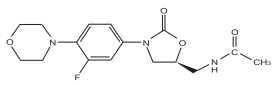
# Ecasil® Tablets / Suspension / Infusion
(Linezolid)

**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:**

**Ecasil® 400mg Tablets**
Each film coated tablet contains:
Linezolid MS.....400mg

**Ecasil® 600mg Tablets**
Each film coated tablet contains:
Linezolid MS.....600mg

**Ecasil® 200mg/100ml Infusion**
Each 100ml contains:
Linezolid MS.....200mg

**Ecasil® 600mg/300ml Infusion**
Each 300ml contains:
Linezolid MS.....600mg

**Ecasil® Dry Powder Suspension 100mg/5ml**
Each 5ml of reconstituted suspension contains:
Linezolid MS.....100mg

**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

**DIRECTION FOR RECONSTITUTION:**
**Ecasil® Dry Powder Suspension 100mg/5ml (60ml)**
Ecasil® suspension is supplied as a dry powder for reconstitution. Shake bottle to loosen the mass. Add one time completely filled provided cup (45ml) with freshly boiled cool water into bottle. Shake well to form uniform suspension. Store reconstituted suspension at the room temperature and consume within 21 days

**INTRAVENOUS (I.V.) ADMINISTRATION:**
Ecasil® (Linezolid) I.V. infusion is supplied in single ready-to-use infusion. Ecasil® (Linezolid) I.V. infusion should be administered by intravenous infusion over a period of 30 to 120 minutes. **Do not use this intravenous infusion in series connections**

Additives should not be introduced into this solution. If Ecasil® (Linezolid) I.V. infusion is to be given concomitantly with another drug, each drug should be given separately in accordance with the recommended dosage and route of administration for each product. In particular, physical incompatibilities resulted when linezolid I.V. infusion was combined with the following drugs during simulated Y - site administration: Amphotericin B, chlorpromazine HCl, diazepam, pentamidine isothionate, erythromycin lactobionate, phenytoin sodium, and trimethoprim / sulfamethoxazole. Additionally, chemical incompatibility resulted when linezolid I.V. infusion was combined with ceftriaxone sodium

Injection may exhibit a yellow color that can intensify with passage of time without adversely affecting potency

**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

**PRESENTATION:**
Ecasil® 400mg tablets in pack of 12's
Ecasil® 600mg tablets in pack of 12's
Ecasil® dry powder suspension 100mg/5ml in pack of 60ml
Ecasil® 200mg/100ml infusion in pack of 1's
Ecasil® 600mg/300ml infusion in pack of 1's

**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

The reconstituted suspension should be kept at room temperature, so that potency of the product remians stable and be used within 21 days

**Caution:** Injection should not be used if container is leaking, solution is cloudy or it contains un-dissolved particle(s)

## ایکاسِل ٹیبلٹ / سسپینشن / انفیوژن
## (لائینزولڈ)

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
تیار شدہ سسپینشن کو کمرے کے درجہ حرارت پر رکھیں تا کہ دوا کی تاثیر برقرار رہے اور ۲۱ یوم کے اندر استعمال کر لیں
تنبیہ: انجکشن کے ایک ہونے، دُھندلا ہونے یا اس میں کوئی غیر حل پذیر شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں

Manufactured by:
**SAMI Pharmaceuticals (Pvt.) Ltd.**
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www.samipharmapk.com

P001948/S R.N-04/HA/10/15

220 mm

71 mm