Linze

200mg/100ml
600mg/300ml
I.V. Infusion

(Linezolid USP)

لنز

۲۰۰ ملی گرام/۱۰۰ ملی لیٹر انفیوژن
۶۰۰ ملی گرام/۳۰۰ ملی لیٹر انفیوژن
I.V. انفیوژن
(لائینزولڈ یو ایس پی)

COMPOSITION:
Each 100ml contains: Linezolid USP ... 200mg. [Surge Specs.]
Each 300ml contains: Linezolid USP ... 600mg. [Surge Specs.]

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.

INDICATIONS: **Linze IV Infusion** 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. **Linze IV Infusion** is not active against infections caused by Gram-negative pathogens. **Linze IV Infusion** should only be initiated in a hospital environment and after consultation with a relevant specialist such as a microbiologist or an infectious diseases specialist.

DOSAGE AND ADMINISTRATION: **Linze IV Infusion** 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 solution for Infusion 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: The safety and efficacy of Linezolid in children aged (< 18 years old) has not been established.
Elderly: No dose adjustment is required.
Renal impairment: No dose adjustment is required
Hepatic impairment: No dose adjustment is required.
Severe renal impairment (i.e. CLCR < 30 ml/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 who are undergoing dialysis and only when the anticipated benefit is considered to outweigh the theoretical risk.
Method of administration: The recommended **Linze IV Infusion** dosage should be administered intravenously (IV) twice daily. The solution for infusion should be administered intravenously over a period of 30 to 120 minutes.

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.

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ADVERSE 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.

OVERDOSAGE: Supportive care is advised together with maintenance of glomerular filtration. Approximately 30% of a Linezolid dose is removed during 3 hours of haemodialysis, but no data are available for the removal of Linezolid by peritoneal dialysis or haemoperfusion. The two primary metabolites of Linezolid are also removed to some extent by haemodialysis.

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.

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 100 mg 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). The effect of rifampicin on the pharmacokinetics of Linezolid was studied in sixteen healthy adult male volunteers administered Linezolid 600mg twice daily for 2.5 days with and without rifampicin 600 mg once daily for 8 days. 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.

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

INSTRUCTIONS: For single I.V. use only. Store below 30°C. Protect from heat & light (Store in orignal package until ready to use in order to protect from light). Keep out of the reach of children. Avoid freezing and do not use if container is leaking, solution is cloudy or it contains undissolved particles.

PRESENTATION: Linze IV Infusion 200mg/100ml & 600mg/300ml (Linezolid) is available in pack of 1's.

ہدایات: صرف ایک دفعہ استعمال کریں۔ ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ روشنی اور گرمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔
منجمد ہونے سے بچائیں۔ بوتل کے لیک ہونے، دھندلا ہونے یا اس میں کوئی غیر حل پزیر شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں۔

Manufactured by: **Surge Laboratories (Pvt.) Ltd.**
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