1. NAME OF THE MEDICINAL PRODUCT

Linezolid Kabi 2 mg/ml Solution for Infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Linezolid Kabi 2 mg/ ml solution for infusion
1 ml contains 2 mg linezolid. 300 ml infusion bags contain 600 mg linezolid.

Excipient(s) with known effect:
Each ml of solution for infusion contains 45.7 mg (i.e. 13.7 g/300 ml) glucose.
Each ml of solution for infusion contains 0.0165 mmol (0.38 mg) sodium.

3. PHARMACEUTICAL FORM

Linezolid Kabi 2mg/ml solution for infusion is supplied as a ready-to-use sterile isotonic solution for intravenous infusion.
Linezolid Kabi contains linezolid 2mg/ml in a clear, colorless to light yellow solution free from visible particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Linezolid formulations are indicated in the treatment of the following infections caused by susceptible strains of the designated microorganisms. Linezolid is active against Gram-positive bacteria only. Linezolid has no clinical activity against Gram-negative pathogens. Specific Gram-negative therapy is required if a concomitant Gram-negative pathogen is documented or suspected.

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

Nosocomial pneumonia caused by *Staphylococcus aureus* (methicillin-susceptible and -resistant strains), or *Streptococcus pneumoniae* (penicillin-susceptible strains). Combination therapy may be clinically indicated if the documented or presumptive pathogens include Gram-negative organisms.

Complicated skin and skin structure infections including diabetic foot infections, without concomitant osteomyelitis caused by *Staphylococcus aureus* (methicillin-susceptible and -resistant strains), *Streptococcus pyogenes*, or *Streptococcus agalactiae*. Linezolid has not been studied in the treatment of decubitus ulcers. Combination therapy may be clinically indicated if the documented or presumptive pathogens include Gram-negative organisms.

Uncomplicated skin and skin structure infections caused by *Staphylococcus aureus* (methicillin-susceptible only) or *Streptococcus pyogenes*.

Community-acquired pneumonia caused by *Streptococcus pneumoniae* (penicillin-susceptible strains only), including cases with concurrent bacteremia, or *Staphylococcus aureus* (methicillin-susceptible strains only).

Due to concerns about inappropriate use of antibiotics leading to an increase in resistant organisms, prescribers should carefully consider alternatives before initiating treatment with linezolid 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 the results of these tests. Once these results become available, antimicrobial therapy should be adjusted accordingly.

4.2 Posology and method of administration

Patients whose therapy is started with linezolid injection may be switched to linezolid tablets, with no dosage adjustment.

Table 1. Dosage Guidelines for Linezolid

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)**	
Complicated skin and skin structure infections	10 mg/kg IV or oral‡ q8h	600 mg IV or oral‡ q12h	10 to 14
Community-acquired pneumonia, including concurrent bacteremia			
Nosocomial pneumonia			
Vancomycin-resistant *Enterococcus faecium* infections, including concurrent bacteremia	10 mg/kg IV or oral‡ q8h	600 mg IV or oral‡ q12h	14 to 28
Uncomplicated skin and skin structure infections	<5 yrs: 10 mg/kg oral‡ q8h 5-11 yrs: 10 mg/kg oral‡ q12h	Adults: 400 mg oral‡ q12h Adolescents: 600 mg oral‡ q12h	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 q12h. Consideration may be given to the use of 10 mg/kg q8h regimen in neonates with a sub-optimal clinical response. All neonatal patients should receive 10 mg/kg q8h by 7 days of life.
‡Oral dosing using Linezolid Tablets.

Elderly patients: No dose adjustment is required.

Patients with renal insufficiency: No dose adjustment is required.

Patients with severe renal insufficiency (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 hemodialysis, linezolid should be given after dialysis in patients receiving such treatment. The primary metabolites of linezolid 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, 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.

To date, there is no experience of linezolid 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 linezolid should be used in such patients only when the anticipated benefit is considered to outweigh the theoretical risk.

Instruction for use

Linezolid solution for infusion is supplied in single-use, ready-to-use infusion bags. Remove overwrap only when ready to use, then check for minute leaks by squeezing the bag firmly. If the bag leaks, do not use as sterility may be impaired. The solution should be visually inspected prior to use and only clear solutions, without particles should be used. **Do not use these bags in series connections.** Any unused solution must be discarded. No special requirements for disposal.
Any unused product or waste should be disposed of in accordance with local requirements.
Do not reconnect partially used bags.

Administer linezolid solution for infusion by intravenous infusion over a period of 30 to 120 minutes. Do not use this intravenous infusion bag in series connections. Do not introduce additives into the intravenous solution. If linezolid 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.

Linezolid solution for infusion was physically incompatible with the following drugs when combined in simulated Y-site administration: amphotericin B, chlorpromazine HCl, diazepam, pentamidine isethionate, phenytoin sodium, erythromycin lactobionate, and trimethoprimsulfamethoxazole.
Linezolid solution for infusion was chemically incompatible when combined with ceftriaxone sodium if the same intravenous line is used for sequential infusion of several drugs, the line should be flushed before and after infusion of linezolid solution for infusion with and infusion solution compatible with linezolid solution for infusion and with any other drug(s) administered via this common line.

Compatible Intravenous Solutions
- 5% glucose intravenous infusion,
- 0.9% sodium chloride intravenous infusion,
- Ringer-lactate solution for injection (Hartmann's solution for injection)

Keep the infusion bags in the overwrap until ready to use. Store at room temperature. Protect from freezing. Linezolid solution for Infusion may exhibit a yellow color that can intensify over time without adversely affecting potency.

Route of Administration:
The recommended linezolid dosage should be administered intravenously twice daily. Route of administration: Intravenous use.
The solution for infusion should be administered over a period of 30 to 120 minutes.

4.3 Contraindications

Linezolid is contraindicated in patients who have previously demonstrated hypersensitivity to linezolid or any of the other product components.

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.

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, phenylpropanolamine), vasopressive agents (e.g., epinephrine, norepinephrine), dopaminergic agents (e.g., dopamine, dobutamine).

Potential Serotonergic Interactions
Unless patients are carefully observed for signs and/or symptoms of serotonin syndrome, 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 or buspirone.

4.4 Special warnings and precautions for use

Reversible myelosuppression (anemia, thrombocytopenia, leukopenia, and pancytopenia) that may be dependent on duration of therapy has been reported in some patients receiving linezolid. Thrombocytopenia may occur more often in patients with severe renal insufficiency, whether or not on dialysis, and in patients with moderate to severe hepatic impairment. Monitoring of complete blood counts should be considered for patients who are at increased risk for bleeding, who have pre-existing myelosuppression, who have severe renal insufficiency or moderate to severe hepatic impairment, who receive concomitant medications that may decrease hemoglobin levels or platelet count or function, or who receive linezolid for more than 2 weeks.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including

linezolid, and may range in severity from mild to life-threatening.

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. 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.

Peripheral and optic neuropathy have been reported in patients treated with linezolid, primarily 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.

If symptoms of visual impairment appear, 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 linezolid for extended periods (greater than or equal to 3 months) and in all patients reporting new visual symptoms regardless of length of therapy with linezolid. If peripheral or optic neuropathy occurs, the continued use of linezolid in these patients should be weighed against the potential risks.

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

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

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

Where administration of linezolid 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.
Hyponatremia and/or Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) have been observed in some patients treated with linezolid. It is recommended that serum sodium levels be monitored regularly in the elderly, in patients taking diuretics, and in other patients at risk of hyponatremia.

In healthy volunteers, co-administration of rifampin with linezolid resulted in a 21% decrease in linezolid Cmax and a 32% decrease in linezolid AUC. The clinical significance of this interaction is unknown.

Linezolid 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. Linezolid 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. Linezolid is not approved for the treatment of patients with catheter-related bloodstream infections.

4.5 Interaction with other medicinal products and other forms of interaction

Linezolid is a weak, reversible, nonselective inhibitor of monoamine oxidase. Therefore, some patients receiving linezolid may experience a mild reversible enhancement on the pressor response induced by pseudoephedrine HCl or phenylpropanolamine HCl. Initial doses of adrenergic agents, such as dopamine or dopamine agonists, should be reduced and titrated to achieve the desired response.

Very rare spontaneous reports of serotonin syndrome with co-administration of linezolid and serotonergic agents have been reported.

Antibiotics: The pharmacokinetics of linezolid were not altered when administered together with either aztreonam or gentamicin. The effect of rifampin on the pharmacokinetics of linezolid was studied in sixteen healthy adult male volunteers administered linezolid 600 mg twice daily for 2.5 days with and without rifampin 600 mg once daily for 8 days. Rifampin decreased the linezolid Cmax and AUC by a mean 21% [90% CI, 15, 27] and a mean 32% [90% CI, 27, 37], respectively.
The mechanism of this interaction and its clinical significance are unknown.

4.6 Fertility, pregnancy and lactation

Reproductive studies performed in mice and rats treated with linezolid showed no evidence of teratogenic effects. Mild fetal toxicity was observed in mice only at maternally toxic dose levels. In rats, fetal toxicity was manifested as decreased fetal body weights and reduced ossification of sternebrae (which is often seen in association with decreased body weights). Reduced pup survival and mild maturational delays occurred in rats. When mated, these same pups showed evidence of a reversible, doserelated increase in pre-implantation loss. There are no adequate and well-controlled studies in pregnant women. Therefore, linezolid should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Linezolid decreased the fertility of male rats.

Linezolid transferred into the breast milk of lactating laboratory rats. It is not known whether linezolid is excreted in human milk. Therefore, caution should be exercised when linezolid is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

The effect of linezolid on the ability to drive or operate machinery has not been systematically evaluated.

4.8 Undesirable effects

System Organ Class	Common	Uncommon	Rare	Unknown
Infections and infestations	Moniliasis			
Blood and lymphatic system disorders	Thrombocytopenia*, Anemia*	Pancytopenia*, Leucopenia*	Sideroblastic anemia*	
Immune system disorders			Anaphylaxis*	
Metabolism and nutrition disorders			Lactic acidosis*	
Nervous system disorders	Headache	Convulsions*, Peripheral neuropathy*, Taste alteration,		
Eye disorders		Optic neuropathy*		
Gastrointestinal disorders	Vomiting, Diarrhea, Nausea, Abdominal pain including abdominal cramps	Abdominal cramps#, Abdominal distension, Tongue discoloration*	Superficial tooth discoloration*	
Skin and subcutaneous tissue disorders	Rash*	Bullous skin disorders, Severe cutaneous adverse reactions, Angioedema*	Hypersensitivity vasculitis*	Toxic epidermal necrolysis*, Stevens-Johnson syndrome*
Investigations	Abnormal liver function tests	Abnormal hematology tests		

*ADR identified post-marketing
The ADR Abdominal cramps is defined by MedDRA LLT and not by PT.

4.9 Overdose

In the event of overdosage, supportive care is advised, with maintenance of glomerular filtration. Hemodialysis removes approximately 30% of a dose of linezolid.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other Antibacterials.
ATC code: J01XX08

General Properties
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, some Gram-negative 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.

Susceptibility
The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

Category
Susceptible organisms **Gram positive aerobes:** *Enterococcus faecalis* *Enterococcus faecium* *Staphylococcus aureus* Coagulase negative staphylococci *Streptococcus agalactiae* *Streptococcus pneumoniae* *Streptococcus pyogenes* Group C streptococci Group G streptococci **Gram positive anaerobes:** *Clostridium perfringens* *Peptostreptococcus anaerobius* *Peptostreptococcus* species
Resistant organisms *Haemophilus influenzae* *Moraxella catarrhalis* *Neisseria* species *Enterobacteriaceae* *Pseudomonas* species

Resistance

Cross resistance

Linezolid's mechanism of action differs from those of other antibiotic classes. In vitro studies with clinical isolates (including methicillin-resistant staphylococci, vancomycin-resistant enterococci, and penicillin- and erythromycin-resistant streptococci) indicate that linezolid is usually active against organisms which are resistant to one or more other classes of antimicrobial agents.

Resistance to linezolid is associated with point mutations in the 23S rRNA.

As documented with other antibiotics when used in patients with difficult to treat infections and/or for prolonged periods, emergent decreases in susceptibility have been observed with linezolid. Resistance to linezolid has been reported in enterococci, Staphylococcus aureus and coagulase negative staphylococci. This generally has been associated with prolonged courses of therapy and the presence of prosthetic materials or undrained abscesses. When antibiotic-resistant organisms are encountered in the hospital it is important to emphasize infection control policies.

5.2 Pharmacokinetic properties

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%).

Plasma linezolid Cmax and Cmin (mean and [SD]) at steady-state following twice daily intravenous dosing of 600 mg have been determined to be 15.1 [2.5] mg/l and 3.68 [2.68] mg/l, respectively.

In another study following oral dosing of 600 mg twice daily to steady-state, Cmax and Cmin were determined to be 21.2 [5.8] mg/l and 6.15 [2.94] mg/l, respectively. Steady-state conditions are achieved by the second day of dosing.

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.
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.

Metabolism
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.

Non-renal clearance accounts for approximately 65% of the total clearance of linezolid. A small degree of non-linearity in clearance is observed with increasing doses of linezolid. This appears to be due to lower renal and non-renal clearance at higher linezolid concentrations. However, the difference in clearance is small and is not reflected in the apparent elimination half-life.

Special Populations

Patients with renal insufficiency: After single doses of 600 mg, there was a 7-8 fold increase in exposure to the two primary metabolites of linezolid in the plasma of patients with severe renal insufficiency (i.e. creatinine clearance < 30 ml/min). However, there was no increase in AUC of parent drug. Although there is some removal of the major metabolites of linezolid by haemodialysis, metabolite plasma levels after single 600 mg doses were still considerably higher following dialysis than those observed in patients with normal renal function or mild to moderate renal insufficiency.

In 24 patients with severe renal insufficiency, 21 of whom were on regular haemodialysis, peak plasma concentrations of the two major metabolites after several days dosing were about 10 fold those seen in patients with normal renal function. Peak plasma levels of linezolid were not affected.

<u>Patients with hepatic insufficiency:</u> Limited data indicate that the pharmacokinetics of linezolid, PNU-142300 and PNU-142586 are not altered in patients with mild to moderate hepatic insufficiency (i.e. Child-Pugh class A or B). The pharmacokinetics of linezolid in patients with severe hepatic insufficiency (i.e. Child-Pugh class C) have 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.

<u>Children and adolescents (<18 years old):</u> In adolescents (12 to 17 years old), linezolid pharmacokinetics were similar to that in adults following a 600 mg dose. Therefore, adolescents administered 600 mg every 12 hours daily will have similar exposure to that observed in adults receiving the same dosage.

In children 1 week to 12 years old, administration of 10 mg/kg every 8 hours daily gave exposure approximating to that achieved with 600 mg twice daily in adults.

In neonates up to 1 week of age, the systemic clearance of linezolid (based on kg body weight) increases rapidly in the first week of life. Therefore, neonates given 10 mg/kg every 8 hours daily will have the greatest systemic exposure on the first day after delivery. However, excessive accumulation is not expected with this dosage regimen during the first week of life as clearance increases rapidly over that period.

Elderly patients: The pharmacokinetics of linezolid are not significantly altered in elderly patients aged 65 and over.

Female patients: Females have a slightly lower volume of distribution than males and the mean clearance is reduced by approximately 20% when corrected for body weight. Plasma concentrations are higher in females and this can partly be attributed to body weight differences. However, because the mean half life of linezolid is not significantly different in males and females, plasma concentrations in females are not expected to substantially rise above those known to be well tolerated and, therefore, dose adjustments are not required.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glucose monohydrate
Sodium citrate
Citric acid anhydrous
Hydrochloric acid
Sodium hydroxide (for pH adjustment)
Water for injections (Solvent)

6.2 Incompatibilities

Linezolid solution for infusion was physically incompatible with the following drugs when combined in simulated Y-site administration: amphotericin B, chlorpromazine HCl, diazepam, pentamidine isothionate, phenytoin sodium, erythromycin lactobionate, and trimethoprimsulfamethoxazole.

Linezolid solution for infusion was chemically incompatible when combined with ceftriaxone sodium.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 30°C. Store in the original package (overwrap and carton) until ready to use. Protect infusion bags from freezing.
After opening: From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.5 Nature and contents of container

Single use, ready-to-use, latex-free, multilayered polyolefine film infusion Freeflex bags sealed inside a foil laminate overwrap.
The bag holds 300 ml solution and is packaged in a box.
Each box contains either 1 infusion bag or 10 infusion bags.

6.6 Special precautions for disposal and other handling

Linezolid solution for infusion is supplied in single-use, ready-to-use infusion bags. Remove overwrap only when ready to use, then check for minute leaks by squeezing the bag firmly. If the bag leaks, do not use as sterility may be impaired. The solution should be visually inspected prior to use and only clear solutions, without particles should be used. **Do not use these bags in series connections.** Any unused solution must be discarded. No special requirements for disposal.
Any unused product or waste should be disposed of in accordance with local requirements.

Do not reconnect partially used bags.

Administer linezolid solution for infusion by intravenous infusion over a period of 30 to 120 minutes. Do not use this intravenous infusion bag in series connections. Do not introduce additives into the intravenous solution. If linezolid 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.

Linezolid solution for infusion was physically incompatible with the following drugs when combined in simulated Y-site administration: amphotericin B, chlorpromazine HCl, diazepam, pentamidine isethionate, phenytoin sodium, erythromycin lactobionate, and trimethoprimsulfamethoxazole.
Linezolid solution for infusion was chemically incompatible when combined with ceftriaxone sodium if the same intravenous line is used for sequential infusion of several drugs, the line should be flushed before and after infusion of linezolid solution for infusion with and infusion solution compatible with linezolid solution for infusion and with any other drug(s) administered via this common line.

<u>Compatible Intravenous Solutions</u>
- 5% glucose intravenous infusion,
- 0.9% sodium chloride intravenous infusion,
- Ringer-lactate solution for injection (Hartmann’s solution for injection)

Keep the infusion bags in the overwrap until ready to use. Store at room temperature. Protect from freezing. Linezolid solution for Infusion may exhibit a yellow color that can intensify over time without adversely affecting potency.

7. MANUFACTURER

HP Halden Pharma AS
Svinesundsveien 80
Halden, 1788, Norway

8. PRODUCT REGISTRATION HOLDER:

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Selangor

9. DATE OF REVISION OF THE TEXT

July 2024