APPROVED PACKAGE INSERT

SCHEDULING STATUS:

S4

PROPRIETARY NAME AND DOSAGE FORM:

ZYVOXID 400 mg (Tablets)

ZYVOXID 600 mg (Tablets)

ZYVOXID 200 mg/100 ml (Solution for Infusion)

ZYVOXID 600 mg/300 ml (Solution for Infusion)

ZYVOXID 20 mg/ml (Granules for Suspension)

COMPOSITION:

ZYVOXID 400 mg Tablets: Each film-coated tablet contains 400 mg linezolid.

ZYVOXID 600 mg Tablets: Each film-coated tablet contains 600 mg linezolid.

ZYVOXID 200 mg/100 ml Solution for Infusion: Each 1 ml contains 2 mg linezolid. The 100 ml infusion bag contains 200 mg linezolid.

ZYVOXID 600 mg/300 ml Solution for Infusion: Each 1 ml contains 2 mg linezolid. The 300 ml infusion bag contains 600 mg linezolid.

ZYVOXID 20 mg/ml Granules for Suspension: Following reconstitution with 123 ml water, each 1 ml contains 20 mg linezolid. Preservative content: Sodium benzoate 0,2 % m/v.

ZYVOXID film-coated tablets contain the following inactive ingredients: maize starch, microcrystalline cellulose, hydroxypropylcellulose, sodium starch glycollate, and magnesium stearate. The film coating contains opadry white and carnauba wax. The printing ink contains black iron oxide (400 mg tablets) or red iron oxide (600 mg tablets).

ZYVOXID 200 mg/100 ml and ZYVOXID 600 mg/300 ml Solution for Infusion contain the following inactive ingredients: sodium citrate dihydrate, citric acid anhydrous, dextrose monohydrate, hydrochloric acid or sodium hydroxide and water for injections.

ZYVOXID 20 mg/ml Granules for Suspension contains the following inactive ingredients: sucrose, citric acid anhydrous, sodium citrate hydrous, microcrystalline cellulose, carboxymethylcellulose sodium, aspartame, xanthan gum, mannitol, sodium benzoate, flavourings (orange, orange cream, peppermint, vanilla), colloidal silicon dioxide anhydrous, sodium chloride, sweeteners (fructose, maltodextrin, monoammonium glycyrrhizinate, sorbitol).

PHARMACOLOGICAL CLASSIFICATION:

A 20.1.1 Broad and medium spectrum antibiotic

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties

Linezolid is a synthetic antibacterial agent of the oxazolidinone class of antibiotics. It has *in vitro* activity against aerobic Gram-positive bacteria and anaerobic microorganisms. It selectively inhibits bacterial protein synthesis through binding to sites on the bacterial ribosome and prevents the formation of a functional 70S-initiation complex that is an essential component of the translation process.

The *in vitro* post-antibiotic effect (PAE) of linezolid for *Staphylococcus aureus* was approximately 2 hours. When measured in animal models, the *in vivo* PAEs were 3,6 and 3,9 hours for *Staphylococcus aureus* and *Streptococcus pneumoniae*, respectively. In animal studies, the key pharmacodynamic parameter for efficacy was the time that the linezolid plasma levels exceeded the minimum inhibitory concentration (MIC) of the infecting organism. Linezolid was efficacious when plasma levels exceeded the MIC of the infecting organism for a minimum of 40 % of the dosing interval.

Susceptibility: The following gives an approximate guidance on the probabilities as to whether microorganisms will be susceptible to linezolid or not. (Only microorganisms relevant to the given clinical indications are presented).

Category	
Susceptible organisms	
Gram-positive aerobes: *Corynebacterium jeikeium* *Enterococcus casseliflavus* *Enterococcus faecalis* (including glycopeptide resistant strains) * *Enterococcus faecium* (including glycopeptide resistant strains) * *Enterococcus gallinarum* *Listeria monocytogenes* *Staphylococcus aureus* (including methicillin resistant strains) * *Staphylococcus aureus* (glycopeptide intermediate strains) *Staphylococcus epidermidis* (including methicillin resistant strains) * *Staphylococcus haemolyticus* *Staphylococcus lugdunensis*	*Streptococcus agalactiae* * *Streptococcus intermedius* *Streptococcus pneumoniae* (including multi-drug resistant strains [MDRSP]) δ *Streptococcus pyogenes* * Group C streptococci Group G streptococci Viridans group streptococci
Gram-positive anaerobes: *Clostridium perfringens* *Peptostreptococcus* species	*Peptostreptococcus anaerobius*
Other: *Chlamydia pneumoniae*	
Intermediately susceptible organisms	
Legionella species *Mycoplasma* species	*Moraxella catarrhalis*
Resistant organisms	
Haemophilus influenzae *Enterobacteriaceae*	*Neisseria* species *Pseudomonas* species
* Clinical efficacy has been demonstrated for susceptible isolates in approved clinical indications δ MDRSP, Multi-drug resistant *Streptococcus pneumoniae* includes isolates previously known as penicillin-resistant *Streptococcus pneumoniae,* and are strains resistant to two or more of the following antibiotics: penicillin, second generation cephalosporins, macrolides, tetracycline, and trimethoprim/sulfamethoxazole.	

Resistance: Linezolid's mechanism of action differs from that of other antibiotics (e.g. the aminoglycosides, beta-lactams, folic acid antagonists, glycopeptides, lincosamides, quinolones, rifamycins, streptogramins, tetracyclines and chloramphenicol). Therefore, there is no cross-resistance between linezolid and these classes of drugs.

In vitro studies have shown that resistance to linezolid develops slowly via multiple step mutations in 23S ribosomal RNA and occurs at frequencies of less than 1×10^{-9} to 1×10^{-11}.

Pharmacokinetic properties

ZYVOXID primarily contains linezolid that is biologically active and is metabolised to form inactive metabolites. The aqueous solubility of linezolid is approximately 3 mg/ml and is independent of pH between pH 3 to 9.

Absorption:

Maximum plasma concentrations are reached within 2 hours of dosing and absolute bioavailability is approximately 100 %. It is not affected by food**.**

Distribution:

The volume of distribution at steady-state averages at about 40 to 50 litres in healthy adults and approximates to total body water. Plasma protein binding is about 31 %.

Linezolid concentrations have been determined in various fluids from a limited number of subjects in volunteer studies following multiple dosing. The ratio of linezolid in saliva and sweat relative to plasma was 1,2:1,0 and 0,55:1,0 respectively. The ratio for epithelial lining fluid and alveolar cells of the lung was 4,5:1,0 and 0,15:1,0, when measured at steady-state C_{max} respectively. In a small study of subjects with ventricular-peritoneal shunts and essentially non-inflamed meninges, the ratio of linezolid in cerebrospinal fluid to plasma at C_{max} was 0,7:1,0 after linezolid dosing.

Metabolism:

Linezolid is metabolised by a non-enzymatic process**.** Metabolic oxidation of the morpholine ring results primarily in two inactive open-ring carboxylic acid derivatives. The hydroxyethyl glycine metabolite (B) is the predominant human metabolite and the amino ethoxy acetic acid metabolite (A) is less abundant. Linezolid is not detectably metabolised by cytochrome P450 (CYP) isoenzymes *in vitro* and it does not inhibit the activities of clinically significant human CYP isoforms (1A2, 2C9, 2C19, 2D6, 2E1, 3A4). Linezolid does not significantly induce major cytochrome P450 isoenzymes in rats and does not induce human CYP2C9.

Elimination:

Under steady-state conditions, linezolid is primarily excreted in the urine as metabolite B (40 %), parent drug (30 - 35 %) and metabolite A (10 %). The elimination half-life of the parent drug averages at about 5 - 7 hours. Non-renal clearance accounts for approximately 65 % of the total clearance of linezolid.

Special populations:

Elderly:

The pharmacokinetics of linezolid is not significantly altered in elderly patients aged 65 and over.

Renal insufficiency:

No dose adjustment is necessary in patients with either mild, moderate or severe renal insufficiency, as linezolid clearance is independent of creatinine clearance. There is evidence that the primary metabolites of linezolid accumulate in patients with severe renal insufficiency (i.e. CL_{CR} < 30 ml/min). The clinical significance of this has not yet been established. As approximately 30 % of a dose is removed during 3 hours of haemodialysis (beginning 3 hours after administration), ZYVOXID should be given after dialysis in patients receiving such treatment.

Hepatic insufficiency:

The pharmacokinetics of linezolid are not altered in patients with mild to moderate hepatic insufficiency. Dose adjustment in such patients is, therefore, not required. The pharmacokinetics of linezolid in patients with severe hepatic insufficiency has not been evaluated. However, as linezolid is metabolised by a non-enzymatic process, impairment of hepatic function would not be expected to significantly alter its metabolism.

Children:

The pharmacokinetics of linezolid following a single IV dose were investigated in paediatric patients ranging in age from birth through 17 years (including premature and full-term neonates).

The C_{max} and the volume of distribution (V_{ss}) are similar regardless of age in paediatric patients. However, clearance of linezolid varies as a function of age. With the exclusion of pre-term neonates less than one week of age, clearance is most rapid in the youngest age groups ranging from > 1 week old to 11 years, resulting in lower single-dose systemic exposure (AUC) and shorter half-life as compared with adults. As age of paediatric patients increases, the clearance of linezolid gradually decreases, and by adolescence mean clearance values approach these observed for the adult population. There is wider inter-subject variability in linezolid clearance and systemic drug exposure (AUC) across all paediatric age groups as compared with adults.

INDICATIONS:

ZYVOXID formulations are indicated for the treatment of patients with the following infections caused by susceptible strains of the designated micro-organisms (see PHARMACOLOGICAL ACTION). ZYVOXID is not indicated for the treatment of Gram-negative infections. It is critical that specific Gram-negative therapy must be initiated immediately if a concomitant Gram-negative pathogen is documented or suspected (see WARNINGS AND SPECIAL PRECAUTIONS).

Vancomycin-resistant *Enterococcus faecium* infections, including cases with concurrent bacteraemia.

Nosocomial pneumonia caused by *Staphylococcus aureus* (methicillin-susceptible and -resistant strains), or *Streptococcus pneumonia*e (including multi-drug resistant *S. pneumoniae* (MDRSP) strains).

Complicated skin and skin structure infections caused by *Staphylococcus aureus* (methicillin-susceptible and -resistant strains), *Streptococcus pyogenes*, or *Streptococcus agalactiae*. ZYVOXID has not been studied in the treatment of decubitus ulcers.

Uncomplicated skin and skin structure infections caused by *Staphylococcus aureus* (methicillin-susceptible and -resistant strains), *Streptococcus pyogenes*.

Community-acquired pneumonia caused by *Streptococcus pneumoniae* (including multi-drug resistant *S. pneumoniae* (MDRSP) strains), including cases with concurrent bacteraemia, or *Staphylococcus aureus* (methicillin-susceptible and -resistant strains).

Due to concern about inappropriate use of antibiotics leading to an increase in resistant organisms, prescribers should carefully consider alternatives before initiating treatment with ZYVOXID in the outpatient setting.

Appropriate specimens for bacteriological examination should be obtained in order to isolate and identify the causative organisms and to determine their susceptibility to linezolid. Therapy may be instituted empirically

while awaiting results of these tests. Once these results become available, antimicrobial therapy should be adjusted accordingly.

CONTRAINDICATIONS:

ZYVOXID formulations are contraindicated for use in patients who have known hypersensitivity to linezolid or any excipients.

Monoamine Oxidase Inhibitors

ZYVOXID 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.

Potential Interactions Producing Elevation of Blood Pressure

Unless patients are monitored for potential increases in blood pressure, ZYVOXID 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, phenylpropanolamine), vasopressive agents (e.g., epinephrine, norepinephrine), dopaminergic agents (e.g., dopamine, dobutamine) (see INTERACTIONS).

Potential Serotonergic Interactions

Unless patients are carefully observed for signs and/or symptoms of serotonin syndrome, ZYVOXID 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 or buspirone (see INTERACTIONS).

WARNINGS AND SPECIAL PRECAUTIONS:

Pseudomembranous colitis has been reported with ZYVOXID, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of this antibacterial agent.

Clostridium difficile associated diarrhoea (CDAD) has been reported with ZYVOXID, and may range in severity from mild diarrhoea to fatal colitis. Treatment with ZYVOXID 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 diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

Reversible myelosuppression (anaemia, thrombocytopenia**,** leukopenia, and pancytopenia) that may be dependent on duration of therapy has been reported in some patients receiving ZYVOXID. Monitoring of complete blood counts should be considered for patients who are at increased risk for bleeding, who have pre-existing myelosuppression, who receive concomitant medications that may decrease haemoglobin levels or platelet count or function, or who receive ZYVOXID for more than 2 weeks.

Peripheral neuropathy and optic neuropathy have been reported in patients treated with ZYVOXID. 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 ZYVOXID for less than 28 days.

If symptoms of visual impairment appear, such as changes in visual acuity, changes in colour vision, blurred vision, or visual field defect, prompt ophthalmic evaluation is recommended. Visual function should be monitored in all patients taking ZYVOXID for extended periods (greater than or equal to 3 months) and in all patients reporting new visual symptoms regardless of length of therapy with ZYVOXID. If peripheral or optic neuropathy occurs, the continued use of ZYVOXID in these patients should be weighed against the potential risks.

Lactic acidosis has been reported with the use of ZYVOXID. Patients who develop recurrent nausea or vomiting, unexplained acidosis, or a low bicarbonate level while receiving ZYVOXID should receive immediate

medical attention.

Convulsions have been reported to occur in patients when treated with ZYVOXID. In some of these cases, a history of seizures or risk factors for seizures were reported.

ZYVOXID has no clinical activity against Gram-negative pathogens and is not indicated for the treatment of Gram-negative infections. Specific Gram-negative therapy is required if a concomitant Gram-negative pathogen is documented or suspected. ZYVOXID should be used with special caution in patients at high risk for life threatening systemic infections, such as those with infections related to central venous catheters in intensive care units. ZYVOXID is not approved for the treatment of patients with catheter-related bloodstream infections.

The use of antibiotics may result in an overgrowth of non-susceptible organisms. Should superinfection occur during therapy, appropriate measures should be taken.

The safety and effectiveness of ZYVOXID when administered for periods longer than 28 days have not been established.

ZYVOXID has not been studied in patients with uncontrolled hypertension, phaeochromocytoma, carcinoid syndrome, or untreated hyperthyroidism.

ZYVOXID should be used with special caution in patients with severe renal insufficiency and only when the anticipated benefit is considered to outweigh the theoretical risk.

It is recommended that ZYVOXID should be used in patients with severe hepatic insufficiency only when the anticipated benefit is considered to outweigh the theoretical risk.

Effects on ability to drive and use machines:

No effects on the ability to drive and use machines have been observed.

INTERACTIONS:

ZYVOXID is not detectably metabolised by the cytochrome P450 (CYP) enzyme system and it does not induce or inhibit the activities of clinically significant human CYP isoforms (1A2, 2C9, 2C19, 2D6, 2E1, 3A4). Therefore, no CYP450-induced drug interactions are expected. Drugs such as warfarin and phenytoin, which are CYP2C9 substrates, may be given with ZYVOXID without changes in dosage regimen.

No interactions have been observed in pharmacokinetic studies with either aztreonam or gentamicin.

ZYVOXID is a reversible, non-selective monoamine oxidase inhibitor (MAOI). Clinical studies have shown that it produces a mild, reversible enhancement of the pressor responses induced by pseudoephedrine and phenylpropanolamine hydrochloride. Thus, the potential for interaction with sympathomimetic or adrenergic agents should be considered and doses of compounds, such as dopamine or adrenalin, should be titrated to achieve the desired response.

No significant pressor response was observed in subjects receiving both ZYVOXID and less than 100 mg tyramine. This suggests that it is only necessary to avoid ingesting large 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).

Although ZYVOXID has the potential for interaction with serotonergic agents, no serotonin effects (e.g. confusion, delirium, restlessness, tremors, blushing, diaphoresis and hyperpyrexia) were observed in subjects receiving linezolid and dextromethorphan.

Spontaneous reports of serotonin syndrome associated with the co-administration of ZYVOXID and serotonergic agents, including antidepressants such as selective serotonin reuptake inhibitors (SSRIs) have been reported.

Where administration of ZYVOXID and concomitant serotonergic agents is clinically appropriate, patients should be closely observed for signs and symptoms of serotonin syndrome such as cognitive dysfunction, hyperpyrexia, hyperreflexia and incoordination. If signs or symptoms occur physicians should consider

discontinuation of either one or both agents. If the concomitant serotonergic agent is withdrawn, discontinuation symptoms can be observed.

In healthy volunteers, co-administration of rifampin with ZYVOXID resulted in a 21 % decrease in linezolid C_{max} and a 32 % decrease in linezolid AUC. The mechanism of this interaction and its clinical significance are unknown.

PREGNANCY AND LACTATION:

The use of ZYVOXID formulations in pregnancy and lactation is contraindicated, as safety has not been demonstrated.

DOSAGE AND DIRECTIONS FOR USE:

ZYVOXID tablets, oral suspension or solution for 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 ZYVOXID has an oral bioavailability of approximately 100 %.

The solution for infusion should be administered over a period of 30 to 120 minutes. The film coated tablets or oral suspension may be taken with or without food.

The recommended ZYVOXID dosage should be administered IV or orally as described in the tables below.

Adult and Adolescent (12 years and older) Patients:

<table>
<tr><th>Infections (including those associated with concurrent bacteraemia)</th><th>Dosage and route of administration</th><th>Duration of treatment</th></tr>
<tr><td>Community-acquired pneumonia, including concurrent bacteraemia</td><td rowspan="2">600 mg IV or orally every 12 hours</td><td rowspan="3">10 – 14 consecutive days</td></tr>
<tr><td>Nosocomial pneumonia, including concurrent bacteraemia</td></tr>
<tr><td>Skin and soft tissue infections, including concurrent bacteraemia</td><td>400 mg to 600 mg orally every 12 hours or</td></tr>
</table>

	600 mg IV every 12 hours depending on clinical severity	
Enterococcal infections, including vancomycin-resistant infections, and those with concurrent bacteraemia	600 mg IV or orally every 12 hours	14 – 28 consecutive days

Paediatric Patients (birth* through to 11 years):

Infections (including those associated with concurrent bacteraemia)	**Dosage and route of administration**	**Duration of treatment**
Community-acquired pneumonia, including concurrent bacteraemia	10 mg/kg IV or oral$^{\delta}$ every 8 hours	10 – 14 consecutive days
Nosocomial pneumonia, including concurrent bacteraemia		
Skin and soft tissue infections, including concurrent bacteraemia		
Enterococcal infections, including vancomycin-resistant infections, and those with concurrent bacteraemia	10 mg/kg IV or oral$^{\delta}$ every 8 hours	14 – 28 consecutive days

***** Pre-term neonates less than 7 days of age (gestational age less than 34 weeks) have lower systemic ZYVOXID clearance values and larger AUC values than many full-term neonates and older infants. By day 7 of age, ZYVOXID clearance and AUC values are similar to those of full-term neonates and older infants.

δ Oral dosing using either ZYVOXID tablets or oral suspension

Elderly patients: No dose adjustment is necessary.

Patients with renal insufficiency: No dose adjustment is required.

Patients with severe renal insufficiency (i.e., CL_{CR} < 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 ZYVOXID in patients with severe renal insufficiency, ZYVOXID 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 ZYVOXID dose is removed during 3 hours of hemodialysis, ZYVOXID should be given after dialysis in patients receiving such treatment. The primary metabolites of ZYVOXID are removed to some extent by hemodialysis, but the concentrations of these metabolites are still very considerably higher

following dialysis than those observed in patients with normal renal function or mild to moderate renal insufficiency.

Therefore, ZYVOXID 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.

To date, there is no experience of ZYVOXID administration to patients undergoing continuous ambulatory peritoneal dialysis (CAPD) or alternative treatments for renal failure (other than hemodialysis).

Patients with hepatic insufficiency: No dose adjustment is required. However, there are limited clinical data and it is recommended that ZYVOXID should be used in such patients only when the anticipated benefit is considered to outweigh the theoretical risk.

Instructions for use/handling:

Intravenous administration:

ZYVOXID Solution for Infusion must be used immediately after the seal is first broken. ZYVOXID Solution for Infusion is supplied in single-use, ready-to-use infusion bags. Parenteral drug products should be inspected visually for particulate matter prior to administration. Check for minute leaks by firmly squeezing the bag. If leaks are detected, discard the solution, as sterility may be impaired.

Administer ZYVOXID Solution for Infusion over a period of 30 to 120 minutes. **Do not use the intravenous infusion bag in series connections. Do not introduce additives into the intravenous solution.** If ZYVOXID Solution for Infusion is to be given concomitantly with another drug, each drug should be given separately, in accordance with the recommended dosage and route of administration for each product.

Compatible infusion solutions: 0,9 % Sodium Chloride Injection, 5 % Dextrose Injection, Lactated Ringer's Injection.

ZYVOXID Solution for Infusion is known to be physically incompatible with the following drugs: amphotericin B, chlorpromazine HCl, diazepam, pentamidine isethionate, phenytoin sodium, erythromycin lactobionate and trimethoprim-sulfamethoxazole.

ZYVOXID Solution for Infusion was chemically incompatible when combined with ceftriaxone sodium.

Constitution of oral suspension:

ZYVOXID Granules for 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 the constituted suspension, gently mix by inverting the bottle several times. **Do not shake.**

SIDE EFFECTS:

Approximately 22 % of patients experienced adverse reactions. Those most commonly reported were headache, diarrhoea, nausea, vomiting, metallic taste, abnormal liver function tests and vaginal moniliasis.

Adverse events considered drug-related in controlled clinical trials with an incidence of at least 1 % were:

Gastrointestinal Disorders: Abdominal pain/cramps/distension, diarrhoea, nausea, vomiting

Infections and Infestations: Moniliasis

Investigations: Abnormal hematology tests, abnormal liver function tests

Nervous System Disorders: Headache, taste alteration

Adverse drug events occurring at frequencies greater than 0,1 % include:

(Common: ≥ 1/100 and < 1/10 or ≥ 1 % and < 10 %

Uncommon: ≥ 1/1 000 and < 1/100 or ≥ 0,1 % and < 1 %)

General body:

Common: headache, moniliasis or fungal infection

Uncommon: chills, fatigue, fever, injection site pain, phlebitis/thrombophlebitis, localised pain, angioedema, anaphylaxis

Blood and the lymphatic system disorders:

Uncommon: reversible anaemia, eosinophilia, leukopenia, neutropenia, thrombocytopenia, pancytopenia

Metabolism and nutrition disorders:

Uncommon: increased serum creatine phosphokinase, hyperglycaemia, lactic acidosis

Nervous system disorders:

Uncommon: dizziness, hypoaesthesia, insomnia, paraesthesia, peripheral neuropathy, convulsions

Special senses:

Common: metallic taste

Uncommon: blurred vision, tinnitus, optic neuropathy

Cardiovascular disorders:

Uncommon: hypertension, hypotension

Gastro-intestinal disorders:

Common: abdominal pain, cramps or distension, diarrhoea, nausea, vomiting

Uncommon: constipation, dry mouth, dyspepsia, gastritis, increased thirst, pancreatitis, stomatitis, tongue discolouration or disorder, superficial tooth discolouration

Skin and subcutaneous tissue disorders:

Uncommon: dermatitis, diaphoresis, pruritus, rash, urticaria, angioedema, bullous skin disorders such described as Stevens Johnson syndrome

Urogenital disorders:

Common: vaginal moniliasis

Uncommon: vulvovaginal disorder, polyuria, vaginitis

Laboratory abnormalities: Chemistry

Common: increased total bilirubin, AST, ALT, LDH, alkaline phosphatase, BUN, creatine kinase, lipase, amylase or non-fasting glucose, decreased total protein, albumin, sodium, calcium, increased or decreased potassium or bicarbonate

Uncommon: increased creatinine, sodium, calcium; decreased non-fasting glucose, increased or decreased chloride

Laboratory abnormalities: Haematology

Common: increased neutrophils or eosinophils, decreased haemoglobin, haematocrit or red blood cell count, increased or decreased platelet or white blood cell counts

Uncommon: increased reticulocyte count; decreased neutrophils

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

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 ZYVOXID dose is removed during 3 hours of haemodialysis, but no data are available for the removal of ZYVOXID by peritoneal dialysis or haemoperfusion.

IDENTIFICATION:

ZYVOXID 400 mg Tablets: A white to off-white, ovaloid tablet, imprinted on one side with black ink “ZYVOXID 400 mg”.

ZYVOXID 600 mg Tablets: A white to off-white, ovaloid tablet, imprinted on one side with red ink “ZYVOXID 600 mg”.

ZYVOXID Solution for Infusion: A ready-to-use infusion bag containing a clear, colourless to yellow solution free of visible particles.

ZYVOXID Granules for Suspension: A white to off-white orange-flavoured granule/powder. The constituted suspension appears as a white to off-white suspension.

PRESENTATION:

ZYVOXID 400 mg Tablets: White HDPE bottles of 10 or 30 tablets or PVC/foil blisters of 10 or 30 tablets.

ZYVOXID 600 mg Tablets: White HDPE bottles of 10 or 30 tablets or PVC/foil blisters of 10 or 30 tablets.

ZYVOXID 200 mg/100 ml Solution for infusion: Single-use infusion bags packaged in a foil overwrap available in a pack size of 100 ml (200 mg linezolid).

ZYVOXID 600 mg/300 ml Solution for infusion: Single-use infusion bags packaged in a foil overwrap available in a pack size of 300 ml (600 mg linezolid).

ZYVOXID Granules for Suspension: Granules for suspension in 240 ml amber glass bottles. Once constituted, the volume of suspension is 150 ml.

STORAGE INSTRUCTIONS:

Tablets: Store at room temperature below 25 °C. Tablets packed in HDPE bottles must be stored in a dry place and protected from light.

Infusion: Store at room temperature below 25 °C. Infusion bags must be kept in overwrap until ready to use. Protect from light. Single-use infusion bags. Do not freeze. Discard any unused solution.

Granules for Suspension: Store at room temperature below 25 °C.

Constituted Suspension: Store at room temperature below 25 °C and use within 21 days.

REGISTRATION NUMBERS:

ZYVOXID 400 mg Tablets: 35/20.1.1/0309

ZYVOXID 600 mg Tablets: 35/20.1.1/0310

ZYVOXID 20 mg/ml Granules for Suspension: 35/20.1.1/0311

ZYVOXID 200 mg/100 ml Solution for Infusion: 35/20.1.1/0312

ZYVOXID 600 mg/300 ml Solution for Infusion: 35/20.1.1/0313

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Pfizer Laboratories (Pty) Ltd

85 Bute Lane

Sandton

2196

South Africa

DATE OF PUBLICATION OF THIS PACKAGE INSERT:

02 March 2012

BOTSWANA: Schedule 2

ZYVOXID 600 mg Tablets: Reg. No.: BOT1202199

ZYVOXID 20 mg/ml Granules for Suspension: Reg. No.: BOT1302358

ZYVOXID 200 mg/100 ml Solution for Infusion: Reg. No.: BOT1302287

ZYVOXID 600 mg/300 ml Solution for Infusion: Reg. No.: BOT1302288

NAMIBIA: S2

ZYVOXID 600 mg Tablets: Reg. No.: 06/20.1.1/0188

ZYVOXID 20 mg/ml Granules for Suspension: Reg. No.:06/20.1.1/0185

ZYVOXID 200 mg/100 ml Solution for Infusion: Reg. No.: 06/20.1.1/0186

ZYVOXID 600 mg/300 ml Solution for Infusion: Reg. No.: 06/20.1.1/0187