Linezolid 600mg tablets AMBER0

When used as a 10-14-day course for the treatment of pneumonia or complicated skin and soft tissue infections on the recommendation of a microbiologist

Information for prescribers - to be read in conjunction with the SPC

Dosage and administration [1]

Consultant microbiologists will request GPs to prescribe up to 14 days of treatment in the community **ONLY**.

If more than 14 days of treatment is required, either as an initial course or if an extension to the initial 14-day course is required, the patient must be referred back into secondary care.

The recommended dose of oral linezolid is 600 mg every 12 hours usually for 10–14 consecutive days (up to 28 days of treatment may be supplied by specialists).

Monitoring [1]

It is recommended that complete blood counts (including haemoglobin levels, platelets, and total and differentiated leucocyte counts) should be monitored **weekly** in primary care for patients who receive linezolid, regardless of baseline blood count (including for short courses of linezolid). If significant myelosuppression occurs during linezolid therapy, treatment should be stopped and discussed with the consultant microbiologist.

Contraindications [1]

- Hypersensitivity to the active substance or to any of the excipients in the product.
- Linezolid should not be used in patients taking any medicinal product which inhibits monoamine oxidases A or B (e.g. phenelzine, isocarboxazid, selegiline, moclobemide) or within two weeks of taking any such medicinal product.
- Unless there are facilities available for close observation and monitoring of blood pressure, linezolid should not be administered to patients with the following underlying clinical conditions or on the following types of concomitant medications:
  - Patients with uncontrolled hypertension, phaeochromocytoma, carcinoid, thyrotoxicosis, bipolar depression, schizoaffective disorder, acute confusional states.
  - Patients taking any of the following medications: serotonin re-uptake inhibitors, tricyclic antidepressants, 5-HT_1 receptor agonists (triptans), directly and indirectly acting sympathomimetic agents (e.g. adrenergic bronchodilators, pseudoephedrine and phenylpropanolamine), vasopressive agents (e.g. epinephrine, norepinephrine), dopaminergic agents (e.g. dopamine, dobutamine), pethidine or buspirone.
- Linezolid and its metabolites may pass into breast milk and, accordingly, breastfeeding should be discontinued prior to and throughout administration.

Cautions [1]

Myelosuppression

Myelosuppression (including anaemia, leucopenia, pancytopenia and thrombocytopenia) has been reported in patients receiving linezolid (see monitoring section above).

Antibiotic-associated diarrhoea and colitis

Antibiotic-associated diarrhoea and antibiotic-associated colitis, including pseudomembranous colitis and *Clostridium difficile*-associated diarrhoea have been reported with nearly all antibacterial agents, including linezolid. In cases of suspected or verified antibiotic-associated colitis, discontinuation of linezolid may be warranted.

Lactic acidosis

Patients who develop signs and symptoms of metabolic acidosis including recurrent nausea or vomiting, abdominal pain, a low bicarbonate level, or hyperventilation while receiving linezolid should receive immediate medical attention. If lactic acidosis occurs, the benefits of continued use of linezolid should be weighed against the potential risks.

Hyponatraemia and SIADH

Hyponatraemia 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 are monitored regularly in patients at risk of hyponatraemia such as elderly patients or patients taking medicines that may lower blood sodium levels.

Peripheral and optic neuropathy

Peripheral neuropathy, as well as optic neuropathy and optic neuritis sometimes progressing to loss of vision, have been reported in patients treated with Linezolid (reports have primarily been in patients treated for longer than the maximum recommended duration of 28 days).

The GP has the responsibility to counsel patients on the potential risk of visual impairment - patients should be advised to read the patient information leaflet given with linezolid, in particular patients should be advised to report symptoms of visual impairment, such as changes in visual acuity, changes in colour vision, blurred vision, or visual field defect. If these occur, then the prescriber should contact the consultant microbiologist. Patients experiencing new visual symptoms (regardless of treatment duration) should be evaluated promptly.

Convulsions

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

Use with tyramine-rich foods

Linezolid is a reversible, non-selective inhibitor of monoamine oxidase (MAOI). Patients should be advised against consuming large amounts of tyramine rich foods.

Superinfection

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

Special populations

Linezolid 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 linezolid should be given to patients with severe hepatic insufficiency only when the perceived benefit outweighs the theoretical risk.

Pregnancy and impairment of fertility

Linezolid should not be used during pregnancy unless clearly necessary i.e. only if the potential benefit outweighs the theoretical risk.

Possible effects of linezolid on the human male reproductive system are not known.

Side effects [2]

Common (≥ 1/100 to < 1/10) or very common (≥ 1/10)

Anaemia; constipation; diarrhoea; dizziness; gastrointestinal discomfort; headache; hypertension; increased risk of infection; insomnia; localised pain; nausea; skin reactions; taste altered; vomiting.

Uncommon (≥ 1/1,000 to < 1/100)

Arrhythmia; chills; dry mouth; eosinophilia; fatigue; gastritis; hyperhidrosis; hyponatraemia; leucopenia; neutropenia; oral disorders; pancreatitis; polyuria; renal failure; seizure; sensation abnormal; thirst; thrombocytopenia; thrombophlebitis; tinnitus; tongue discolouration; transient ischaemic attack; vision disorders; vulvovaginal disorder.

Rare (≥ 1/10,000 to < 1/1,000) or very rare (< 1/10,000)

Antibiotic associated colitis; bone marrow disorders; tooth discolouration.

Frequency not known

Alopecia; angioedema; lactic acidosis; nerve disorders; serotonin syndrome; severe cutaneous adverse reactions (SCARs).

Drug Interactions [1]

- Monoamine oxidase inhibitors (**see contraindications**).
- Potential interactions producing elevation of blood pressure (see contraindications).
- Potential serotonergic interactions including use with tyramine-rich foods (see contraindications and cautions).
- Rifampicin - The mechanism of this interaction and its clinical significance are unknown.
- Warfarin - There are insufficient data from patients who have received warfarin and linezolid to assess the clinical significance, if any, of these findings.

Version Number	Date	Amendments Made	Author
1.0	March 2021	New document	PT, AG
1.1	April 2024	Update	JG

References

[1] Electronic Medicines Compendium, "Summary of Product Characteristics Linezolid 600 mg tablets," Amarox Limited, 06 September 2023. [Online]. Available: https://www.medicines.org.uk/emc/product/13583/smpc. [Accessed 29 April 2024].

[2] Joint Formulary Committee, "British National Formulary (online)," London BMJ Group and Pharmaceutical Press, [Online]. Available: https://bnf.nice.org.uk/drugs/linezolid/. [Accessed 29 April 2024].