Linezolid Contraindications

The following list of linezolid contraindications should not be considered exhaustive. For further information please see the current Summary of Product Characteristics via https://www.medicines.org.uk/emc or the current BNF via http://www.medicinescomplete.com

1. Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of SPC.
2. Unless there are facilities available for close observation and monitoring of blood pressure linezolid should not be administered to patients with the following conditions: uncontrolled hypertension, phaeochromocytoma, carcinoid, thyrotoxicosis, bipolar depression, schizoaffective disorder, acute confusional states.
3. Breastfeeding should be discontinued prior to and throughout administration of linezolid
4. Lactose: patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption

Linezolid monitoring

Monitor	Reason for monitoring	Action to be taken
LFTs, U&Es, and FBC	Myelosuppression (including anaemia, leucopenia, pancytopenia and thrombocytopenia) have been reported. Risk of these effects appears to be related to duration of treatment, elderly patients. Thrombocytopenia may occur more commonly with patients with severe renal impairment Linezolid can also cause abnormal LFTs (reported as common on SPC >1/100 to <1/10) and incidence of renal failure (reported as uncommon Linezolid should be used with special caution in patients with severe renal and hepatic insufficiency and only when the anticipated benefit is considered to outweigh potential risk	If abnormalities are detected, this should be discussed with the acute care microbiology or infectious disease consultant as soon as possible
Peripheral and optical neuropathy	Peripheral neuropathy, as well as optic neuropathy and optic neuritis sometimes progressing to loss of vision- these reports have primarily been in patients treated for longer than the max recommended duration of 28 days	Patients experiencing new visual symptoms should be evaluated promptly and referred to an ophthalmologist if necessary. This should also be reported and discussed with acute care microbiology or infectious disease consultant as soon as possible Vision should be monitored regularly if treatment is required for longer than 28 days. Patients should be asked to report any visual disturbances or impairment
Lactic acidosis	Lactic acidosis (frequency no known) and hyponatraemia (uncommon) has been reported with use of linezolid. Patients who develop signs and symptoms of metabolic including recurrent nausea or vomiting, abdominal pain, a low bicarbonate level, or hyperventilation	This should be reported and discussed with the OPAT service or the acute care microbiology or infectious diseases consultant as soon as possible

Convulsion risk	Convulsion have been reported in patients with linezolid- in most of these cases, a history of seizures or risk factors for seizures was reported	Patient should be advised to inform if they have a history of seizure. Linezolid should be avoided in patients at risk of seizures
Gastrointestinal disorders:	Diarrhoea, nausea/ vomiting, localised or general abdominal pain, constipation, dyspepsia reported as common. Pancreatitis, gastritis, abdominal distension reported as uncommon Antibiotic-associated diarrhoea and antibiotic-associated colitis, including pseudomembranous colitis have been reported with linezolid.	If these symptoms become severe or persistent or stools contain blood or mucus, linezolid therapy should be stopped. Consider stool sample
Skin disorders:	Urticaria, dermatitis and rash reported common to uncommon Bullous disorders such as those described as Stevens-Johnson syndrome and toxic epidermal necrolysis reported as rare (>1/10,000 to <1/1000)	Mild skin disorders should be managed appropriately. In more severe cases the use of ongoing linezolid should be weighed against the potential risks. Encourage patient to report

Drug Interactions with Linezolid

Interactive agent	**Effect**	**Management**
Alpha blockers	Enhanced hypotensive effects	Monitor BP
Analgesics/ Opioids	Pethidine, Nefopam- CNS excitation (hypertension) or depression (hypotension) Opioids with serotonergic effects- fentanyl/ alfentanil, methadone Tramadol- increase serotonergic effects and risk of convulsions	Avoid where possible. If co-administration is considered essential patients will require close observation and monitoring for serotonin syndrome.
Antiepileptics	MAOIs possibly antagonize anticonvulsant effects of antiepileptics by lowering seizure threshold	Avoid concurrent use
Antipsychotics	CNS effects of MAOIs possibly increased	Monitor for CNS effects
Axomoxetine	Possible increased risk of convulsions	Atomoxetine should not be used within a minimum of 2 weeks after discontinuing therapy with MAOI. Treatment with MAOI should not be initiated within 2 weeks after discontinuing atomoxetine
Buproprion	Increase the risk of additive hypertension: a case of severe, intermittent, intraoperative hypertension appears to support this	Manufacturer advises avoid for 2 weeks after stopping MAOI
Dopaminergics	Possible increased risk of serotonin syndrome when MAOIs given with levodopa, entacapone and tolcapone.	Monitor. Concurrent treatment should be stopped if serotonin syndrome occurs
Food/ Drink containing tyramine	No significant pressor reported in subjects receiving both linezolid and less than 100mg tyramine.	Avoid consuming excessive amounts of food with high tyramine contents e.g. mature cheese, yeast extracts, undistilled alcoholic beverages and fermented soya bean products

	However, eating large quantity of tyramine content can raise blood pressure to a dangerous level and the risk of hypertensive crisis	such as soy sauce
Other MAOI	Linezolid is a reversible MAOI inhibitor and therefore it is contra-indicated with MAOI inhibitors There are very limited data from drug interaction studies and on the safety of linezolid when administered to patients on concomitant medications that might put them at risk from MAO inhibition	The concurrent use of linezolid is contraindicated with or within 2 weeks of taking any other drug that inhibits MAO-A or MAO-B e.g phenelzine, moclobemide, selegiline, rasagiline, isocarboxazide, tranylpromine
Rifampicin	Rifampicin reduces linezolid concentrations (AUC reduced by 30%). This is not a CYP450 mediated interaction but is thought to be due to induction of p-glycoprotein transporter and subsequent increased linezolid excretion	It is no longer recommended to co-prescribe these antibiotics and rifampicin should be stopped 2 weeks prior to starting linezolid
Serotonin reuptake inhibitors, Tricyclic antidepressants, Serotonergic antiemetics, Serotonin 5HT1 receptor agonists (triptans)	Increased risk of hypertension and CNS excitation and serotonin syndrome Examples of: SSRIs: citalopram, paroxetine, escitalopram, sertraline), *Dapoxetine (SSRI) indicated for premature ejaculation Tricyclic antidepressants: amitriptyline) Serotonergic antiemetics: ondansetron *Metoclopramide also thought to increase risk Serotonin 5HT1 agonists: sumatriptan, rizatriptan	Monitor for confusion, restlessness, agitation, tremors, incoordination, blushing, diaphoresis (excessive sweating), diarrhoea, rapid heart rate and high blood pressure and hyperpyrexia Whilst co-administration is contraindicated the management of patients for whom treatment with linezolid and a serotonergic antidepressant agent is considered essential will require close observation and monitoring For dapoxetine, manufacturers advise avoiding concurrent use during and for 14 days after stopping linezolid. Linezolid should not be started for at least 7 days after stopping dapoxetine
Sympathomemetics/ Vasopressive agents	Risk of hypertensive crisis. Medications include adrenergic bronchodilators, pseudoephedrine, xylomethazoline, phenylpropanolamine, adrenaline, noradrenaline, dopamine, dobutamine	Avoid if possible. Advised not to buy and use OTC decongestant products (Sudafed®, Otrivine®) without first consulting their medical team
Warfarin	When warfarin was added to linezolid therapy at steady-state, there was a 10% reduction in mean maximum INR on co-administration with a 5% reduction in AUC INR.	Monitor INR There are insufficient data from patients who have received warfarin and linezolid to assess the clinical significance, if any, of these findings

The following list of drug interactions should not be considered exhaustive. For further information refer to the current Summary of Product Characteristics via https://www.medicines.org.uk/emc current BNF http://www.medicinescomplete.com and UK Medicines Information via https://www.sps.nhs.uk/articles/what-is-serotonin-syndrome-and-which-medicines-causeit-2/

References:

1. SPC for Linezolid www.medicines.org.uk
2. NHS GGC Adult Protocol Clinical Guidelines on Linezolid
3. NHS Tayside Clinical Guidelines on Linezolid
4. Stockley Drug Interaction
5. SPC for Axomoxetine www.medicines.org.uk

Author: Evelyn Yoong (antimicrobial pharmacist)

Approved: OPAT services DGRI, ADTC 26/4/23 Next review: 26/4/26