Obzitic™ (Linezolid)

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QUALITATIVE AND QUANTITATIVE COMPOSITION

Obzitic 600 mg Tablet

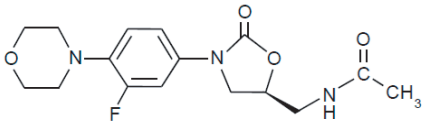
Each film coated Tablet contains:

Linezolid USP.....600 mg

DESCRIPTION

Obzitic 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:



CLINICAL INFORMATION

Indications

- **Vancomycin-Resistant Enterococcus faecium infections**, including cases with concurrent bacteremia
- **Nosocomial pneumonia** caused by Staphylococcus aureus (methicillin-susceptible and resistant strains), or Streptococcus pneumoniae (including multi-drug resistant strains [MDRSP]).
- **Complicated skin and skin structure infections**, including diabetic foot infections, without concomitant osteomyelitis, caused by Staphylococcus aureus (methicillin-susceptible and resistant strains), Streptococcus pyogenes, or Streptococcus agalactiae.
- **Uncomplicated skin and skin structure infections** caused by Staphylococcus aureus (methicillin-susceptible only) or Streptococcus pyogenes.
- **Community-acquired pneumonia** caused by Streptococcus pneumoniae (including multi-drug resistant strains [MDRSP]*), including cases with concurrent bacteremia, or Staphylococcus aureus (methicillin-susceptible strains only).

*MDRSP refers to isolates resistant to two or more of the following antibiotics: penicillin, second-generation cephalosporins, macrolides, tetracycline, and trimethoprim/sulfamethoxazole

DOSAGE AND ADMINISTRATION

INFECTION	DOSAGE AND ROUTE OF ADMINISTRATION (12 YEARS AND OLDER)	RECOMMENDED DURATION OF TREATMENT
Complicated skin and skin structure infections	600 mg oral q12h	10 to 14 days
Community-acquired pneumonia, including concurrent bacteremia		
Nosocomial pneumonia		
Vancomycin-resistant Enterococcus faecium infections, including concurrent bacteremia		14 to 28 days
Uncomplicated skin and skin structure infections		10 to 14 days

Dosage adjustment

Renal impairment

No dose adjustment is recommended for patients with renal insufficiency. Dialysis patients should take Linezolid tablet after dialysis treatment.

Hepatic impairment

No data

Administration requirements

Swallow the whole film coated tablet with some water.

Contraindications

- Known hypersensitivity to linezolid or any of the other product components.
- **Monoamine Oxidase Inhibitors:** Linezolid should not be used in patients taking any medicinal product which inhibits monoamine oxidases A or B (e.g., phenelzine, isocarboxazid) or within two weeks of taking any such medicinal product.

Warning and Precautions

- **Myelosuppression:** including anemia, leukopenia, pancytopenia, and thrombocytopenia may occur in patients receiving linezolid. Discontinuation of therapy with linezolid should be considered in patients who develop or have worsening myelosuppression.
- **Peripheral and Optic Neuropathy:** Can occur in patients treated for longer than 28 days. If patients experience symptoms of visual impairment, prompt ophthalmic evaluation is recommended.
- **Hypoglycemia:** Symptomatic hypoglycemia can occur 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.
- **Clostridioides difficile-Associated Diarrhea:** Evaluate if diarrhea occurs.
- **Potential Interactions producing elevation of blood pressure:** Linezolid should not be administered to patients with uncontrolled hypertension, pheochromocytoma, thyrotoxicosis and/or patients taking any of the following types of medications: directly and indirectly acting sympathomimetic agents (e.g., pseudoephedrine), vasopressive agents (e.g., epinephrine, norepinephrine), dopaminergic agents (e.g., dopamine, dobutamine).
- **Potential Serotonergic Interactions:** Linezolid should not be administered to patients with carcinoid syndrome and/or patients taking any of the following medications: serotonin re-uptake inhibitors, tricyclic antidepressants, serotonin 5-HT_1 receptor agonists (triptans), meperidine or buspirone.
- Lactic acidosis can occur with the use of linezolid.
- Convulsions can occur in patients when treated with linezolid.

Drug Interactions

Drugs Metabolized by Cytochrome P450: Linezolid does not inhibit the activities of clinically significant human CYP isoforms (e.g., 1A2, 2C9, 2C19, 2D6, 2E1, 3A4). Therefore, linezolid is not expected to affect the pharmacokinetics of other drugs metabolized by these major enzymes.

Antibiotics:

Rifampin: Co-administration of rifampin with linezolid resulted in a decrease in linezolid C_{max} and $AUC_{0\text{-}12}$.

Monoamine Oxidase Inhibition: Linezolid is a reversible, nonselective inhibitor of monoamine oxidase. Therefore, linezolid has the potential for interaction with adrenergic and serotonergic agents.

Adrenergic Agents: A significant pressor response can occur in normal adults receiving linezolid and tyramine. Therefore, patients receiving linezolid need to avoid consuming large amounts of foods or beverages with high tyramine content. A reversible enhancement of the pressor response of either pseudoephedrine HCl (PSE) or phenylpropanolamine HCl (PPA) is observed when linezolid is administered to healthy normotensive subjects.

Pregnancy and Breast Feeding

Pregnancy Category C: The effect of Linezolid in pregnant women is not known. Therefore it should not be taken in pregnancy unless advised by doctor. Should not breast-feed when taking Linezolid tablets because it passes into breast milk and could affect the baby.

Effects on ability to drive and use machines

Patients may feel dizzy or experience problems with vision. If this happens, do not drive or operate any machinery.

Adverse Reactions

Hepatobiliary

- Severe diarrhea containing blood and/or mucus (antibiotic associated colitis including pseudomembranous colitis), which in very rare circumstances may develop into complications that are life-threatening (rare).
- Recurrent nausea or vomiting, abdominal pain or rapid breathing (not known).
- Inflammation of the pancreas (uncommon).

Hematologic

- Unexplained bleeding or bruising, which may affect blood clotting or lead to anemia (common).
- Changes in numbers of certain cells in the blood which may affect your ability to fight infection (common) some signs of infection include: any fever (common), sore throat (uncommon), mouth ulcers (uncommon) and tiredness (uncommon).

Vision and Hearing

- Blurred vision (uncommon), changes in colour vision (not known) and difficulty in seeing detail (not known) or field of vision becomes restricted (rare).

• "Ringing" in the ears (tinnitus) (uncommon).
• Numbness, tingling or blurred vision can occur in patients who have been given Linezolid tablets for more than 28 days.

Nervous system disorders
• Fits or seizures (uncommon). Patient should inform if they experience agitation, confusion, delirium, rigidity, tremor, incoordination and seizure while also taking antidepressants like SSRI's (not known).

Psychiatric disorders
Convulsions (uncommon)

Skin and Appendages
• Severe skin disorder swelling, particularly around the face and neck (not known). Skin reactions such as red sore skin and flaking (dermatitis) (uncommon), rash (common), itching (common). Transient ischemic attacks (temporary disturbance of blood flow to the brain causing short term symptoms such as loss of vision, leg and arm weakness, slurring of speech and loss of consciousness) (uncommon).

Overdose
In the event of overdosage, supportive care is advised, with maintenance of glomerular filtration. Haemodialysis may facilitate more rapid elimination of linezolid.

PHARMACOLOGICAL PROPERTIES
Pharmaco therapeutic group
Linezolid is a synthetic antibacterial agent of a new class of antibiotics, the oxazolidinones, 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.

Mechanism of Action
Linezolid inhibits bacterial protein synthesis through a mechanism of action different from that of other antibacterial agents; therefore, cross-resistance between linezolid and other classes of antibiotics is unlikely. 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 an essential component of the bacterial translation process.

Microbiology

Aerobic and facultative Gram-positive microorganisms
Enterococcus faecium (vancomycin-resistant strains only), Staphylococcus aureus (including methicillin-resistant strains), Streptococcus agalactiae, Streptococcus pneumoniae (including multi-drug resistant isolates [MDRSP]) and Streptococcus pyogenes.

Aerobic and facultative Gram-positive microorganisms
Enterococcus faecalis (including vancomycin-resistant strains), Enterococcus faecium (vancomycin-susceptible strains), Staphylococcus epidermidis (including methicillin-resistant strains), Staphylococcus haemolyticus and Viridans group streptococci.

Aerobic and facultative Gram-negative microorganisms
Pasteurella multocida

Pharmacokinetic properties
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.
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 C_{max} 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
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, 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
Nonrenal 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 40 mL/min). 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. However, the difference in clearance was small and was not reflected in the apparent elimination half-life.

Special Populations
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.

PHARMACEUTICAL INFORMATION
Shelf life
2 Years

Special Precautions for Storage
Do not store above 30°C.
Protect from light and moisture.
Keep out of the reach of children.

ہدایات:
۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں۔
دوا کو روشنی اور نمی سے محفوظ رکھیں۔ بچوں کی پہنچ سے دور رکھیں۔

NATURE AND CONTENTS OF CONTAINER
Obzitic (Linezolid) 600 mg tablets are available in a pack of 12's (2 x 6's).

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