CLINICAL GUIDELINE

Linezolid, adult treatment protocol initiation, monitoring, discharge & outpatient supply

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

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Important Note:

The online version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

ADULT LINEZOLID TREATMENT PROTOCOL: INITIATION, MONITORING, DISCHARGE & OUTPATIENT SUPPLY

NHS Greater Glasgow and Clyde

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Guideline Summary

1. Linezolid treatment should only be initiated on the advice of a Microbiologist or Infectious Diseases physician.

2. Linezolid is a 'Protected' antibiotic, supply requires completion of a 'Protected' Antibiotic form Protected Form.

3. **Before** starting a patient on Linezolid

- Check for contraindications, cautions and interactions.
- Undertake baseline investigations
  - ✓ U&Es
  - ✓ LFTs
  - ✓ FBC (including haemoglobin, platelets and differential leucocyte counts)

4. Ensure appropriate ongoing monitoring

- Weekly U&Es, LFTs and FBC including haemoglobin, platelets and total differentiated leucocyte counts. **NOTE:** More frequent monitoring of the above is recommended in those with pre-existing myelosuppression, severe renal impairment or receiving concomitant medicines that may affect blood counts.

- There is a limited evidence base to support the use of therapeutic drug monitoring (TDM) to optimise linezolid dosing in patient with renal impairment or extremes of body weight. The OPAT service may undertake or advise linezolid TDM on rare occasions.

Be vigilant for the development of undesirable effects

- ✓ Monitor for symptoms and signs of lactic acidosis e.g. recurrent nausea and/or vomiting, abdominal pain, a low bicarbonate level or hyperventilation.
- ✓ Monitor for symptoms and signs of peripheral (e.g. any numbness or tingling in the extremities) and optic (e.g. changes in visual acuity, changes in colour vision, blurred vision or visual field defects) neuropathy. **Note**: there is no definitive evidence to support the use of pyridoxine supplements to reduce the risk of linezolid induced peripheral or optic neuropathy.
- ✓ In any patient requiring longer than 28 days linezolid therapy visual function should be checked regularly.
- ✓ If a patient experiences new visual symptoms whilst taking linezolid they should be referred to ophthalmology.
- ✓ Close inpatient blood pressure monitoring and/or monitoring for signs and symptoms of serotonin syndrome will be required in some patients where the concomitant administration of interacting drugs is considered necessary. **Note:** on rare occasions where treatment options are limited patients under the care of the OPAT service may be discharged on interacting medications with an OPAT monitoring plan in place.

5. Provide patient/carer education, a linezolid patient information leaflet (see Appendix 1) or available at PrintOnTheWeb (TimeHarvest-Server.local) and a low tyramine diet advice sheet (see Appendix 2) or available at www.pennutrition.com.

6. Linezolid has excellent oral bioavailability so the oral route should be used whenever possible.

7. In any patient where linezolid therapy is ongoing at discharge ensure the linezolid discharge checklist is completed **prior** to discharge Linezolid Discharge Checklist.

NOTE: if linezolid therapy is to continue for > 7 days post discharge the patient **must** also be referred to the Outpatient Antibiotic Therapy (OPAT) Service via TrakCare **prior** to discharge to ensure an adequate plan is in place for ongoing patient monitoring and linezolid supply.

1 INDICATION AND FORMULATIONS

Generic drug name:	Linezolid
Intended indication:	Treatment of infection on the advice of a consultant microbiologist or infectious diseases (ID) physician
Formulations:	600mg Tablet 100mg/5ml granules for oral suspension IV Infusion 600mg/300ml

2 DOSE & TREATMENT DURATION

Recommended starting dose:	***Linezolid can only be initiated on the advice of a microbiologist or an infectious diseases (ID) physician*** Oral 600mg twice daily IV 600mg twice daily Please see link below for mycobacterium infections
Titration of dose:	None
Maximum dose:	Oral 600mg twice daily IV 600mg twice daily
Conditions requiring dose adjustment:	None
Duration of treatment	Treatment duration should be discussed with a microbiologist/ID consultant at initiation. The shortest possible duration should be prescribed. Usual maximum treatment course of 10-14 days. Maximum licensed duration of treatment 28 days. With microbiologist/ ID consultant approval some infections may require treatment courses for longer than 28 days. **NOTE**: this is unlicensed and will increase the risk of adverse effects so increased monitoring of the patient is required.
Mycobacterium Infection	For the use of linezolid in the treatment of mycobacterium infection please refer to http://www.tbdrugmonographs.co.uk/linezolid.html

3 INITIATING A PATIENT ON LINEZOLID THERAPY

Linezolid can only be initiated on the advice of a microbiologist or an infectious diseases (ID) physician.

3.1 Responsibilities of microbiologist or ID physician recommending linezolid

- Inform the prescribing doctor to refer to this document "Adult Linezolid Treatment Protocol: Initiation, Monitoring, Discharge and Outpatient Supply" available via NHSGGC Clinical Guideline Platform to ensure appropriate patient baseline checks are undertaken before initiating linezolid and ensure appropriate ongoing patient management.
- Inform the prescribing doctor to complete a "Protected Antibiotic" form available via NHSGGC Clinical Guideline Platform (see Section 16).
- Inform the local antimicrobial pharmacist (See Section 15) of the recommendation to start linezolid.

3.2 Responsibilities of the doctor prescribing linezolid

- Discuss prescription with microbiologist/ID consultant and complete "Protected Antibiotic" form available via NHSGGC Clinical Guideline Platform (see Section 16) and send to pharmacy department.
- Check for contraindications (see Section 7) cautions (see Section 8) and interactions (see Section 9) prior to initiating treatment.

- Undertake baseline investigations (see Section 10) and ongoing monitoring (see Section 11) and be vigilant for the development of undesirable effects (see Section 12).
- Provide patient education and a linezolid patient information leaflet (PIL) and low tyramine diet sheet (see Section 16) and document this in the patient's medical notes.
- Prescribe linezolid on the inpatient medicine chart and inform the ward pharmacist and nurse looking after the patient to ensure supply available.
- Linezolid has high oral bioavailability so the oral route should be used as soon as reliably available.
- Linezolid tablets are considerably cheaper than the oral suspension (see Section 14). Prescribe linezolid tablets where possible.
- Ensure the discharge checklist (see Section 4.1) is completed if the patient is discharged on ongoing linezolid therapy.

4 DISCHARGING A PATIENT ON LINEZOLID THERAPY OR SUPPLYING LINEZOLID VIA OUTPATIENTS

4.1 Doctor Checklist for Discharge/Outpatient Supply

If patient requires ≤ 7 days linezolid to complete their treatment course the prescribing doctor must:

- Ensure patient monitoring (see Section 11.1) is complete and up to date prior to discharge/outpatient supply.
- Ensure patient has been educated and provided with a linezolid PIL and low tyramine diet sheet (see Section 16) prior to discharge/outpatient supply.
- Complete the 'Linezolid Discharge and Outpatient Supply Checklist' (see Section 16) and forward to pharmacy. The linezolid supply will not be released from pharmacy until this document has been received.

If patient requires > 7 days linezolid to complete their treatment course the prescribing doctor must:

- Ensure **prior** to discharge the patient is referred to the Outpatient Antibiotic Therapy (OPAT) Service via TrakCare to ensure an adequate plan is in place for ongoing patient monitoring and supply of linezolid.
- The patient must **not** be discharged until OPAT have arranged patient follow up monitoring and supply of linezolid. This plan must be documented in the patient's medical notes and the patient's immediate discharge letter. **NOTE**: If patient monitoring to be carried out by the GP (Section 11.2) this **must** be discussed and agreed with the GP **and** the OPAT team **prior** to the patient being discharged from hospital.
- Ensure patient monitoring (Section 11.1) is complete and up to date prior to discharge.
- Ensure patient has been educated and a linezolid PIL and low tyramine diet sheet (see Section 16) provided prior to discharge. The details of the patient's follow up appointment should be documented on the patient information leaflet.
- Complete the 'Linezolid Discharge and Outpatient Supply Checklist' (see Section 16) and forward to the local hospital pharmacy department. The linezolid supply will not be released from pharmacy until a completed checklist has been received.

4.2 Pharmacy Checklist for Discharge/Outpatient Supply

If patient requires ≤ 7 days linezolid to complete their treatment course pharmacy must:

- Screen discharge/outpatient prescription.
- Ensure 'Linezolid Discharge and Outpatient Supply Checklist' (see Section 16) has been completed and received prior to releasing linezolid supply.
- Dispense prescription in usual manner.

If patient requires > 7 days linezolid to complete their treatment course pharmacy must:

- Screen discharge/outpatient prescription.
- Ensure 'Linezolid Discharge and Outpatient Supply Checklist' (see Section 16) has been completed and received prior to releasing linezolid supply.

- Supply a maximum 7 day supply of linezolid to the patient at a time. Ensure the discharging/outpatient medical team are aware only one week will be supplied at a time.

5 RESPONSIBILITIES OF OUTPATIENT ANTIBIOTIC THERAPY (OPAT) SERVICE

- To assess inpatient referrals for patients being discharged on > 7 days linezolid treatment to ensure ongoing linezolid is appropriate and if appropriate to agree a plan for patient monitoring and ongoing linezolid supply.
- To assess referrals for patients commenced on linezolid therapy via outpatient clinics to ensure linezolid is appropriate and if appropriate to agree a plan for patient monitoring and ongoing linezolid supply.
- OPAT will not take responsibility for patients discharged without formal assessment and agreement by the OPAT nurse specialist.

6 RESPONSIBILITIES OF THE PATIENT OR THEIR CARER

- Inform the prescribing doctor of all current medications including prescribed and over the counter products.
- To take linezolid as prescribed.
- To attend scheduled hospital and clinic appointments.
- To refer to the information in the linezolid patient information leaflet and dietary advice sheet.
- To be aware of the importance of reporting any adverse effects to their doctor, nurse or pharmacist.
- If the adverse effect occurs in the community to be aware of the contact advice in the linezolid patient information leaflet to report adverse effects.

7 CONTRAINDICATIONS

NOTE: 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

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of SPC.
- 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 conditions: uncontrolled hypertension, phaeochromocytoma, carcinoid, thyrotoxicosis, bipolar depression, schizoaffective disorder, acute confusional states.
- Unless there are facilities available for close observation and monitoring of blood pressure linezolid should not be administered to patients taking any of the following medications: serotonin re-uptake inhibitors, tricyclic antidepressants, serotonin 5-HT1 receptor agonists (triptans), directly or indirectly acting sympathomimetic agents (including the adrenergic bronchodilators, pseudoephedrine and phenylpropanolamine), vasopressive agents (e.g. epinephrine, norepinephrine), dopaminergic agents (e.g. dopamine, dobutamine), pethidine or buspirone. **Note:** on rare occasions where treatment options are limited patients under the care of the OPAT service may be discharged on interacting medications with an OPAT monitoring plan in place.
- It is recommended breastfeeding should be discontinued prior to and throughout administration of linezolid. In patients where treatment options are limited contact Medicines Information for additional breastfeeding specialist services advice.

8 CAUTIONS

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

- Myelosuppression (including anaemia, leucopenia, pancytopenia and thrombocytopenia). Linezolid should only be administered to such patients when close monitoring (See section 11.1) of haemoglobin levels, blood counts and platelet counts is possible. If significant myelosuppression occurs linezolid should be stopped. If considered absolutely necessary to continue therapy, intensive monitoring of blood counts and appropriate management strategies should be implemented.
- Antibiotic-associated diarrhoea and antibiotic-associated colitis, including pseudomembranous colitis have been reported with linezolid. Linezolid should be discontinued, if possible, if such symptoms develop.
- Lactic acidosis has been reported with the use of linezolid. Patients who develop signs and symptoms of metabolic acidosis (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.
- Serotonin syndrome associated with the co-administration of linezolid and serotonergic agents, including antidepressants such as selective serotonin re-uptake inhibitors (SSRIs) and opioids have been reported. Concomitant use of such agents is contra-indicated unless considered essential. In such cases close **INPATIENT** monitoring for signs and symptoms of serotonin syndrome is necessary. If symptoms occur consideration should be given to discontinuation of either one or both agents. Note discontinuation of the serotonergic agent may result in withdrawal symptoms. **Note:** on rare occasions where treatment options are limited patients under the care of the OPAT service may be discharged on interacting medications with an OPAT monitoring plan in place.
- 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 (e.g. thiazide diuretics such as hydrochlorothiazide).
- Peripheral neuropathy, as well as optic neuropathy and optic neuritis sometimes progressing to loss of vision, have been reported in patients treated with linezolid; these reports have primarily been in patients treated for longer than the maximum recommended duration of 28 days. If peripheral or optic neuropathy occurs, the continued use of Linezolid should be weighed against the potential risks. There may be an increased risk of neuropathies when linezolid is used in patients currently taking or who have recently taken antimycobacterial medications for the treatment of tuberculosis. **Note:** there is no definitive evidence to support the use of pyridoxine supplement to reduce the risk of linezolid induced peripheral or optic neuropathy.
- Convulsions have been reported to occur in patients when treated with linezolid. Linezolid should be used with caution in patients with a history or risk of developing seizures.
- Tyramine rich foods/drinks should be avoided in patients taking linezolid due to the risk of developing hypertensive crisis.
- Severe renal impairment: 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. There is a limited evidence base to support the use of therapeutic drug monitoring (TDM) to optimise linezolid dosing in patient with renal impairment or extremes of body weight. The OPAT service may undertake or advise TDM of linezolid on rare occasions.
- Severe hepatic impairment: it is recommended that linezolid should be given to patients with severe hepatic insufficiency only when the perceived benefit outweighs the theoretical risk.
- Pregnancy: treatment with linezolid during pregnancy should be avoided unless clinically necessary i.e. only if the potential benefit outweighs the theoretical risk.
- Lactose: patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption

9 DRUG INTERACTIONS

NOTE: The following list should not be considered exhaustive. For further information refer to the current Summary of Product Characteristics https://www.medicines.org.uk/emc current BNF http://www.medicinescomplete.com Stockley's Drug Interactions Checker MedicinesComplete — Interactions Checker Stockley's Interactions Checker (oclc.org) and Serotonin syndrome - Symptoms, diagnosis and treatment | BMJ Best Practice

Linezolid is a reversible non-selective monoamine oxidase inhibitor (MAOI)

- **Food/Drink**: No significant pressor response was observed in subjects receiving both linezolid and less than 100 mg tyramine. This suggests that it is only necessary to avoid ingesting excessive 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). Refer to low tyramine diet advice sheet (see appendix) or available at www.pennutrition.com.
- **Other MAOI:** 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, selegiline, rasagiline, isocarboxazide, tranylpromine.
- **Alpha blockers:** enhanced hypotensive effect when MAOIs given with alpha blockers.
- **Analgesics:** including pethidine [CNS excitation (hypertension) or depression (hypotension) when given with MAOIs], tramadol [possible increased serotonergic effects and increased risk of convulsions when given with MAOIs], nefopam [CNS excitation (hypertension) or depression (hypotension) when given with MAOIs], and other opioids which have serotonergic effects e.g. fentanyl/alfentanil, methadone. Co-administration of linezolid and opioids which have serotonergic effects e.g. pethidine, fentanyl, alfentanyl, tramadol, methadone, dextromethorphan, pentazocine, oxycodone, tapentadol should be avoided where possible. If co-administration is considered essential patients will require close observation and monitoring for serotonin syndrome.
- **Antidepressants** increased risk of hypertension and CNS excitation and serotonin syndrome when MAOIs given with antidepressants including: SSRIs (e.g. citalopram, paroxetine, escitalopram, sertraline), and tricyclic antidepressants (e.g. amitriptyline). 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.
- **Serotonergic antiemetics** e.g. ondansetron, metoclopramide increased risk of serotonin syndrome. Monitor patients for symptoms of serotonin syndrome such as fever, tremors, diarrhoea, and agitation. Concurrent treatment should be stopped if serotonin syndrome occurs.
- **Antiepileptics**: MAOIs possibly antagonise anticonvulsant effect of antiepileptics by lowering seizure threshold. Where possible linezolid should be avoided in patients with increased risk of seizure.
- **Antipsychotics**: CNS effects of MAOIs possibly increased.
- **Atomoxetine**: possible increased risk of convulsions when given with MAOIs.
- **Bupropion:** The concurrent use of bupropion and linezolid is predicted to 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.
- **Dapoxetine**: increased risk of serotonergic effects when given with MAOIs. If both drugs are given, patients should be closely monitored for signs of serotonin syndrome such as agitation, fever, diarrhoea, and tremor. 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.
- **Dopaminergics**: possible increased risk of serotonin syndrome when MAOIs given with levodopa, entacapone and tolcapone. Concurrent treatment should be stopped if serotonin syndrome occurs.
- **5HT1 receptor agonists**: risk of CNS toxicity and serotonin syndrome when MAOIs given with rizatriptan or sumatriptan. The manufacturers of linezolid contraindicate its use with the triptans unless concurrent use is essential. If both drugs are given, patients should be closely monitored for signs of serotonin syndrome.
- **Sympathomemetics:** risk of hypertensive crisis when MAOIs given with sympathomemetics e.g. adrenaline, noradrenaline, dopamine, dobutamine.

10 BASELINE INVESTIGATIONS

- Baseline LFTs, U&Es and FBC (including haemoglobin, platelets, and total differentiated leucocyte counts).
- Baseline monitoring of blood pressure is required in patients where the concomitant administration of interacting drugs is considered necessary (see Section 9).

11 ONGOING MONITORING

11.1 ***Acute Setting:*** Patients receiving treatment with linezolid should receive the following monitoring:

- Weekly FBC including haemoglobin, platelets and total differentiated leucocyte counts.
- Weekly LFTs and U&Es.
- Symptoms and signs of lactic acidosis e.g. recurrent nausea and/or vomiting, abdominal pain, a low bicarbonate level or hyperventilation.
- All patients should be advised to report any numbness or tingling in the extremities.
- All patients should be advised to report any symptoms of visual impairment. These include changes in visual acuity, changes in colour vision, blurred vision or visual field defects.
- Any patient experiencing new visual symptoms whilst taking linezolid should be referred to ophthalmology.
- Visual function should be monitored regularly if treatment is required for longer than 28 days.
- Close monitoring of blood pressure is required in patients where the concomitant administration of interacting drugs is considered necessary (see section 9).

Note: more frequent monitoring is recommended in the following patients

- Receiving longer than 10-14 days of treatment.
- With pre-existing myelosuppression.
- Receiving concomitant medicines that might affect their blood counts.
- With severe renal insufficiency.

11.2 ***Primary care:***

In exceptional circumstances, if a patient **does not require inpatient monitoring** and is suitable for discharge, if there are barriers to the patient attending OPAT or the acute setting on a weekly basis, then bloods may be taken in primary care for monitoring.

- The patient must be referred to the OPAT Service and there must be an agreed plan for monitoring and supply of linezolid between the GP and the acute setting. This plan must be documented in the patient's medical notes and discharge letter.
- If appropriate the following monitoring (see table below) can be undertaken in primary care if the patient is unable to attend the acute setting or the OPAT service.

Monitoring Parameters	Frequency	Action to be taken
LFTs, U&Es, and FBC including haemoglobin, platelets and total differentiated leucocyte counts	Weekly	If any abnormalities are detected this should be discussed with the OPAT service or the acute care microbiology or infectious diseases consultant as soon as possible.
Visual function	All patients should be advised to report visual changes whilst taking linezolid. If treatment is required for longer than 28 days visual function should be checked regularly.	Any patient experiencing new visual symptoms whilst taking linezolid should be evaluated promptly and referred to an ophthalmologist if necessary. This should be reported and discussed with the OPAT service or the acute care microbiology or infectious diseases consultant as soon as possible.

Metabolism and nutrition disorders: Lactic acidosis, hyponatraemia	All patients should be advised to report any signs of metabolic disorder whilst taking linezolid.	Any patients who develop signs and symptoms of metabolic acidosis including: recurrent nausea or vomiting, abdominal pain, a low bicarbonate level or hyperventilation, should receive immediate medical attention. This should be reported and discussed with the OPAT service or the acute care microbiology or infectious diseases consultant as soon as possible.

12 UNDESIRABLE EFFECTS

NOTE: The following list should not be considered exhaustive. For further documented adverse drug reactions (ADRs) and details of likelihood etc, see the current Summary of Product Characteristics available via https://www.medicines.org.uk/emc or current BNF http://www.medicinescomplete.com

Any serious adverse drug reactions should be reported via the CSM Yellow Card scheme. Yellow Cards and guidance on its use are available at the back of the BNF or online at http://yellowcard.mhra.gov.uk/

ADR details	Management of ADR
Peripheral and optic neuropathy, loss of vision, changes in visual acuity and visual field defects, blurred vision	All patients should be advised to report any numbness or tingling in the extremities or any symptoms of visual impairment. These include changes in visual acuity, changes in colour vision, blurred vision or visual field defects. Patients experiencing new visual symptoms should be evaluated promptly and referred to an ophthalmologist if necessary. Vision should be monitored regularly if treatment is required for longer than 28 days. If peripheral or optic neuropathy occurs, the continued use of linezolid should be weighed against the potential risks. **Note:** there is no definitive evidence to support the use of pyridoxine supplement to reduce the risk of linezolid induced peripheral or optic neuropathy.
Blood disorders: Myelosuppression , leucopenia, neutropenia, thrombocytopenia, eosinophilia, pancytopenia, anaemia and sideroblastic anaemia	Monitor full blood count (FBC) at baseline, then weekly. Close monitoring of FBC is recommended in patients who: • require longer than 10-14 days treatment • have pre-existing myelosuppression • are receiving concomitant medicines that may affect their blood counts • have severe renal insufficiency **NOTE:** if significant myelosuppression occurs during linezolid therapy, treatment should be stopped. If it is considered absolutely necessary to continue therapy, intensive monitoring of blood counts and appropriate management strategies should be implemented.
Anaphylaxis	Linezolid should be avoided in patients with known hypersensitivity to linezolid or any of the excipients.
Metabolism and nutrition disorders: Lactic acidosis, hyponatraemia	The continued use of linezolid should be weighed against the potential risks. Patients who develop signs and symptoms of metabolic acidosis including: recurrent nausea or vomiting, abdominal pain, a low

	bicarbonate level or hyperventilation, should receive immediate medical attention.
Serotonin syndrome	Linezolid should be avoided in contraindicated patients (See section 7). If concurrent use of linezolid with a serotonergic drug is considered essential then close inpatient monitoring should be undertaken for signs of serotonin syndrome which include: hypertension, confusion, delirium, restlessness, tremor or blushing (see Section 9). **Note:** on rare occasions where treatment options are limited, patients under the care of the OPAT service may be discharged on interacting medications with an OPAT monitoring plan in place.
Convulsions	Linezolid can lower seizure threshold and should be avoided where possible in patients at increased risk of seizure.
Gastrointestinal disorders: diarrhoea, nausea and vomiting, pancreatitis, gastritis, abdominal pain	If these symptoms become severe or persistent or stools contain blood or mucus, linezolid therapy should be stopped. Patients should also avoid medicines that stop or slow bowel movements and seek medical attention.
Vascular disorders: hypertension, phlebitis, thrombophlebitis	The continued use of linezolid should be weighed against the potential risks. **NOTE:** patients taking linezolid should avoid interacting drugs and food with high tyramine content due to the risk of developing hypertension (see Section 9).
Hepato-biliary disorders: abnormal liver function test, increased AST, ALT or alkaline phosphatase. Increased total bilirubin.	The continued use of linezolid should be weighed against the potential risks.
Skin disorders: urticaria, dermatitis and rash. Bullous disorders such as those described as Stevens-Johnson syndrome and toxic epidermal necrolysis	Mild skin disorders should be managed appropriately. In more severe cases the use of ongoing linezolid should be weighed against the potential risks.
Renal disorders: Increased BUN, polyuria, increased creatinine, renal failure	The continued use of linezolid should be weighed against the potential risks. **Note:** There is a limited evidence base to support the use of TDM to optimise linezolid dosing in patient with renal impairment. The OPAT service may undertake or advice TDM of linezolid under certain clinical conditions.
Oral and vaginal thrush	Patients should receive appropriate anti-fungal treatment. Check FBC to ensure patient does not have myelodepression.

13 PHARMACEUTICAL ASPECTS

Refer to the most recent Linezolid Summary of Product Characteristics. This is available via https://www.medicines.org.uk/emc

14 COST: BRITISH NATIONAL FORMULARY (BNF)

• 7 day course tablets:	£57.40	14 day course:	£114.80
• 7 day course oral suspension	£667.50	14 day course:	£1335.00
• 7 day course IV:	£623.00	14 day course:	£1246.00

15 ACUTE CARE CONTACT INFORMATION

Name	Designation	Acute Site	Contact Information
OPAT Service Mon-Sun 8am-4pm	OPAT Team	Queen Elizabeth University Hospital	0141 452 3107 or 07989470541 Non urgent referral requests can be made via Trakcare under **OPAT GGC**
OPAT Service out with the above times	Infectious Diseases Registrar/Consultant	Ward 5c Queen Elizabeth University Hospital	0141 452 2470 Non urgent referral requests can be made via Trakcare under **OPAT GGC**
Consultant Microbiologist Service		Glasgow North & Clyde Glasgow South Online referral (Mon-Fri 9am-5pm)	0141 201 8551 0141 354 9132 Clinical Advice Referral Form
Rachael Rodger	Antimicrobial Pharmacist	Royal Alexandra Hospital (Mon, Tue, Thur) & Vale of Leven Hospital (Wed)	0141 314 6146 0141 314 7294 pg 56260 Rachael.Rodger@nhs.scot
Lee Stewart	Antimicrobial Pharmacist	Queen Elizabeth University Hospital	0141 451 6263 or 0141 201 1100 pg 16055 Lee.Stewart3@nhs.scot
Fiona Robb	Antimicrobial Pharmacist	Gartnavel General Hospital (Tues) Queen Elizabeth University Hospital (Mon, Wed & Thur)	0141 451 6261 or 0141 201 1100 pg 15008 Fiona.Robb3@nhs.scot
Siobhan Carty	Antimicrobial Pharmacist	Queen Elizabeth University Hospital	0141 451 6260 or DECT Phone 0141 232 4083 Siobhan.Carty2@nhs.scot
Amy Robertson	Antimicrobial Pharmacist	Queen Elizabeth University Hospital (Fri only)	0141 451 6261 or 0141 201 1100 pg 15008 Amy.Robertson7@nhs.scot
Scott Gillen	Antimicrobial Pharmacist	Glasgow Royal Infirmary	0141 201 3246 0141 211 4000 pg 13997 Scott.Gillen@nhs.scot
Anna Reuben	Antimicrobial Pharmacist	Glasgow Royal Infirmary (Wed only)	0141 201 3246 0141 211 4000 pg 12009 Anna.Rueben2@nhs.scot
Karen Downie	Antimicrobial Pharmacist	Inverclyde Royal Hospital (Wed & Thur)	0141 314 9504 Ex 04070 pg 51072 Karen.Downie@nhs.scot

16 LINKS TO SUPPORTING DOCUMENTATION

16.1 Protected Antimicrobial Form available via this link protected-antimicrobial-order-form

16.2 Linezolid Patient Information Leaflet - see appendix 1 or PrintOnTheWeb (TimeHarvest-Server.local)

16.3 Eating Guidelines for a Low Tyramine Diet – see appendix 2 or available at www.pennutrition.com

16.4 Linezolid Discharge and Outpatient Supply Checklist- available via this link- Linezolid Discharge Checklist

- Medicines.org.uk, (2024). *Linezolid 600mg film-coated tablets- Summary of Product Characteristics (SPC) - (eMC)*. [online] Available at: http://www.medicines.org.uk/emc/medicine/31542 [Accessed 17th December 2024]
- Joint Formulary Committee. *British National Formulary* (online) London: BMJ Group and Pharmaceutical Press http://www.medicinescomplete.com [Accessed 17th December 2024]
- Serotonin syndrome - Symptoms, diagnosis and treatment | BMJ Best Practice

APPENDIX 1

Help & Advice

If you notice any other side-effects or have any other concerns please discuss them with your GP, hospital doctor or NHS 24 on ☎ **111** as soon as possible.

The Outpatient Parenteral Antibiotic Therapy (OPAT) services can also provide advice on ☎ **0141 452 3107** (Mon-Sun 8am-4pm) or ✆ **07989 470541** outside these times.

Can I take all my current medicines with linezolid?

Your doctor or pharmacist will review your regular prescribed medications before starting treatment. If you are taking any other medicines or herbal remedies or planning to start any you must check with your doctor or pharmacist that it is safe to take with linezolid.

You should not use Linezolid if you are taking or have taken within the last two weeks any medicines known as a **monoamine oxidase inhibitors** (MAOIs, for example phenelzine, isocarboxazid, selegiline, rasagiline, moclobemide). These may be used to treat depression or Parkinson's disease.

If you are taking serotonin re-uptake inhibitors (SSRIs), tricyclic antidepressants, 5-HT1 agonists (triptans), opiates (avoid with pethidine and methadone), your doctor will need to decide if linezolid is suitable.

What about pregnancy or breastfeeding?

We do not usually give linezolid in pregnancy. Please tell your doctor if you are pregnant, think you may be pregnant or trying to get pregnant.

You should not breastfeed if you are taking linezolid. Please tell your doctor if you are currently breastfeeding.

Where do I get supplies of linezolid from?

You will normally get linezolid from the hospital pharmacy. As you will need weekly blood tests, we will normally only give you a one-week supply of linezolid at a time.

Further information

You can find further information about linezolid in the manufacturer's information leaflet that comes with your medicine or you can ask your doctor or pharmacist.

Follow Up Appointment Date	Time and Venue

AUC Approved: February 2028
Review Date: February 2028

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NHS Greater Glasgow and Clyde

Information about

Linezolid

Your information	
Name	
Address	
CHI number	
Email	
Date started on Linezolid	

This leaflet contains **important** information about the medicine linezolid you have been prescribed.

A nurse, doctor, pharmacist or pharmacy technician will go through the information in this leaflet with you and answer any questions you may have.

Please keep a note of all follow up appointment details.

What is linezolid and what are the benefits of taking it?

Linezolid is an antibiotic used to treat infections. It works by stopping the growth of certain types of bacteria.

The main benefit of this antibiotic is you can take it as a tablet or a liquid. This means you may not need to have an intravenous drip to receive your antibiotic and may be able to have treatment at home.

How do I take linezolid?

You should take it twice a day every 12 hours, for example at 8 o'clock in the morning and then at 8 o'clock at night.

Occasionally for certain infections your doctor may tell you to take this medicine once a day only. You can take it before, with or after food.

How long will I need to take linezolid?

Your doctor will decide how long you need to take linezolid. Do not stop taking this medicine when you start to feel better unless told to stop by your doctor. If you stop too soon, surviving bacteria may cause the infection to come back.

How will I be monitored whilst on linezolid?

If you are prescribed linezolid for more than a week, we will ask you to return to the hospital for a weekly blood test. If a follow up appointment has not been arranged for you, please ask your doctor.

Your doctor should also monitor your eyesight if you are taking linezolid for more than 28 days. If you have been taking linezolid for more than 28 days and not had a vision check, please ask your doctor, pharmacist or staff at the Outpatient Parenteral Antibiotic Therapy (OPAT) Clinic.

You may also need regular blood pressure monitoring if taking certain medicines that interact with linezolid.

What side-effects might I experience on linezolid?

Like all medicines Linezolid has side effects. For a complete list see the manufacturer's leaflet that comes with this medicine.

Important - if you develop any of the following symptoms whilst taking linezolid contact NHS 24 on ☎**111** immediately or go to your nearest Accident and Emergency (A&E)

- Severe throbbing headache
- Unexplained bleeding or bruising
- Blurred vision or other problems with eyesight
- Tingling or numbness in your hands or feet
- Severe or persistent diarrhoea
- Recurrent nausea and vomiting, abdominal pain or increased breathing rate

Do I need to change my diet whilst on linezolid?

Eating foods high in **tyramine** may increase your blood pressure when you are taking linezolid.

You should 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.

You can find further advice on avoiding foods high in tyramine at: 🌐 **www.pennutrition.com** under **Eating Guidelines for a Low Tyramine Diet**. We can also provide a printed copy of this dietary advice if helpful.

If you develop a throbbing headache after eating or drinking whilst taking linezolid contact NHS 24 on ☎ **111** immediately or go to your nearest Accident and Emergency (A&E).

APPENDIX 2

BDA The Association of UK Dietitians

PEN The Global Resource for Nutrition Practice

Eating Guidelines for a Low Tyramine Diet

Tyramine is a substance found naturally in some foods. Most of the time, there are only small amounts of tyramine in food. The amount of tyramine in food can increase when food has been aged, cured, fermented or is spoiled. Improvements in food production and storage have led to a decrease in tyramine within foods.

For most people, tyramine is not harmful. If you are taking certain types of monoamine oxidase inhibitors (MAOIs) your body cannot process tyramine very well. While many MAOIs are being replaced with drugs with fewer side effects they are still used to treat depression and movement disorders such as Parkinson's disease.

Eating foods high in tyramine at the same time you take these medications can cause high blood pressure, which may become dangerously high. Signs and symptoms include:

- severe headaches
- heart palpitations (rapid heart beats)
- chest pain
- blurry vision.

Talk to your health care provider right away if you develop any signs and symptoms. Your reaction to tyramine levels in food may be different from someone else.

This fact sheet provides information about how to avoid eating foods that may be high in tyramine if you have been advised to follow a low tyramine diet by your health care provider.

Steps you can take

1. Buy, cook and eat fresh foods.
   - Look for fruits and vegetables that are not bruised or damaged and buy cold or frozen food at the end of your grocery shopping.
   - Prepare and eat fresh foods whenever you can. Most fresh foods have very low tyramine levels. Tyramine levels can go up when foods are stored.

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- Check the "Best Before" or expiry date of foods. Do not eat foods which are outdated or expired.

2. Eat and store foods safely.
   - Store all dairy products and packaged meat, fish, poultry and eggs immediately after returning home from the grocery store.
   - Refrigerate leftovers, including canned food put into a storage container, as soon as possible. Maintain storage temperatures at 4°C or lower.
   - Eat leftovers within 48 hours, or freeze them. Cooking does not lower the amount of tyramine in foods.

3. Avoid eating foods that may be high in tyramine levels. These include:
   - Foods that have been aged, cured, fermented, pickled or smoked such as aged cheese and processed meat. Be aware of mixed dishes such as stir-fry with soya sauce or pizza with pepperoni that may contain foods that are high in tyramine.
   - Leftovers with meat, fish, poultry or eggs that are more than 48 hours old.
   - Food that is over ripe or spoiled and past its "Best Before" date.

Use the chart below as a guide to know which foods are more likely to be high in tyramine. This is not a complete list. You may tolerate small amounts of tyramine over larger amounts.

Continue to follow a low tyramine diet for at least two weeks after stopping your MAOI medications, or as advised by your health care provider.

Always double check with your health care provider or registered dietitian if you are concerned about what foods to eat. Using a food and symptom journal can help you to track your reactions to any foods and drinks.

Type of Food	Foods that may be high in tyramine	Foods that contain very little or no tyramine
Milk and Milk Products	Mature or aged cheese such as Blue (Roquefort, stilton),	Cottage cheese Plain cream cheese

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Type of Food	Foods that may be high in tyramine	Foods that contain very little or no tyramine
	camembert, cheddar, Emmental, aged feta, gouda, gruyere, parmesan, Romano and edam Yogurt made from fermented yak-milk Any milk products past their "Best Before" date Any milk products made with raw (unpasteurized) milk	Ricotta cheese Sour cream All other pasteurized milk and milk products
Protein Foods	Aged, dried and pickled meats such as aged beef, mortadella, Chinese dried duck Pickled and smoked fish such as pickled herring, lox, caviar in a glass or can, smoked salmon and trout Cured, smoked, dried and processed meats such as bacon, bologna, corned beef, hot dogs, pepperoni, salami, sausage and jerky Fava beans (broad beans) and fava beans eaten with their pods Any leftovers with meat, fish, poultry or eggs that are more than 48 hours old	All fresh meat, fish and poultry - store these in the refrigerator and eat them as soon as possible Freshly cooked eggs Cooked beans, peas, and lentils (except fava beans) Canned meat, poultry, and fish Non-fermented soy products such as non-fermented tofu, fortified soy beverages and soy yogurt

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Type of Food	Foods that may be high in tyramine	Foods that contain very little or no tyramine
	Spoiled or improperly stored meat, fish or poultry	
Processed/ Fermented Soy Products	Miso and miso based soup Tempeh or sufu (fermented tofu) Soy sauce and other soy based products like soybean paste	
Vegetables and Fruit	Spoiled or over ripe fresh, frozen, dried and canned fruits and vegetables, including over-ripe avocados and bananas Fermented or pickled vegetables, including sauerkraut and kimchi (fermented cabbage)	Fresh, frozen and canned unspoiled vegetables and fruit
Grain Products	Sourdough breads Breads made with aged cheese, aged meat or yeast extracts or some artisan breads	All others
Alcoholic Beverages When alcohol is consumed on an empty stomach, tyramine is absorbed quickly and may cause unpleasant	Draft or tap beer Unpasteurized beer, including some craft varieties Some homemade beer and wine While improvements in production and hygiene have	Check with your health care provider about the type and amount of alcohol that is safe for you to drink

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Type of Food	Foods that may be high in tyramine	Foods that contain very little or no tyramine
symptoms. If you do consume alcohol have something to eat first. Alcohol may trigger a headache in some people.	reduced tyramine levels, the amount of tyramine in beer and wine can vary	
Miscellaneous Foods Drinking fewer caffeinated beverages than usual may trigger a headache.	Fish sauce or paste Yeast extract spreads Protein supplements (may contain yeast extracts) Salad dressings made with aged cheese, such as blue cheese dressing	Butter and margarine Salad dressings made without aged cheese Vegetable oils

Additional Resources

- Safe food storage https://www.canada.ca/en/health-canada/services/general-food-safety-tips/safe-food-storage.html
- Food and symptom journal https://www.pennutrition.com/viewhandout.aspx?Portal=UbY=&id=J8frWQ0=&PreviewHandout=bA==

These resources are provided as sources of additional information believed to be reliable and accurate at the time of publication and should not be considered an endorsement of any information, service, product or company.

Notes

Distributed by:

NHS Greater Glasgow & Clyde Antimicrobial Pharmacist Team

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