SHARED CARE GUIDELINE

Drug: d-Penicillamine

Introduction	**Indications**: Licensed: Severe active rheumatoid arthritis, including juvenile forms, Wilson's disease (hepatolenticular degeneration) in adults and children (0 to 18 years). **Background:** Penicillamine is an effective chelator of copper, zinc, mercury and lead and promotes their excretion in urine. It is effective in diseases caused by toxic levels of these metals e.g. Wilson's disease. Penicillamine has been shown to be effective in the treatment of rheumatoid arthritis not adequately controlled by NSAID therapy, an effect probably not associated with its metal binding properties. [2,3] **Definitions:** Stable dose – the dose will be titrated to achieve efficacy at the lowest dose. Once efficacy achieved and provided the patient can tolerate the dose, this will be termed "stable dose" Stable bloods – results of blood tests remain below the "alert" thresholds as set by national guidelines and have stayed at similar levels for at least two consecutive tests. N.B. The patient can continue to have active disease despite being on a stable dose or having stable bloods, so the "patient" is not referred to as "stable"
Form	d-Penicillamine tablets 125mg d-Penicillamine tablets 250mg
Dose and Administration	Typical regimen, oral route of administration: 125-250mg/day increasing by 125mg every 4-12 weeks to 500-750mg/day. Maximum dose is 1.5g/day.
Secondary Care Responsibilities	• Confirm the diagnosis. • Check for absence of pregnancy in women of child-bearing age and ensure the patient understands the importance of contraception. • Discuss the benefits and side effects of treatment with the patient. Ensure that the patient understands which warning signs and symptoms to report. • Perform pre-treatment screening: FBC, U&Es, creatinine/ eGFR and urinary dipstick for protein. • Ensure that the patient understands not to expect improvement for at least 6-12 weeks after treatment is initiated. • Provide the patient with prescriptions for penicillamine until on stable dose and they have undergone monthly monitoring for a minimum of 3 months. • Provide the patient with a monitoring and dosage record booklet and ensure that the patient knows where and when to attend for monitoring. Encourage the patient to take responsibility for ensuring that results of tests are entered in the monitoring booklet. • Make arrangements for shared care with the patient's GP. • Review the patient regularly to monitor the patient's response to therapy. • Advise the GP on frequency of monitoring, management of any dose adjustments and when to stop treatment. • Ensure that clear backup arrangements exist for GPs to obtain advice.
Primary Care Responsibilities	• Provide the patient with prescriptions for penicillamine once on stable dose and having undergone monthly monitoring for a minimum of 3 months. Monitor at the recommended frequencies (see MONITORING below) and ensure that test results are recorded in the monitoring booklet. • Report any adverse events to the consultant or specialist nurse and stop treatment on their advice or immediately if an urgent need arises. (See MONITORING below). • Report any worsening of control of the condition to the consultant or the specialist nurse. • Follow recommended immunisation programme.
Common Drug Interactions	• Antacids, iron or zinc supplements: absorption is reduced if taken within 2 hours • Antipsychotic drugs: may increase risk of agranulocytosis • Digoxin: Levels of digoxin can be reduced by concurrent use of Penicillamine • Levodopa Not an exhaustive list, please refer to current BNF and SPC for further drug interactions
Cautions	• Renal impairment

	• Elderly • Patients allergic to penicillin • Patients who have shown a sensitivity to gold • Oral iron, digoxin or antacids not to be given within 2 hours of penicillamine • Concomitant use of NSAIDs and other nephrotoxic drugs may increase the risk of renal damage
Contraindications	• Hypersensitivity to penicillamine or any of the ingredients • Moderate to severe renal insufficiency • Systemic lupus erythematosus History of penicillamine induced agranulocytosis, aplastic anaemia or severe thrombocytopenia • Co-prescribing of gold salts, chloroquine, clozapine, hydroxychloroquine, or immunosuppressive drugs • Pregnancy & lactation should be avoided in rheumatology patients.
This guidance does not replace the SPC's, which should be read in conjunction with this guidance	

MONITORING AND ADVERSE EFFECTS

Treatment Status	FBC	U+Es	Creatinine/ eGFR	ESR or CRP	Urinalysis
Initial monitoring (first 2 months)	Every 2 weeks	Every 2 weeks	Every 2 weeks	Every 3 months (for RA only)	Weekly
After 2 months	Monthly	Monthly	Monthly	Every 3 months (for RA only)	Monthly

***Please note:** If the patient is also being treated with **leflunomide**, increased monthly monitoring is required, as specified in the leflunomide shared care guidance. (Where other biologic/DMARDs are used in combination with penicillamine, the standard monitoring requirements, as outlined above, continue to apply).

As per secondary care responsibilities, for clarity the frequency of monitoring should be specified in the initial shared care request.

- Patients to be asked about the presence of rash or oral ulceration at each visit
- If 2+ proteinuria or more check MSSU. If infection present treat appropriately.

In the event of the following adverse laboratory results or patient reported symptoms, withhold d-Penicillamine until discussed with specialist team and repeat the test after two weeks:

- WCC < 3.5 x 10^9/L or less than the lower limit of reference range as per lab
- Neutrophils < 1.6 x 10^9/L or less than the lower limit of reference range as per lab
- Platelets < 140 x 10^9/L or less than the lower limit of reference range as per lab
- If urinalysis sterile and 2+ proteinuria or more persisting on two consecutive occasions
- Severe or late onset rash. Late rashes are more serious than early ones
- Oral ulceration
- Abnormal bruising or severe sore throat. (Check FBC immediately)
- Haematuria – requires investigation

Other adverse reactions:

- Nausea – taking medication before bed may reduce nausea
- Alteration of taste. This may settle spontaneously.

This list is not exhaustive, please refer to SPCs and BNF

References

1. Summary of product characteristics. Penicillamine 250mg Tablets and Pendramine 250mg Tablets. Kent Pharma UK Ltd. Last updated on the EMC 21st June 2016. Accessed via: https://www.medicines.org.uk/emc/medicine/1240 [accessed online: 21st June 2022].
2. Summary of product characteristics. Penicillamine 125mg Tablets and Pendramine 125mg Tablets. Kent Pharma UK Ltd. Last updated on the EMC 21st June 2016. Accessed via: https://www.medicines.org.uk/emc/medicine/1241 [accessed online: 21st June 2022].
3. Ledingham et al. BSR/BHPR Non-Biologic DMARD Guidelines, June 2017. Accessed via: https://academic.oup.com/rheumatology/article/56/6/865/3053478

4. Flint et al. BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding, January 2016. Accessed via: https://academic.oup.com/rheumatology/article/55/9/1693/1744535
5. UK Health Security Agency. Immunisation Against Infectious Disease 'The Green Book', 2021. Department of Health and Social Care. London, UK.

RELEVANT CONTACT LIST

Speciality	
Name and Title	Tel. No.

The Shared Care agreement form is available here: https://www.lancashireandsouthcumbriaformulary.nhs.uk/docs/files/dmards-shared-care-agreement-v1.1.docx