Tablets/Dry Suspension

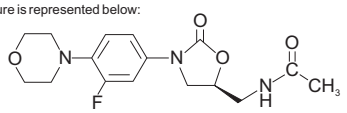
LINEZERT

(LINEZOLID)

لینزرٹ

(لائینزولِڈ) گولیاں/ڈرائی سسپینشن

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



COMPOSITION:

1) LINEZERT 400mg Tablets
Each film coated tablet contains:
Linezolid ... 400mg
(As per Innovator's Specification)

2) LINEZERT 600mg Tablets
Each film coated tablet contains:
Linezolid ... 600mg
(As per Innovator's Specification)

3) LINEZERT Dry Suspension
Each 5ml contain:
Linezolid ... 100mg
(As per Innovator's Specification)

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 inhibit bacterial protein synthesis through a unique mechanism of action. Linezolid binds to sites on the bacterial 23S ribosomal RNA of the 50S subunit and prevents the formation of functional 70s initiation complex which is an essential component of tile bacterial translation process. The mechanism of action of Linezolid (Oxazolidinones) differ from that of other antibiotic classes (e.g., Aminoglycosides, beta-lactams, folic acid , antagonists, glycopeptides, lincosamide, quinilones, rifamycins, streptogramins, tetracyclines, chloramphenicol). Therefore crossresisaence between linezolid and the mentioned classes of antibiotics is unlikely. Linezolid is active against 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 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 protine binding of linezolide is approximately 31% and is concentration independent.The volume of distribution (VD) of Linezolid at steady-state averaged 40 to 50 litters.

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 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 approximately65% 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 40 ml/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:
Vancomycin-resistant Enterococcus faecium(VREF) infection:
linezolid is indicated for the treatment of 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 pneumonia (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 infection:
Caused by staphylococcus aureus (methicillin-susceptible strains only) or streptococcus pyogenes.

DosageIndications	Adults (12 years and older)	Recommended dosage
Vancomycin- resistant Enterococcus faecium (VREF) infection	600mg-12hr I.V. or oral	10-28 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	400mg-12 hr oral	10-14 days

Or
As directed by the physician

CONTRAINDICATIONS:
Linezolid is contraindicated for use in patients who have known hypersensitivity to linezolid or any of the 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 dose of more than 100mg. therefore patients receiving linezolid need to avoid consuming large amount of foods and beverage 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 inhibitor 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, physician 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 no alerted when administered together.
Gentamicin - the pharmacokinetics of linezolid or gentamicin are no alerted 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 potential benefits justify the potential risk to the fetus.

Nursing mothers
Linezolid and its metabolites are excreted in 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 were observed between elderly patients and young 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, Gl 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 while receiving linezolid and should be advised not to drive or operate machinery if dizziness occur.

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

PRESENTATION:
Linezert 400mg tablets in blister pack of 12
Linezert 600mg tablets in blister pack of 12.
Linezert Dry Suspension...100mg/5ml ...60ml bottle

INSTRUCTIONS:
Keep out of reach of children
Avoid exposure to heat, light and humidity.
Store below 30°C.

خوراک:
ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔
ہدایات:
دوا کو روشنی، نمی اور گرمی سے بچائیں۔
دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

صرف رجسٹرڈ ڈاکٹر کے نسخے پر فروخت کریں۔

Manufactured by:

Albert Pharmaceuticals (Pvt.) Ltd.
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