as metabolite A The elimination half-life of linezolid averages at about 5-7 hours

INDICATIONS, CLINICAL USE & DOSAGE:
Linezolid tablets / suspension / infusion are indicated for:

- **Vancomycin-resistant *Enterococcus faecium* (VREF) Infections**: Linezolid is indicated for the treatment of the intra-abdominal, skin and skin-structure, and urinary tract infections (Including cases associated with concurrent bacteremia)
- **Nosocomial pneumonia**: Caused by *Staphylococcus aureus* (Methicillin-susceptible and resistant [MRSA] strains), or *Streptococcus pneumoniae* (Including multi-drug resistant strains [MDRS]). Combination therapy may be clinically indicated if the documented or presumptive pathogens include gram-negative organisms
- **Community-acquired pneumonia:** Caused by *Streptococcus pneumoniae* (Including MDRS) including cases with concurrent bacteremia or *Staphylococcus aureus* (Methicillin-susceptible and–resistant [MRSA] strains)
- **Complicated skin and skin structure infections:** Including non-limb threatening diabetic foot infections, without concomitant osteomyelitis, caused by *Staphylococcus aureus* (Methicillin-susceptible and-resistant [MRSA] strains), *Streptococcus pyogenes*, or *Streptococcus agalactiae*
- **Uncomplicated skin and skin structure infections:** Caused by *Staphylococcus aureus* (Methicillin-susceptible strains only) or *Streptococcus pyogenes*

Dosage

Indications	Paediatric Patients (Birth to 11 years)	Adults (12 years and older)	Recommended Dosage
Vancomycin-resistant Enterococcus faecium (VREF) infections	10mg/kg 8hrs, I.V. or Oral	600mg 12hrs, I.V. or Oral	14 - 28 days
Nosocomial pneumonia (Including MDRS - multi-drug resistant strains)			10 - 14 days
Community acquired pneumonia			
Complicated skin and skin structure infections			
Uncomplicated skin and skin structure infections	Less than 5 yrs.: 10mg/kg Oral - 8hrs. 5-11 yrs.: 10mg/kg Oral - 12hrs.	400mg 12hrs, I.V. or Oral	10 - 14 days

OR
As directed by the physician

CONTRAINDICATIONS:
Linezolid tablet / suspension / infusion are contraindicated for use in patients who have known hypersensitivity to linezolid or any of the other product components

DRUG INTERACTIONS:
Monoamine Oxidase Inhibitors: Linezolid is a mild reversible nonselective inhibitor of MAO-A and MAO-B. Therefore, linezolid has the potential for interaction with adrenergic and serotonergic agents
Adrenergic Agents: A significant pressor response has been observed in normal adult subjects receiving linezolid and tyramine doses of more than 100mg. Therefore, patients receiving linezolid need to avoid consuming large amounts of foods or beverages with high tyramine content. Initial doses of adrenergic agents, such as dopamine or epinephrine, should be reduced and titrated to achieve the desired response
Serotonergic Agents: No significant differences were found in the pharmacodynamic measures of temperature, digit symbol substitution, nurse-rated sedation, blood pressure, or pulse when subjects were administered dextromethorphan with or without linezolid. The effects of other serotonin-reuptake inhibitors have not been studied. Very rare spontaneous reports of serotonin syndrome with co-administration of linezolid and serotonergic agents have been reported. Since there is limited experience with concomitant administration of linezolid and serotonergic agents, physicians should be alert to the possibility of signs and symptoms of serotonin syndrome (e.g. Hyperpyrexia, and cognitive dysfunction) in patients receiving such concomitant therapy
Antibiotics: Aztreonam-the pharmacokinetics of linezolid or aztreonam are not altered when administered together. Gentamicin-the pharmacokinetics of linezolid or gentamicin are not altered when administered together
Antacids: No studies have been conducted with antacids and chelating agents. Based on the chemical structure, concurrent administration with these agents is not expected to affect absorption of linezolid

PRECAUTIONS:
Pregnancy Category: C
Linezolid should be used during pregnancy only if the potential benefits justify the potential risk to the fetus
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, cautions should be exercised when linezolid is administered to a nursing mother
Paediatrics
No overall differences in safety or effectiveness of linezolid were observed between elderly patients and younger patients

ADVERSE REACTIONS:
Linezolid is very well tolerated with relative few side effects which include headache, insomnia, convulsions, dizziness, vertigo, dermatologic rash, pharyngitis, diarrhea, vomiting, nausea, generalized and localized abdominal pain, GI bleeding, loose stools, constipation, altered taste, tongue discoloration, oral moniliasis, vaginal moniliasis, anemia, thrombocytopenia, eosinophilia, leucopenia, hypokalemia, generalized edema & lactic acidosis

Effects on ability to drive & use machinery
Patients should be warned about the potential for dizziness whilst receiving linezolid and should be advised not to drive or operate machinery if dizziness occurs

OVERDOSAGE:
Supportive care is advised in the events of overdosage, with maintenance of glomerular filtration. Hemodialysis may facilitate more rapid elimination of linezolid

STABILITY:
See expiry on the pack

INSTRUCTIONS:
Keep out of reach of children
Avoid exposure to heat, light, humidity and freezing
Store between 15 to 30°C. Improper storage may deteriorate the medicine

ڈائیزولڈ ۶۰۰ ملی گرام
(لنزولڈ) ۱۲ ٹیبلٹس

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں
ہدایات: بچوں کی پہنچ سے دور رکھیں
دوا کو دھوپ، گرمی، روشنی، نمی اور منجمد ہونے سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی

Manufactured by:
Dyson Research Laboratories (Pvt) LTD.
28th-KM Ferozepur Road, Lahore, Pakistan.