

## **PACKAGE LEAFLET: INFORMATION FOR THE PATIENT**

### **LINEZOLID 2 mg/ml SOLUTION FOR INFUSION**

Linezolid

**Read all of this leaflet carefully before you start receiving this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

#### **What is in this leaflet:**

1. What Linezolid is and what it is used for
2. What you need to know before you are given Linezolid
3. How Linezolid is given
4. Possible side effects
5. How to store Linezolid
6. Contents of the pack and other information

#### **1. What Linezolid is and what it is used for**

Linezolid is an antibiotic of the oxazolidinones group that works by stopping the growth of certain bacteria (germs) that cause infections. It is used to treat pneumonia and some infections in the skin or under the skin. Your doctor will have decided if Linezolid is suitable to treat your infection.

#### **2. What you need to know before you are given Linezolid**

##### **You should not be given Linezolid:**

- if you are allergic to linezolid or any of the other ingredients of this medicine (listed in section 6).
- if you are taking or have taken within the last 2 weeks any medicines known as monoamine oxidase inhibitors (MAOIs for example phenelzine, isocarboxazid, selegiline, moclobemide). These may be used to treat depression or Parkinson's disease.
- if you are breast-feeding. This is because it passes into breast milk and could affect the baby.

##### **Warnings and precautions**

Talk to your doctor, pharmacist or nurse before receiving Linezolid.

Linezolid may not be suitable for you if you answer **yes** to any of the following questions. In this case tell your doctor as he/she will need to check your general health and your blood pressure before and during your treatment or may decide that another treatment is better for you.

Ask your doctor if you are not sure whether any of the following categories apply to you.

- Do you have high blood pressure, whether or not you are taking medicines for this?
- Have you been diagnosed with an overactive thyroid?
- Do you have a tumour of the adrenal glands (phaeochromocytoma) or carcinoid syndrome (caused by tumours of the hormone system with symptoms of diarrhoea, flushing of the skin, wheezing)?
- Do you suffer from manic depression, schizoaffective disorder, mental confusion or other mental problems?
- Are you taking any of the following medicines?
  - decongestant, cold or flu remedies containing pseudoephedrine or phenylpropanolamine

- medicines used to treat asthma such as salbutamol, terbutaline, fenoterol
- antidepressants known as tricyclics or SSRIs (selective serotonin reuptake inhibitors) for example amitriptyline, citalopram, clomipramine, desvenlafaxine, doxepin, fluoxetine, fluvoxamine, imipramine, lofepramine, paroxetine, sertraline
- medicines used to treat migraine such as sumatriptan and zolmitriptan
- medicines used to treat sudden, severe allergic reactions such as adrenaline (epinephrine)
- medicines which increase your blood pressure, such as noradrenaline (norepinephrine), dopamine and dobutamine
- medicines used to treat moderate to severe pain, such as pethidine
- medicines used to treat anxiety disorders, such as buspirone
- an antibiotic called rifampicin
- medicines used to treat similar medical conditions which can cause monoamine oxidase inhibition. Please check with your doctor.

Tell your doctor before you are treated with this medicine if you:

- bruise and bleed easily
- are anaemic
- are prone to getting infections
- have a history of seizures
- have liver problems or kidney problems particularly if you are having dialysis
- have diarrhoea.

Tell your doctor immediately if during treatment you suffer from:

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

### Children and adolescents

Linezolid is not recommended for use in children and adolescents under the age of 18.

### Other medicines and Linezolid

There is a risk that Linezolid may sometimes interact with certain other medicines to cause side effects such as changes in blood pressure, temperature or heart rate.

**Tell your doctor if you are taking or have taken within the last 2 weeks** the following medicines as Linezolid **must not** be taken if you are already taking these medicines or have taken them recently (see also Section 2 above “You should not be given Linezolid”):

- monoamine oxidase inhibitors (MAOIs: for example phenelzine, isocarboxazid, selegiline, moclobemide). These may be used to treat depression or Parkinson’s disease.

Also tell your doctor if you are taking any of the following medicines. Your doctor may still decide to give you Linezolid, but will need to check your general health and your blood pressure before and during your treatment. In other cases, your doctor may decide that another treatment is better for you.

- decongestant cold or flu remedies containing pseudoephedrine or phenylpropanolamine
- some medicines used to treat asthma such as salbutamol, terbutaline, fenoterol
- certain antidepressants known as tricyclics or SSRIs (selective serotonin reuptake inhibitors). There are many of these including amitriptyline, citalopram, clomipramine, desvenlafaxine, doxepin, fluoxetine, fluvoxamine, imipramine, lofepramine, paroxetine, sertraline
- medicines used to treat migraine such as sumatriptan and zolmitriptan

- medicines used to treat sudden, severe allergic reactions such as adrenaline (epinephrine)
- medicines which increase your blood pressure, such as noradrenaline (norepinephrine), dopamine and dobutamine
- medicines used to treat moderate to severe pain, such as pethidine
- medicines used to treat anxiety disorders, such as buspirone
- medicines that stop blood clotting, such as warfarin.

**Tell your doctor or pharmacist if you are taking or have recently or might take any other medicines.**

#### **Linezolid with food, drink and alcohol**

- you can take Linezolid either before, during or after a meal.
- avoid eating large amounts of mature cheese, yeast extracts, or soya bean extracts (e.g. soy sauce) and drinking alcohol, especially draught beers and wine. This is because this medicine may react with a substance called tyramine which is naturally present in some foods to cause an increase in your blood pressure.
- if you develop a throbbing headache after eating or drinking, tell your doctor or pharmacist immediately.

#### **Pregnancy and breast-feeding**

The effect of Linezolid in pregnant women is not known. Therefore it should not be taken in pregnancy unless advised by your doctor. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before being given this medicine.

You should not breast-feed when taking Linezolid because it passes into breast milk and could affect the baby.

Ask your doctor or pharmacist for advice before taking any medicine.

#### **Driving and using machines**

Linezolid may make you feel dizzy or experience problems with your vision. If this happens, do not drive or operate any machinery. Remember that if you are unwell your ability to drive or operate machinery may be affected.

#### **Linezolid contains Glucose and Sodium**

Each 1 ml of Linezolid solution for infusion contains 45.7 mg glucose (13.710 g glucose in one bag). This should be taken into account in patients with diabetes mellitus.

Each 1 ml of Linezolid solution for infusion contains 0.38 mg sodium (0.165 mmol) (114.0 mg sodium in one bag). To be taken into consideration by patients on a controlled sodium diet.

Please tell your doctor if you are on a low sodium diet.

### **3. How Linezolid is given**

#### **Adults**

This medicine will be given to you through a drip (by infusion into a vein) by a doctor or healthcare professional. The recommended dose for adults (18 years and older) is 300 ml (600 mg linezolid) twice daily which is given directly into the blood stream (intravenously) by a drip over a period of 30 to 120 minutes.

If you are on kidney dialysis, you should be given Linezolid after dialysis.

A course of treatment usually lasts 10 to 14 days, but can last up to 28 days. The safety and effectiveness of this medicine have not been established for treatment periods longer than 28 days. Your doctor will decide how long you should be treated.

While you are taking Linezolid, your doctor should perform regular blood tests to monitor your blood count.

Your doctor should monitor your eyesight if you take Linezolid for more than 28 days.

#### **Use in children and adolescents**

Linezolid is not recommended to treat children and adolescents (under 18 years old).

#### **If you receive more Linezolid than you should**

If you are concerned that you may have been given too much Linezolid, tell your doctor or nurse immediately.

#### **If you miss a dose of Linezolid**

As you will be given this medicine under close supervision, it is very unlikely that you will miss a dose. If you think that you have missed a dose of treatment, tell a doctor or nurse immediately.

If you have any further questions on the use of this product, ask your doctor, pharmacist or nurse.

### **4. Possible side effects**

Like all medicines, Linezolid can cause side effects, although not everybody gets them.

**Tell your doctor or pharmacist immediately** if you notice any of these side effects during your treatment with Linezolid:

- skin reactions such as red sore skin and flaking (dermatitis), rash, itching, or swelling, particularly around the face and neck. This may be the sign of an allergic reaction and it may be necessary for you to stop taking Linezolid.
- problems with your vision such as blurred vision, changes in colour vision, difficulty in seeing detail or if your field of vision becomes restricted.
- severe diarrhoea containing blood and/or mucus (antibiotic associated colitis including pseudomembranous colitis), which in rare circumstances may develop into complications that are life-threatening.
- recurrent nausea or vomiting, abdominal pain or over breathing.
- fits or seizures have been reported with Linezolid. You should let your doctor know if you experience agitation, confusion, delirium, rigidity, tremor, incoordination and seizure while also taking antidepressants known as SSRIs (see section 2).

Numbness, tingling or blurred vision have been reported by patients who have been given Linezolid for more than 28 days. If you experience difficulties with your vision you should consult your doctor as soon as possible.

#### **Other side effects include:**

**Common** (may affect up to 1 in 10 people):

- fungal infections especially vaginal or oral “thrush”
- headache
- metallic taste in the mouth
- diarrhoea, nausea or vomiting
- changes in some blood test results including those measuring your kidney or liver function or blood sugar levels

- unexplained bleeding or bruising, which may be due to changes in the numbers of certain cells in the blood which may affect blood clotting or lead to anaemia
- difficulty in sleeping
- increased blood pressure
- anaemia (low red blood cell)
- changes in numbers of certain cells in the blood which may affect your ability to fight infection
- skin rash
- itching skin
- dizziness
- localised or general abdominal pain
- constipation
- indigestion
- localised pain
- fever

**Uncommon** (may affect up to 1 in 100 people):

- inflammation of the vagina or genital area in women
- sensations such as tingling or feeling numb
- blurred vision
- 'ringing' in the ears (tinnitus)
- inflammation of the veins
- dry or sore mouth, swollen, sore or discoloured tongue
- pain at and around the place where the infusion (drip) was given
- a need to urinate more often
- chills
- feeling tired or thirsty
- inflammation of the pancreas
- increased sweating
- changes in proteins, salts or enzymes in the blood which measure kidney or liver function
- convulsions
- hyponatraemia (low blood sodium levels)
- kidney failure
- reduction in platelets
- abdominal bloating
- transient ischaemic attacks (temporary disturbance of blood flow to the brain causing short term symptoms such as loss of vision, leg and arm weakness, slurring of speech and loss of consciousness)
- inflammation of the skin
- increase in creatinine
- stomach pain
- changes in heart rate (e.g. increase rate)

**Rare** (may affect up to 1 in 1,000 people):restricted field of vision

- superficial tooth discolouration, removable with professional dental cleaning (manual descaling)

**Not known** (frequency cannot be estimated from the available data):

- serotonin syndrome (symptoms include fast heart rate, confusion, abnormal sweating, hallucinations, involuntary movements chills and shivering)
- lactic acidosis (symptoms include recurrent nausea and vomiting, abdominal pain, rapid breathing)
- severe skin disorders
- sideroblastic anaemia (a type of anaemia (low red blood cells))

- alopecia (hair loss)
- changes in colour vision or difficulty in seeing detail
- decrease of the blood cell count
- weakness and/or sensory changes

### **Reporting of side effects**

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA

Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517.

Website: [www.hpra.ie](http://www.hpra.ie); E-mail: [medsafety@hpra.ie](mailto:medsafety@hpra.ie). By reporting side effects you can help provide more information on the safety of this medicine.

## **5. How to store Linezolid**

**Keep this medicine out of the sight and reach of children.**

Do not use medicine after the expiry date which is stated on the bag label after EXP. The expiry date refers to the last day of that month.

### **Storage conditions:**

*Before opening:* Do not store above 30°C. Do not refrigerate or freeze. Store in the original package (overpouch) until ready to use in order to protect from light.

#### *After opening:*

Linezolid 2 mg/ml solution for infusion is physically and chemically stable for at least four hours at room temperature after first opening. From a microbiological point of view unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

#### *After dilution:*

Linezolid 2 mg/ml solution for infusion is physically and chemically stable for at least four hours at room temperature after dilution with 0.9% sodium chloride, 5% glucose or Ringer lactate solution. From a microbiological point of view unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

For single use only. Discard any unused solution.

Do not use Linezolid if you notice any visible particles, if the solution is unclear or if the bag is damaged.

Medicines should not be disposed of via wastewater or household waste. Your doctor should dispose of medicines that are no longer required. These measures will help to protect the environment.

## **6. Contents of the pack and other information**

### **What Linezolid contains**

- The active substance is linezolid. 1 ml of solution for infusion contains 2 mg of linezolid. 300 ml of solution for infusion contains 600 mg of linezolid.
- The other ingredients are citric acid anhydrous (E330), sodium citrate dihydrate (E331), glucose monohydrate (a type of sugar) and water for injections.

### **What Linezolid looks like and contents of the pack**

Linezolid is presented as a clear, colourless solution, in a one or two port plastic infusion bag fitted with a twist off connector plastic spike port. The infusion bag is contained in a plastic overpouch.

Pack sizes: 300 ml bags (600 mg linezolid) in packs of 1, 10 or 30 bags.  
Not all pack sizes may be marketed.

## **Marketing Authorisation Holder and Manufacturer**

### Marketing Authorisation Holder

Teva Pharma B.V., Swensweg 5, 2031GA Haarlem, The Netherlands.

### Manufacturer

Teva Pharmaceutical Works Private Limited Company, Táncsics Mihály út 82, H-2100 Gödöllő, Hungary

## **This medicinal product is authorised in the Member States of the EEA under the following names:**

Denmark:	Linozid
Bulgaria:	ZOLINID 2 mg/ml solution for infusion
Czech Republic:	Linezolid Teva 2 mg/ml, infuzní roztok
Spain:	Linezolid Teva 2 mg/ml solución para perfusión
Ireland:	Linezolid 2 mg/ml Solution for Infusion
Romania:	Linezolid Teva 2 mg/ml soluție perfuzabilă

**This leaflet was last revised in 05/2016.**

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## **The following information is intended for medical or healthcare professionals only:**

### **IMPORTANT: Refer to the Summary of Product Characteristics before prescribing**

Linezolid is not active against infections caused by Gram negative pathogens. Specific therapy against Gram negative organisms must be initiated concomitantly if a Gram negative pathogen is documented or suspected.

### **Dosage and Method of Administration**

Linezolid should only be initiated in a hospital environment and after consultation with a relevant specialist such as a microbiologist or infectious diseases specialist.

Patients who commence treatment on the parenteral formulation may be switched to either oral presentation when clinically indicated. In such circumstances, no dose adjustment is required as linezolid has an oral bioavailability of approximately 100%.

The solution for infusion should be administered over a period of 30 to 120 minutes.

**Recommended dosage and duration of treatment for adults:** The duration of treatment is dependent on the pathogen, the site of infection and its severity, and on the patient's clinical response.

The following recommendations for duration of therapy reflect those used in the clinical trials. Shorter treatment regimens may be suitable for some types of infection but have not been evaluated in clinical trials.

The maximum treatment duration is 28 days. The safety and effectiveness of linezolid have not been established for treatment periods longer than 28 days.

No increase in the recommended dosage or duration of treatment is required for infections associated with concurrent bacteraemia.

The dose recommendation for the solution for infusion is as follows:

Infections	Dosage	Duration of treatment
Nosocomial pneumonia	600 mg twice daily	10-14 Consecutive days
Community acquired pneumonia	600 mg twice daily	10-14 Consecutive days
Complicated skin and soft tissue infections	600 mg twice daily	10-14 Consecutive days

**Children:** There are insufficient data on the safety and efficacy of linezolid in children and adolescents (<18 years old) to establish dosage recommendations. Therefore, until further data are available, use of linezolid in this age group is not recommended.

**Elderly patients:** No dose adjustment is required.

**Patients with renal insufficiency:** No dose adjustment is required.

**Patients with severe renal insufficiency (i.e. creatinine clearance ( $CL_{CR}$ )  $\leq 30$  ml/min):** No dose adjustment is required. Due to the unknown clinical significance of higher exposure (up to 10 fold) to the two primary metabolites of linezolid in patients with severe renal insufficiency, linezolid should be used with special caution in these patients and only when the anticipated benefit is considered to outweigh the theoretical risk.

As approximately 30% of a linezolid dose is removed during 3 hours of haemodialysis, linezolid should be given after dialysis in patients receiving such treatment. The primary metabolites of linezolid are removed to some extent by haemodialysis, 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 haemodialysis).

**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.

**Method of administration:** The recommended linezolid dosage should be administered intravenously twice daily.

### Overdose

No specific antidote is known.

No cases of overdose have been reported. However, the following information may prove useful:

Supportive care is advised together with maintenance of glomerular filtration. Approximately 30% of a linezolid dose is removed during 3 hours of haemodialysis, but no data are available for the removal of linezolid by peritoneal dialysis or haemoperfusion.

### Instructions for use and handling

For single use only.

Remove overpouch 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. Do not reconnect partially used bags.

Linezolid Solution for Infusion is compatible with the following solutions:

Glucose 50 mg/ml (5%) solution for infusion,

Sodium chloride 9 mg/ml (0.9%) solution for infusion,

Ringer-lactate solution for injection (Hartmann's solution for injection).

**Incompatibilities:**

Additives should not be introduced into this solution. If linezolid is to be given concomitantly with other medicinal products, each medicinal product should be given separately in accordance with its own directions for use. Similarly, if the same intravenous line is to be used for sequential infusion of several medicinal products, the line should be flushed prior to and following linezolid administration with a compatible infusion solution.

Linezolid solution for infusion is known to be physically incompatible with the following compounds: amphotericin B, chlorpromazine hydrochloride, diazepam, pentamidine isethionate, erythromycin lactobionate, phenytoin sodium and sulphamethoxazole/trimethoprim. Additionally, it is chemically incompatible with ceftriaxone sodium.

**Shelf life: 2 years**

**After opening:**

Chemical and physical in-use stability has been demonstrated for 4 hours at room temperature. From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

**After dilution:**

0.9% sodium chloride: the solution is physically and chemically stable for 4 hours at  $25\pm 2.5^{\circ}\text{C}$ .

5% glucose: the solution is physically and chemically stable for 4 hours at  $25\pm 2.5^{\circ}\text{C}$ .

Ringer lactate: the solution is physically and chemically stable for 4 hours at  $25\pm 2.5^{\circ}\text{C}$ . From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

**Special precautions for Storage**

Do not store above  $30^{\circ}\text{C}$ . Do not refrigerate or freeze. Store in the original package (overpouch) until ready to use in order to protect from light.

**Disposal**

Any unused solution must be disposed of in accordance with local requirements.