NOCOQUE
Linezolid Tablets 600 mg

COMPOSITION
Each Film Coated Tablet Contains:
Linezolid USP 600 mg
Excipients q.s.
Colour: Titanium Dioxide BP

DESCRIPTION
NOCOQUE contains Linezolid belongs to the class of medicines called oxazolidinones used to treat bacterial infections of the lungs (pneumonia), and skin.

PHARMACODYNAMICS
Pharmacotherapeutic group: Other antibacterials, ATC code: J 01 X X 08.
Mode of action
Linezolid is a synthetic, antibacterial agent that belongs to a new class of antimicrobials, the oxazolidinones. It has in vitro activity against aerobic Gram positive bacteria and anaerobic micro-organisms. 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
Absorption
Linezolid is rapidly and extensively absorbed following oral dosing. Maximum plasma concentrations are reached within 2 hours of dosing. Absolute oral bioavailability of linezolid (oral and intravenous dosing in a crossover study) is complete (approximately 100%). Absorption is not significantly affected by food and absorption from the oral suspension is similar to that achieved with the film-coated tablets.
Distribution
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.
Biotransformation
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.
Elimination
In patients with normal renal function or mild to moderate renal insufficiency, linezolid is primarily excreted under steady-state conditions in the urine as PNU-142586 (40%), parent drug (30%) and PNU-142300 (10%). Virtually no parent drug is found in the faeces whilst approximately 6% and 3% of each dose appears as PNU-142586 and PNU-142300, respectively. The elimination half-life of linezolid averages at about 5-7 hours.

THERAPEUTIC INDICATIONS
NOCOQUE is indicated for the treatment of infections caused by susceptible strains of the designated microorganisms in the specific conditions listed below.
NOCOQUE is not indicated for the treatment of Gram-negative infections. It is critical that specific Gram-negative therapy be initiated immediately if a concomitant Gram-negative pathogen is documented or suspected
-Pneumonia
Nosocomial pneumonia caused by *Staphylococcus aureus (methicillin-susceptible and -resistant isolates) or Streptococcus pneumoniae.*
Community-acquired pneumonia *caused by Streptococcus pneumoniae, including cases with concurrent bacteremia, or Staphylococcus aureus* (methicillin-susceptible isolates only)
-Skin and Skin Structure Infections
Complicated skin and skin structure infections, including diabetic foot infections, concomitant osteomyelitis, *caused by Staphylococcus aureus (methicillin-susceptible and -resistant isolates), Streptococcus pyogenes, or Streptococcus agalactiae.*
NOCOQUE has not been studied in the treatment of decubitus ulcers
Uncomplicated skin and skin structure infections caused by *Staphylococcus aureus* (methicillin-susceptible isolates only) or *Streptococcus pyogenes*
-Vancomycin-resistant *Enterococcus faecium Infections*
Vancomycin-resistant *Enterococcus faecium infections,* including cases with concurrent bacteremia

POSOLOGY AND METHOD OF ADMINISTRATION
The recommended dosage for NOCOQUE formulations for the treatment of infections is described in Table.

Infection*	Dosage, Route and Frequency of Administration		Recommended Duration of Treatment (consecutive days)
	Pediatric Patients† (Birth through 11 Years of Age)	Adults and Adolescents (12 Years and Older)	
Nosocomial pneumonia	10 mg/kg intravenously or oral‡every 8 hours	600 mg intravenously or oral‡every 12 hours	10 to 14
mmunity acquired pneumonia, including concurrent bacteremia			
Complicated skin and skin structure infections			
Vancomycin resistant Enterococcus faecium infections, including concurrent bacteremia	10 mg/kg intravenously or oral‡every 8 hours	600 mg intravenously or oral‡every 12 hours	14 to 28
Uncomplicated skin and skin structure infections	less than 5 yrs: 10 mg/kg oral‡every 8 hours 5-11 yrs: 10 mg/kg oral‡ every 12 hours	Adults: 400 mg oral‡every 12 hours Adolescents: 600 mg oral‡every 12 hours	10 to 14

Due to the designated pathogens
†Neonates <7 days: Most pre-term neonates <7 days of age (gestational age <34 weeks) have lower systemic linezolid clearance values and larger AUC values than many full-term neonates and older infants. These neonates should be initiated with a dosing regimen of 10 mg/kg every 12 hours. Consideration may be given to the use of 10 mg/kg every 8 hours regimen in neonates with a sub-optimal clinical response. All neonatal patients should receive 10 mg/kg every 8 hours by 7 days of life.
‡Oral dosing using either NOCOQUE Tablets or NOCOQUE for Oral Suspension
No dose adjustment is necessary when switching from intravenous to oral administration.

Method of administration:
Route of administration: Oral use.

CONTRAINDICATION
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.

SPECIAL WARNING AND PRECAUTION FOR USE
Do not take Linezolid Tablets:
- if you are allergic to linezolid or any of the other ingredients of this medicine.
- if you are taking or have taken within the last 2 weeks any medicines known as monoamine oxidase inhibitors (MAOIs, for example phenelzine, isocarboxazid, selegiline, moclobemide). These medications may be used to treat depression or Parkinson's disease.
- if you are breast-feeding. This is because it passes into breast milk and could affect the baby.

Take special care with Linezolid
Talk to your doctor or pharmacist before taking Linezolid Tablets if you:
- bruise and bleed easily
- are anaemic (have low red blood cells)
- are prone to getting infections
- have a history of seizures
- have liver problems or kidney problems particularly if you are on have dialysis
- have diarrhoea.

Tell your doctor immediately if you suffer from any of the following during treatment:
- problems with your vision such as blurred vision, changes in colour vision, difficulty in seeing detail or if your field of vision becomes restricted.
- loss of sensitivity in your arms or legs or a sensation of tingling or pricking in your arms or legs.
- you may develop diarrhoea while taking or after taking antibiotics, including Linezolid. If this becomes severe or persistent or you notice that your stools contains blood or mucus, you should stop taking Linezolid tablets immediately and consult your doctor. In this situation, you should not take medicines that stop or slow bowel movement.
- recurrent nausea or vomiting, abdominal pain or rapid breathing.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION
- **Drug-Drug Interactions:** LINEZOLID may have interaction with anti-asthma (albuterol, ipratropium), antihistamine (diphenhydramine), diuretics (furosemide), anti-emetic (ondansetron), anti-hypertensive agent (metoprolol).
- **Drug-Food Interactions:** Avoid foods and drinks containing tyramine such as cheese, yeast extracts, soybean extracts, alcohol, beer or wine while taking LINEZOLID as it may react with tyramine and lead to increase in blood pressure.
- **Drug-Disease Interactions:** LINEZOLID may have interactions with colitis (inflammation in the lining of the colon), seizures, high blood pressure, acidosis (increased acidity in the blood), carcinoid syndrome (cancerous tumour which secretes chemicals into the bloodstream), hemodialysis, hypoglycaemia (low blood sugar levels), neuropathy, kidney and liver dysfunction.

PREGNACY, LACTATION & FERTILITY
Pregnancy
There are limited data from the use of linezolid in pregnant women.
Linezolid should not be used during pregnancy unless clearly necessary i.e. only if the potential benefit outweighs the theoretical risk.
Breast-feeding
Linezolid is excreted in human milk. A risk to the suckling child cannot be excluded.
Breast-feeding should be discontinued during treatment with Linezolid 600 mg Tablets.
Fertility
In animal studies, 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.
UNDESIRABLE EFFECTS
Like all medicines, this medicine can cause side effects, although not everybody gets them.
The serious side effects of Linezolid tablets are:
- Severe skin disorder (not known), swelling particularly around the face and neck (not known), wheezing and/or difficulty breathing (not known). This may be the sign of an allergic reaction and it may be necessary for you to stop taking these tablets. Skin reactions such as red sore skin and flaking (dermatitis) (uncommon), rash (common), itching (common).
- Problems with your vision such as blurred vision (uncommon), changes in colour vision (not known), difficulty in seeing detail (not known) or if your field of vision becomes restricted (rare).
- Severe diarrhoea containing blood and/or mucus (antibiotic associated colitis including pseudomembranous colitis), which in rare circumstances may develop into complications that are life-threatening (rare).
- Recurrent nausea or vomiting, abdominal pain or rapid breathing (not known).
- Fits or seizures (uncommon) have been reported with Linezolid Tablets. You should let your doctor know if you experience agitation, confusion, delirium, rigidity, tremor, incoordination and seizure while also taking antidepressants known as SSRIs (not known).
- Unexplained bleeding or bruising, which may be due to changes in the numbers of certain cells in the blood which may affect blood clotting or lead to anaemia (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).
- Inflammation of the pancreas (uncommon).
- Convulsions (uncommon).
- Transient ischaemic 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).
- "Ringing" in the ears (tinnitus) (uncommon).
- Numbness, tingling or blurred vision have been reported by patients who have been given Linezolid Tablets for more than 28 days. If you experience difficulties with your vision you should consult your doctor as soon as possible.

Other side effects include:
Common (may affect up to 1 in 10 people):
- Fungal infections especially vaginal or oral "thrush"
- Headache
- Metallic taste in the mouth
- Diarrhoea, nausea or vomiting
- Changes in some blood test results including those measuring your kidney or liver function or blood sugar levels
- Difficulty in sleeping
- Increased blood pressure
- Anaemia (low red blood cell)
- Dizziness
- Localised or general abdominal pain
- Constipation
- Indigestion
- Localised pain

Uncommon (may affect up to 1 in 100 people)
- Inflammation of the vagina or genital area in women
- Sensations such as tingling or feeling numb
- Inflammation of the veins (IV only)
- sore, swollen or discoloured tongue
- A need to urinate more often
- Chills
- Feeling thirsty
- Increased sweating
- Changes in proteins, salts or enzymes in the blood which measure kidney or liver function.
- Hyponatraemia (low blood sodium levels)
- Kidney failure
- Reduction in platelets
- Abdominal bloating
- Injection site pain
- Increase in creatinine
- Stomach pain
- Changes in heart rate (e.g. increase rate)

Rare (may affect up to1 in 1000 people):
- Restricted field of vision
- Superficial tooth discolouration, removable with professional dental cleaning (manual descaling)

The following side effects have also been reported not known (frequency cannot be estimated from the available data):
- Alopecia (hair loss)
- Decrease of the blood cell count
- Weakness and/or sensory changes

OVERDOSE
No specific antidote is known.
No cases of overdose have been reported. However, the following information may prove useful:
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.

INCOMPATIBILITY
Not applicable.

SHELF LIFE:
36 months

PACKAGING
10 Tablets are packed in Alu-Alu Blister and such 1 blister is packed in a printed carton along with pack insert.

STORAGE
Store at a temperature below 30^{0}C. Protect from direct sunlight, heat and moisture.
Keep the medicine out of reach of children.

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MANUFACTURED BY:
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