Oxzorid Tablet
Linezolid

آگزورڈ ٹیبلیٹ
(لینزولیڈ)

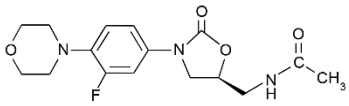
400mg, 600mg Tablets
100mg/5ml Dry Powder Suspension

۴۰۰ ملی گرام، ۶۰۰ ملی گرام ٹیبلیٹس
۱۰۰ ملی گرام/۵ ملی لیٹر ڈرائی پاؤڈر سسپنشن

1 DESCRIPTION

OXZORID Tablets, and OXZORID for Oral Suspension 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 C16H20FN3O4. Its molecular weight is 337.35, and its chemical structure is represented below:



COMPOSITION:
Oxzorid 400 mg Tablets:
Each film-coated tablet contains 400 mg linezolid.
(USP Specification)

Oxzorid 600 mg Tablets:
Each film-coated tablet contains 600 mg linezolid.
(USP Specification)

Oxzorid Dry Powder Suspension:
Each 5ml reconstituted suspension contains 100mg linezolid.
(As per Innovator Specification)

2 INDICATIONS AND USAGE

OXZORID is indicated for the treatment of infections caused by susceptible strains of the designated microorganisms in the specific conditions listed below. OXZORID 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 [see Warnings and Precautions.

2.1 Pneumonia
Nosocomial pneumonia caused by Staphylococcus aureus (methicillin-susceptible and -resistant isolates) or Streptococcus pneumoniae [see Clinical Studies.

Community-acquired pneumonia caused by Streptococcus pneumoniae, including cases with concurrent bacteremia, or Staphylococcus aureus (methicillin-susceptible isolates only) [see Clinical Studies.

2.2 Skin and Skin Structure Infections
Complicated skin and skin structure infections, including diabetic foot infections, without concomitant osteomyelitis, caused by Staphylococcus aureus (methicillin-susceptible and -resistant isolates), Streptococcus pyogenes, or Streptococcus agalactiae. OXZORID has not been studied in the treatment of decubitus ulcers [see Clinical Studies].

Uncomplicated skin and skin structure infections caused by Staphylococcus aureus (methicillin-susceptible isolates only) or Streptococcus pyogenes [see Clinical Studies.

2.3 Vancomycin-resistant Enterococcus faecium Infections
Vancomycin-resistant Enterococcus faecium infections, including cases with concurrent bacteremia [see Clinical Studies].

2.4 Usage
To reduce the development of drug-resistant bacteria and maintain the effectiveness of OXZORID and other antibacterial drugs, OXZORID should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

The safety and efficacy of OXZORID formulations given for longer than 28 days have not been evaluated in controlled clinical trials.

3 DOSAGE AND ADMINISTRATION

3.1 General Dosage and Administration
The recommended dosage for OXZORID formulations for the treatment of infections is described in Table 1.

Infection *	Dosage and Route 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 Community-acquired pneumonia, including concurrent bacteremia Complicated skin and skin structure infections	10 mg/kg intravenously or oral ‡ every 8 hours	600 mg intravenously or oral ‡ every 12 hours	10 to 14
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	<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 [see Indications and Usage (1)]
† 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 [see Use in Specific Populations (8.4) and Clinical Pharmacology (12.3)]. ‡ Oral dosing using either OXZORID Tablets or OXZORID for Oral Suspension [see How Supplied/Storage and Handling.

No dose adjustment is necessary when switching from intravenous to oral administration.

3.2 Constitution of Oral Suspension
OXZORID for Oral Suspension is supplied as a powder/granule for constitution. Gently tap bottle to loosen powder. Add a total of 123 mL distilled water in two portions. After adding the first half, shake vigorously to wet all of the powder. Then add the second half of the water and shake vigorously to obtain a uniform suspension. After constitution, each 5 mL of the suspension contains 100 mg of linezolid. Before using, gently mix by inverting the bottle 3 to 5 times. Do not shake. Store constituted suspension at room temperature. Use within 21 days after constitution.

4 CONTRAINDICATIONS

4.1 Hypersensitivity
OXZORID formulations are contraindicated for use in patients who have known hypersensitivity to linezolid or any of the other product components.

4.2 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.

5 WARNINGS AND PRECAUTIONS

5.1 Myelosuppression
Myelosuppression (including anemia, leukopenia, pancytopenia, and thrombocytopenia) has been reported in patients receiving linezolid. In cases where the outcome is known, when linezolid was discontinued, the affected hematologic parameters have risen toward pretreatment levels. Complete blood counts should be monitored weekly in patients who receive linezolid, particularly in those who receive linezolid for longer than two weeks, those with pre-existing myelosuppression, those receiving concomitant drugs that produce bone marrow suppression, or those with a chronic infection who have received previous or concomitant antibiotic therapy. Discontinuation of therapy with linezolid should be considered in patients who develop or have worsening myelosuppression.

5.2 Peripheral and Optic Neuropathy
Peripheral and optic neuropathies have been reported in patients treated with OXZORID, primarily in those patients treated for longer than the maximum recommended duration of 28 days. In cases of optic neuropathy that progressed to loss of vision, patients were treated for extended periods beyond the maximum recommended duration. Visual blurring has been reported in some patients treated with OXZORID for less than 28 days. Peripheral and optic neuropathy has also been reported in children.

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. Visual function should be monitored in all patients taking OXZORID for extended periods (≥ 3 months) and in all patients reporting new visual symptoms regardless of length of therapy with OXZORID. If peripheral or optic neuropathy occurs, the continued use of OXZORID in these patients should be weighed against the potential risks.

5.3 Serotonin Syndrome

Spontaneous reports of serotonin syndrome including fatal cases associated with the co-administration of OXZORID 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 [see Drug Interactions (7) and Clinical Pharmacology.

In some cases, a patient already receiving a serotonergic antidepressant or buspirone may require urgent treatment with linezolid. If alternatives to linezolid are not available and the potential benefits of linezolid outweigh the risks of serotonin syndrome or NMS-like reactions, the serotonergic antidepressant should be stopped promptly and linezolid administered. The patient should be monitored for two weeks (five weeks if fluoxetine was taken) or until 24 hours after the last dose of linezolid, whichever comes first. Symptoms of serotonin syndrome or NMS-like reactions include hyperthermia, rigidity, myoclonus, autonomic instability, and mental status changes that include extreme agitation progressing to delirium and coma. The patient should also be monitored for discontinuation symptoms of the antidepressant (see package insert of the specified agent(s) for a description of the associated discontinuation symptoms).

5.4 Mortality Imbalance in an Investigational Study in Patients with Catheter-Related Bloodstream Infections, including those with catheter-site infections

An imbalance in mortality was seen in patients treated with linezolid relative to vancomycin/dicloxacillin/oxacillin in an open-label study in seriously ill patients with intravascular catheter-related infections [78/363 (21.5%) vs.
58/363 (16.0%); odds ratio 1.426, 95% CI 0.970, 2.098]. While causality has not been established, this observed imbalance occurred primarily in linezolid-treated patients in whom either Gram-negative pathogens, mixed Gram- negative and Gram-positive pathogens, or no pathogen were identified at baseline, but was not seen in patients with Gram-positive infections only.

Linezolid is not approved and should not be used for the treatment of patients with catheter-related bloodstream infections or catheter-site infections.

Linezolid has no clinical activity against Gram-negative pathogens and 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 [see Indications and Usage.

5.5 Clostridium difficile Associated Diarrhea

Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including OXZORID, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of C. difficile.

C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of C. difficile cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use.

Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against C. difficile may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic treatment of C. difficile, and surgical evaluation should be instituted as clinically indicated.

5.6 Potential Interactions Producing Elevation of Blood Pressure

Unless patients are monitored for potential increases in 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) [see Drug Interactions (7) and Clinical Pharmacology .

5.7 Lactic Acidosis

Lactic acidosis has been reported with the use of OXZORID. In reported cases, patients experienced repeated episodes of nausea and vomiting. Patients who develop recurrent nausea or vomiting, unexplained acidosis, or a low bicarbonate level while receiving OXZORID should receive immediate medical evaluation.

5.8 Convulsions

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.

5.9 Hypoglycemia

Postmarketing cases of symptomatic hypoglycemia have been reported in patients with diabetes mellitus receiving insulin or oral hypoglycemic agents when treated with linezolid, a reversible, nonselective MAO inhibitor. Some MAO inhibitors have been associated with hypoglycemic episodes in diabetic patients receiving insulin or hypoglycemic agents. While a causal relationship between linezolid and hypoglycemia has not been established, diabetic patients should be cautioned of potential hypoglycemic reactions when treated with linezolid.

If hypoglycemia occurs, a decrease in the dose of insulin or oral hypoglycemic agent, or discontinuation of oral hypoglycemic agent, insulin, or linezolid may be required.

5.10 Development of Drug-Resistant Bacteria

Prescribing OXZORID in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Adults:

The safety of OXZORID formulations was evaluated in 2046 adult patients enrolled in seven Phase 3 comparator- controlled clinical trials, who were treated for up to 28 days.

Of the patients treated for uncomplicated skin and skin structure infections (uSSSIs), 25.4% of OXZORID-treated and 19.6% of comparator-treated patients experienced at least one drug-related adverse event. For all other indications, 20.4% of OXZORID -treated and 14.3% of comparator-treated patients experienced at least one drug-related adverse event.

Table 2 shows the incidence of all-causality, treatment-emergent adverse reactions reported in at least 1% of adult patients in these trials by dose of OXZORID.

ADVERSE REACTIONS	Uncomplicated Skin and Skin Structure Infections		All Other Indications	
	OXZORID400 mg by mouth every 12 hours (n=548)	Clarithromycin 250 mg by mouth every 12 hours (n=537)	OXZORID 600 mg every 12 hours (n=1498)	All Other Comparators* (n=1464)
Headache	8.8	8.4	5.7	4.4
Diarrhea	8.2	6.1	8.3	6.4
Nausea	5.1	4.5	6.6	4.6
Vomiting	2.0	1.5	4.3	2.3
Dizziness	2.6	3.0	1.8	1.5
Rash	1.1	1.1	2.3	2.6
Anemia	0.4	0	2.1	1.4
Taste alteration	1.8	2.0	1.0	0.3
Vaginal moniliasis	1.8	1.3	1.1	0.5
Oral moniliasis	0.5	0	1.7	1.0
Abnormal liver function tests	0.4	0.2	1.6	0.8
Fungal infection	1.5	0.2	0.3	0.2
Tongue discoloration	1.3	0	0.3	0
Localized abdominal pain	1.3	0.6	1.2	0.8
Generalized abdominal pain	0.9	0.4	1.2	1.0

* Comparators included cefpodoxime proxetil 200 mg by mouth every 12 hours; ceftriaxone 1 g intravenously every 12 hours; dicloxacillin 500 mg by mouth every 6 hours; oxacillin 2 g intravenously every 6 hours; vancomycin 1 g intravenously every 12 hours.

Of the patients treated for uSSSIs, 3.5% of OXZORID -treated and 2.4% of comparator-treated patients discontinued treatment due to drug-related adverse events. For all other indications, discontinuations due to drug-related adverse events occurred in 2.1% of OXZORID -treated and 1.7% of comparator-treated patients. The most common reported drug-related adverse events leading to discontinuation of treatment were nausea, headache, diarrhea, and vomiting.

Pediatric Patients:
The safety of OXZORID formulations was evaluated in 215 pediatric patients ranging in age from birth through 11 years, and in 248 pediatric patients aged 5 through 17 years (146 of these 248 were age 5 through 11 and 102 were age 12 to 17). These patients were enrolled in two Phase 3 comparator-controlled clinical trials and were treated for up to 28 days. In the study of hospitalized pediatric patients (birth through 11 years) with Gram-positive infections, who were randomized 2 to 1 (linezolid: vancomycin), mortality was 6.0% (13/215) in the linezolid arm and 3.0% (3/101) in the vancomycin arm. However, given the severe underlying illness in the patient population, no causality could be established.

Of the pediatric patients treated for uSSSIs, 19.2% of OXZORID-treated and 14.1% of comparator-treated patients experienced at least one drug-related adverse event. For all other indications, 18.8% of OXZORID- treated and 34.3% of comparator-treated patients experienced at least one drug-related adverse event.

Table 3 shows the incidence of all-causality, treatment-emergent adverse reactions reported in more than 1% of pediatric patients (and more than 1 patient) in either treatment group in the comparator-controlled Phase 3 trials.

ADVERSE REACTIONS	Uncomplicated Skin and Skin Structure Infections*		All Other Indications†	
	ZYVOX (n=248)	Cefadroxil (n=251)	ZYVOX (n=215)	Vancomycin (n=101)
Diarrhea	7.8	8.0	10.8	12.1
Vomiting	2.9	6.4	9.4	9.1
Headache	6.5	4.0	0.9	0
Anemia	0	0	5.6	7.1
Thrombocytopenia	0	0	4.7	2.0
Nausea	3.7	3.2	1.9	0
Generalized abdominal pain	2.4	2.8	0.9	2.0
Localized abdominal pain	2.4	2.8	0.5	1.0
Loose stools	1.6	0.8	2.3	3.0
Eosinophilia	0.4	0.8	1.9	1.0
Pruritus at non-application site	0.8	0.4	1.4	2.0
Vertigo	1.2	0.4	0	0

* Patients 5 through 11 years of age received ZYVOX 10 mg/kg by mouth every 12 hours or cefadroxil 15 mg/kg by mouth every 12 hours. Patients 12 years or older received ZYVOX 600 mg by mouth every 12 hours or cefadroxil 500 mg by mouth every 12 hours.
† Patients from birth through 11 years of age received ZYVOX 10 mg/kg intravenously by mouth every 8 hours or vancomycin 10 to 15 mg/kg intravenously every 6-24 hours, depending on age and renal clearance.

Of the pediatric patients treated for uSSSIs, 1.6% of OXZORID-treated and 2.4% of comparator-treated patients discontinued treatment due to drug-related adverse events. For all other indications, discontinuations due to drug-related adverse events occurred in 0.9% of OXZORID-treated and 6.1% of comparator-treated patients.

7 DRUG INTERACTIONS

7.1 Monoamine Oxidase Inhibitors
Linezolid is a reversible, nonselective inhibitor of monoamine oxidase. [see Contraindications.

7.2 Adrenergic and Serotonergic Agents
Linezolid has the potential for interaction with adrenergic and serotonergic agents. [see Warnings and Precautions.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Teratogenic Effects – Pregnancy Category C
Linezolid was not teratogenic in mice, rats, or rabbits at exposure levels 6.5-fold (in mice), equivalent to (in rats), or 0.06-fold (in rabbits) the expected human exposure level, based on AUCs. However, embryo and fetal toxicities were seen (see Non-teratogenic Effects). There are no adequate and well-controlled studies in pregnant women. OXZORID should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Non-teratogenic Effects
In mice, embryo and fetal toxicities were seen only at doses that caused maternal toxicity (clinical signs and reduced body weight gain). A dose of 450 mg/kg/day (6.5-fold the estimated human exposure level based on AUCs) correlated with increased postimplantational embryo death, including total litter loss, decreased fetal body weights, and an increased incidence of costal cartilage fusion.

In rats, mild fetal toxicity was observed at 15 and 50 mg/kg/day (exposure levels 0.22-fold to approximately equivalent to the estimated human exposure, respectively, based on AUCs). The effects consisted of decreased fetal body weights and reduced ossification of sternebrae, a finding often seen in association with decreased fetal body weights. Slight maternal toxicity, in the form of reduced body weight gain, was seen at 50 mg/kg/day.

In rabbits, reduced fetal body weight occurred only in the presence of maternal toxicity (clinical signs, reduced body weight gain and food consumption) when administered at a dose of 15 mg/kg/day (0.06-fold the estimated human exposure based on AUCs).

When female rats were treated with 50 mg/kg/day (approximately equivalent to the estimated human exposure based on AUCs) of linezolid during pregnancy and lactation, survival of pups was decreased on postnatal days 1 to 4. Male and female pups permitted to mature to reproductive age, when mated, showed an increase in preimplantation loss.

8.2 Nursing Mothers
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, caution should be exercised when OXZORID is administered to a nursing woman.

8.3 Pediatric Use
The safety and effectiveness of OXZORID for the treatment of pediatric patients with the following infections are supported by evidence from adequate and well-controlled studies in adults, pharmacokinetic data in pediatric patients, and additional data from a comparator-controlled study of Gram-positive infections in pediatric patients ranging in age from birth through 11 years [see Indications and Usage (1), Clinical Pharmacology and Clinical Studies:

- nosocomial pneumonia
- complicated skin and skin structure infections
- community-acquired pneumonia (also supported by evidence from an uncontrolled study in patients ranging in age from 8 months through 12 years)
- vancomycin-resistant Enterococcus faecium infections

The safety and effectiveness of OXZORID for the treatment of pediatric patients with the following infection have been established in a comparator-controlled study in pediatric patients ranging in age from 5 through 17 years:

- uncomplicated skin and skin structure infections caused by Staphylococcus aureus (methicillin-susceptible strains only) or Streptococcus pyogenes

Pharmacokinetic information generated in pediatric patients with ventriculoperitoneal shunts showed variable cerebrospinal fluid (CSF) linezolid concentrations following single and multiple dosing of linezolid; therapeutic concentrations were not consistently achieved or maintained in the CSF. Therefore, the use of linezolid for the empiric treatment of pediatric patients with central nervous system infections is not recommended.

The pharmacokinetics of linezolid have been evaluated in pediatric patients from birth to 17 years of age. In general, weight-based clearance of linezolid gradually decreases with increasing age of pediatric patients. However, in preterm (gestational age < 34 weeks) neonates < 7 days of age, linezolid clearance is often lower than in full-term neonates < 7 days of age. Consequently, preterm neonates < 7 days of age may need an alternative linezolid dosing regimen of 10 mg/kg every 12 hours [see Dosage and Administration (2.1) and Clinical Pharmacology.

In limited clinical experience, 5 out of 6 (83%) pediatric patients with infections due to Gram-positive pathogens with minimum inhibitory concentrations (MICs) of 4 mcg/mL treated with OXZORID had clinical cures. However, pediatric patients exhibit wider variability in linezolid clearance and systemic exposure (AUC) compared with adults. In pediatric patients with a sub-optimal clinical response, particularly those with pathogens with MIC of 4 mcg/mL, lower systemic exposure, site and severity of infection, and the underlying medical condition should be considered when assessing clinical response [see Clinical Pharmacology (12.3) and Dosage and Administration.

8.4 Geriatric Use
Of the 2046 patients treated with OXZORID in Phase 3 comparator-controlled clinical trials, 589 (29%) were 65 years or older and 253 (12%) were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

9 OVERDOSAGE

In the event of overdosage, supportive care is advised, with maintenance of glomerular filtration. Hemodialysis may facilitate more rapid elimination of linezolid. In a Phase 1 clinical trial, approximately 30% of a dose of linezolid was removed during a 3-hour hemodialysis session beginning 3 hours after the dose of linezolid was administered. Data are not available for removal of linezolid with peritoneal dialysis or hemoperfusion. Clinical signs of acute toxicity in animals were decreased activity and ataxia in rats and vomiting and tremors in dogs treated with 3000 mg/kg/day and 2000 mg/kg/day, respectively.

OXZORID for Oral Suspension is supplied as an orange-flavored granule/powder for constitution into a suspension for oral administration. Following constitution, each 5 mL contains 100 mg of linezolid. Inactive ingredients are sucrose, citric acid, sodium citrate, microcrystalline cellulose and carboxymethylcellulose sodium, aspartame, xanthan gum, mannitol, sodium benzoate, colloidal silicon dioxide, sodium chloride, and flavors [see Patient Counseling Information (17)]. The sodium (Na+) content is 8.52 mg/5 mL (0.4 mEq/5 mL).

10 NONCLINICAL TOXICOLOGY

10.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Lifetime studies in animals have not been conducted to evaluate the carcinogenic potential of linezolid. Neither mutagenic nor clastogenic potential was found in a battery of tests including: assays for mutagenicity (Ames bacterial reversion and CHO cell mutation), an in vitro unscheduled DNA synthesis (UDS) assay, an in vitro chromosome aberration assay in human lymphocytes, and an in vivo mouse micronucleus assay.

Linezolid did not affect the fertility or reproductive performance of adult female rats. It reversibly decreased fertility and reproductive performance in adult male rats when given at doses 50 mg/kg/day, with exposures approximately equal to or greater than the expected human exposure level (exposure comparisons are based on AUCs). The reversible fertility effects were mediated through altered spermatogenesis. Affected spermatids contained abnormally formed and oriented mitochondria and were non-viable. Epithelial cell hypertrophy and hyperplasia in the epididymis was observed in conjunction with decreased fertility.

In sexually mature male rats exposed to drug as juveniles, mildly decreased fertility was observed following treatment with linezolid through most of their period of sexual development (50 mg/kg/day from days 7 to 36 of age, and 100 mg/kg/day from days 37 to 55 of age), with exposures up to 1.7-fold greater than mean AUCs observed in pediatric patients aged 3 months to 11 years. Decreased fertility was not observed with shorter treatment periods, corresponding to exposure in utero through the early neonatal period (gestation day 6 through postnatal day 5), neonatal exposure (postnatal days 5 to 21), or to juvenile exposure (postnatal days 22 to 35). Reversible reductions in sperm motility and altered sperm morphology were observed in rats treated from postnatal day 22 to 35.

11 PATIENT COUNSELING INFORMATION

Patients should be counseled that antibacterial drugs including OXZORID should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When OXZORID is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by OXZORID or other antibacterial drugs in the future.

Patients should be advised that:

- OXZORID may be taken with or without food.
- They should inform their physician if they have a history of hypertension.
- Large quantities of foods or beverages with high tyramine content should be avoided while taking OXZORID.
- Foods high in tyramine content include those that may have undergone protein changes by aging, fermentation, pickling, or smoking to improve flavor, such as aged cheeses ,fermented or air-dried meats ,sauerkraut , soy sauce, tap beers, and red wines. The tyramine content of any protein-rich food may be increased if stored for long periods or improperly refrigerated.
- They should inform their physician if taking medications containing pseudoephedrine HCl or phenylpropanolamine HCl, such as cold remedies and decongestants.
- They should inform their physician if taking serotonin re-uptake inhibitors or other antidepressants.
- Phenylketonurics: Each 5 mL of the 100 mg/5 mL OXZORID for Oral Suspension contains 20 mg phenylalanine.
- The other OXZORID formulations do not contain phenylalanine. Contact your physician or pharmacist.
- They should inform their physician if they experience changes in vision.
- They should inform their physician if they have a history of seizures.
- Diarrhea is a common problem caused by antibiotics, which usually ends when the antibiotic is discontinued.
- Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible.
- Inform patient, particularly those with diabetes mellitus that hypoglycemic reactions, such as diaphoresis and tremulousness, along with low blood glucose measurements may occur when treated with linezolid. If such reactions occur, patients should contact a physician or other health professional for proper treatment.

12 HOW SUPPLIED/STORAGE AND HANDLING

STORAGE:

- Store at 25ºC (77ºF). Protect from light.
- Keep bottle tightly closed to protect from moisture.
- Keep out of the reach of children.

PACK SIZE:

- **Oxzorid Tablets 400mg:**
  Box containing 12 tablets in blister pack.
- **Oxzorid Tablets 600mg:**
  Box containing 12 tablets in blister pack
- **Oxzorid Dry Powder suspension**:
  Amber glass bottle 60ml after reconstitution

آگزورڈ ٹیبلیٹ

(لینزولیڈ)

۴۰۰ ملی گرام، ۶۰۰ ملی گرام ٹیبلیٹس

۱۰۰ ملی گرام/۵ ملی لیٹر ڈرائی پاؤڈر سسپنشن

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات: صرف مُستند ڈاکٹر کے نسخے پر فروخت کی جائے۔

۲۵ ڈگری سے کم درجہ حرارت پر رکھیں۔ روشنی سے بچائیں۔

نمی سے بچانے کیلئے بوتل کو مضبوطی سے بند کریں۔

بچوں کی پہنچ سے دور رکھیں۔

MANUFACTURED BY:

NAWAN LABORATORIES (PVT) LTD.

136, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan.