Linox
Tablets / Oral Suspension
(Linezolid) USP

لینوکس
ٹیبلیٹس/اورل سسپنشن
(لائینزولڈ)

COMPOSITION:
Linox 400mg Tablets
Each film coated tablet contains: Linezolid USP ... 400mg. [USP Specs.]

Linox 600mg Tablets
Each film coated tablet contains: Linezolid USP ... 600mg. [USP Specs.]

Linox 100mg/5ml Oral Suspension
Each 5ml of reconstituted suspension contains: Linezolid USP ... 100mg. [Innovator's Specs.]

DESCRIPTION: Linox 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.

INDICATIONS: Linox is indicated in adults for the treatment of community acquired pneumonia and nosocomial pneumonia when known or suspected to be caused by susceptible Gram-positive bacteria, also indicated in adults for the treatment of complicated skin and soft tissue infections only when microbiological testing has established that the infection is known to be caused by susceptible Gram-positive bacteria. **Linox** is not active against infections caused by Gram-negative pathogens. **Linox** should only be initiated in a hospital environment and after consultation with a relevant specialist such as a microbiologist or an infectious diseases specialist. Consideration should be given to official guidance on the appropriate use of antibacterial agents.

DOSAGE AND ADMINISTRATION: Linezolid film coated tablets or oral suspension may be used as initial therapy. Patients who commence treatment on the parenteral formulation may be switched to either oral presentation when clinically indicated. In such circumstances, no dose adjustment is required as linezolid has an oral bioavailability of approximately 100%.The duration of treatment is dependent on the pathogen, the site of infection and its severity, and on the patient's clinical response. The maximum treatment duration is 28 days. The safety and effectiveness of Linezolid when administered for periods longer than 28 days have not been established. No increase in the recommended dosage or duration of treatment is required for infections associated with concurrent bacteraemia.
The dose recommendation for the tablets/oral suspension is the following:

Infections	Dosage	Duration of treatment
Nosocomial pneumonia	600mg twice daily	10-14 Consecutive days
Community acquired pneumonia		
Complicated skin and soft tissue infections	600mg twice daily	

Paediatric population: **Linox** should not be administered in children aged < 18 years old.
Elderly: No dose adjustment is required.
Renal & Hepatic impairment: No dose adjustment is required.
Severe renal impairment (i.e. CLCR < 30ml/min): No dose adjustment is required. Due to the unknown clinical significance of higher exposure (up to 10 fold) to the two primary metabolites of Linezolid in patients with severe renal insufficiency, Linezolid should be used with special caution in these patients and only when the anticipated benefit is considered to outweigh the theoretical risk. As approximately 30% of a Linezolid dose is removed during 3 hours of haemodialysis, Linezolid should be given after dialysis in patients receiving such treatment. The primary metabolites of Linezolid are removed to some extent by haemodialysis, therefore, Linezolid should be used with special caution in patients with severe renal insufficiency that are undergoing dialysis and only when the anticipated benefit is considered to outweigh the theoretical risk.
Method of reconstitution of granules for oral suspension: Loosen the powder by shaking the bottle. To prepare 60ml oral suspension use provided measuring cup to add 45ml boiled cool water. Close the cap tightly and shake vigorously. Reconstituted suspension should be used within 3 weeks. The appearance after reconstitution is a white to yellow-orange suspension. Before use, gently invert the bottle a few times. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
Method of administration: The recommended Linezolid dosage should be administered orally twice daily. The oral suspension or film coated tablets may be taken with or without food. The film-coated tablets should be swallowed whole with some water. A 600mg dose is provided by 30ml of reconstituted suspension (i.e. six 5ml spoonful).

CLINICAL PHARMACOLOGY: Pharmacodynamics: Linezolid selectively inhibits bacterial protein synthesis via a unique mechanism of action. Specifically, it binds to a site on the bacterial ribosome (23S of the 50S subunit) and prevents the formation of a functional 70S initiation complex which is an essential component of the translation process.
Pharmacokinetics: Linezolid primarily contains (s)-Linezolid which is biologically active and is metabolised to form inactive derivatives. Linezolid is 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, without regards to the timings of meal. Volume of distribution at steady-state averages at about 40-50 litres in healthy adults and approximates to total body water. Plasma protein binding is about 31% and is not concentration dependent. Linezolid is primarily metabolised by oxidation of the morpholine ring resulting mainly in the formation of two inactive open-ring carboxylic acid derivatives; the aminoethoxyacetic acid metabolite (PNU-142300) and the hydroxyethyl glycine metabolite (PNU-142586). The hydroxyethyl glycine metabolite (PNU-142586) is the predominant human metabolite and is believed to be formed by a non-enzymatic process. The aminoethoxyacetic acid metabolite (PNU-142300) is less abundant. Other minor, inactive metabolites have been characterised. In patients with normal renal function or mild to moderate renal insufficiency, Linezolid is primarily excreted under steady-state conditions in the urine. Virtually no parent drug is found in the faeces. The elimination half-life of Linezolid averages at about 5-7 hours.

Rev: 07-23/1/NQ.

CONTRAINDICATIONS: Hypersensitivity to Linezolid or to any of the excipients.Linezolid should not be used in patients taking any medicinal product which inhibits monoamine oxidases A or B (e.g. phenelzine, isocarboxazid, selegiline, moclobemide) or within two weeks of taking any such medicinal product. Unless there are facilities available for close observation and monitoring of blood pressure, Linezolid should not be administered to patients with the following underlying clinical conditions or on the following types of concomitant medications: • Patients with uncontrolled hypertension, phaeochromocytoma, carcinoid, thyrotoxicosis, bipolar depression, schizoaffective disorder, acute confusional states. • Patients taking any of the following medications: serotonin re-uptake inhibitors, tricyclic antidepressants, serotonin 5-HT1 receptor agonists (triptans), directly and indirectly acting sympathomimetic agents (including the adrenergic bronchodilators, pseudoephedrine and phenylpropanolamine), vasopressive agents (e.g. epinephrine, norepinephrine), dopaminergic agents (e.g. dopamine, dobutamine), pethidine or buspirone.

WARNING & PRECAUTION: Myelosuppression has been reported in patients receiving Linezolid. Discontinuation of therapy with Linezolid should be considered in patients who develop or have worsening myelosuppression. Peripheral and optic neuropathies have been reported in patients treated with Linezolid, primarily in those patients treated for longer than the maximum recommended duration of 28 days. If patients experience symptoms of visual impairment, such as changes in visual acuity, changes in color vision, blurred vision, or visual field defect, prompt ophthalmic evaluation is recommended. If peripheral or optic neuropathy occurs, the continued use of Linezolid in these patients should be weighed against the potential risks. Spontaneous reports of serotonin syndrome including fatal cases associated with the co-administration of Linezolid and serotonergic agents, including antidepressants such as selective serotonin reuptake inhibitors (SSRIs), have been reported. Unless clinically appropriate and patients are carefully observed for signs and/or symptoms of serotonin syndrome or neuroleptic malignant syndrome-like (NMS-like) reactions, 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-HT1 receptor agonists (triptans), meperidine, bupropion, or buspirone). Linezolid is not approved and should not be used for the treatment of patients with catheter-related bloodstream infections or catheter-site infections. Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including Linezolid, and may range in severity from mild diarrhea to fatal colitis. Patients who develop recurrent nausea or vomiting, unexplained acidosis, or a low bicarbonate level while receiving Linezolid should receive immediate medical evaluation. Convulsions have been reported in patients when treated with Linezolid. In some of these cases, a history of seizures or risk factors for seizures was reported.

FERTILITY, PREGNANCY AND LACTATION:
Pregnancy: Linezolid should not be used during pregnancy unless clearly necessary i.e. only if the potential benefit outweighs the theoretical risk.
Breast-feeding: Breast-feeding should be discontinued prior to and throughout administration.
Fertility: Linezolid caused a reduction in fertility.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES: Patients should be warned about the potential for dizziness or symptoms of visual impairment whilst receiving Linezolid and should be advised not to drive or operate machinery if any of these symptoms occurs.

SIDE EFFECTS: Those most commonly reported side effects were diarrhoea (8.4%), headache (6.5%), nausea (6.3%) and vomiting (4.0%). The other commonly reported drug-related adverse events which led to discontinuation of treatment were headache, diarrhoea, nausea and vomiting. Other common adverse effects include: Candidiasis, oral candidiasis, vaginal candidiasis, fungal infections, anemia, insomnia, headache, taste perversion (metallic taste) dizziness, hypertension, diarrhoea, nausea, vomiting, localized or general abdominal pain, constipation, dyspepsia, abnormal liver function test; increased AST, ALT or alkaline, phosphatase, pruritus, rash, Increased BUN, fever, localised pain, increased LDH, creatine kinase, lipase, amylase or non-fasting glucose, decreased total protein, albumin, sodium or calcium, increased or decreased potassium or bicarbonate, *haematology* increased neutrophils or eosinophils, decreased haemoglobin, haematocrit or red blood cell count, increased or decreased platelet or white blood cell counts.

DRUG INTERACTION: Linezolid is a reversible, non-selective inhibitor of monoamine oxidase (MAOI). Therefore, co-administration is contraindicated. Co-administration of Linezolid with either pseudoephedrine or phenylpropanolamine resulted in mean increases in systolic blood pressure of the order of 30-40 mmHg, compared with 11-15 mmHg increases with Linezolid alone, 14-18 mmHg with either pseudoephedrine or phenylpropanolamine alone and 8-11 mmHg with placebo. During clinical use of Linezolid with serotonergic agents, including antidepressants such as selective serotonin reuptake inhibitors (SSRIs), cases of serotonin syndrome have been reported. Therefore, co-administration is contraindicated. No significant pressor response was observed in subjects receiving both Linezolid and less than 100mg tyramine. This suggests that it is only necessary to avoid ingesting excessive amounts of food and beverages with a high tyramine content (e.g. mature cheese, yeast extracts, undistilled alcoholic beverages and fermented soya bean products such as soy sauce). Linezolid is not detectably metabolised by the cytochrome P450 (CYP) enzyme system and it does not inhibit any of the clinically significant human CYP isoforms (1A2, 2C9, 2C19, 2D6, 2E1, 3A4). When warfarin was added to Linezolid therapy at steady-state, there was a 10% reduction in mean maximum INR on co-administration with a 5% reduction in AUC INR.

OVERDOSAGE: No specific antidote is known. Supportive care is advised together with maintenance of glomerular filtration. Approximately 30% of a linezolid dose (primary metabolites of linezolid) is removed during 3 hours of haemodialysis.

INSTRUCTIONS: Store below 30° C. Protect from heat, light and moisture. Keep out of the reach of children. Keep the bottle tightly closed.

PRESENTATION:
Linox Tablet 400mg are available in pack of 12's.
Linox Tablet 600mg are available in pack of 12's.
Linox 100mg/5ml Oral Suspension is available in pack size of 60ml.

ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔ استعمال کے بعد ڈھکن کو اچھی طرح بند کردیں۔

Manufactured by:
NABIQASIM INDUSTRIES (PVT.) LTD.
17/24, Korangi Industrial Area, Karachi-Pakistan.
PHARMA
Rev: 07-23/1/NQ.