Penicillamine: Guidelines for its use in Wilson's disease

Shared Care Guideline

Executive summary

- Penicillamine is used to promote copper excretion in the urine, reducing copper deposition in the liver and other organs. It is potentially toxic and therefore the drug must be monitored.
- The responsibilities of the hospital specialist, primary care clinician and patient for this shared care guideline can be found within this document (see section 11).

Sharing of care depends on communication between the specialist, primary care clinician and the patient or their parent/ carer. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. The doctor/ healthcare professional who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

1. Scope

Prescribing and monitoring by primary care clinicians.

2. Aim

This shared care guideline outlines the responsibility of primary and secondary care clinicians in managing penicillamine for use in Wilson's disease.

3. Introduction

Penicillamine is used to promote copper excretion in the urine, reducing copper deposition in the liver and other organs. Penicillamine may also act by inducing metallothionein. It is potentially toxic and therefore the drug must be monitored.

4. Abbreviations

ICS	Integrated Care System
CUH	Cambridge University Hospitals NHS Foundation Trust
ESR	erythrocyte sedimentation rate
FBC	full blood count
GP	general practitioner
MSU	mid-stream urine
NSAID	non-steroidal anti-inflammatory drug
SPC	summary of product characteristics
WBC	white blood (cell) count

5. Dose and administration

All daily doses should be taken in divided doses;

- Start with 1.5-2 g daily, adjusted to response.
- Maintenance dose should be approximately 0.75- 1.5g daily.
- The maximum recommended dosage is 2g daily.
- Dosing in the elderly is recommended at 20mg/kg daily.
  Please note penicillamine therapy can be continued throughout pregnancy.

Women on penicillamine therapy should not be advised against breastfeeding.

Please refer the patient to discuss with the hospital specialist if they have concerns.

6. Adverse effects

- Rashes/ anorexia/ taste disturbance/ nausea.
- Bone marrow suppression, causing thrombocytopenia, neutropenia and rarely anaemia. Warn patients to report sore throat, or abnormal bleeding/ bruising/ rashes, mouth ulcer.
- Renal damage indicated by proteinuria/ haematuria on urinalysis.
- Rarely febrile reactions, myasthenia, drug-induced lupus.

7. Cautions

- Care should be exercised in patients with renal insufficiency; modification of dosage may be necessary.
- Especially careful monitoring is necessary in the elderly since increased toxicity has been observed in this patient population regardless of renal function. See section 5 for dosing.
- Concomitant use of NSAIDs and other nephrotoxic drugs may increase the risk of renal damage, see section 9.
- Penicillamine should be used with caution in patients who have had adverse reactions to gold.
- Note that there are no restrictions on vaccinations in patients treated with penicillamine.

8. Contraindications

- Hypersensitivity to penicillamine or any of the ingredients.
- Agranulocytosis, aplastic anaemia or severe thrombocytopenia due to penicillamine.
- Lupus erythematosus.
- Moderate or severe renal impairment.

9. Interactions

- Concomitant use of clozapine should be avoided – increased risk of agranulocytosis.
- Concomitant use of NSAIDs and other nephrotoxic drugs may increase the risk of renal damage.
- Iron supplements, zinc supplements and antacids may reduce absorption of penicillamine – do not take within two hours of penicillamine.

Further information about dose and administration, adverse effects, cautions, contraindications and interactions can be found in the Summary of Product Characteristics.

10. Monitoring standards and actions to take in the event of abnormal test results/ symptoms

a) Secondary/ Tertiary Care

Monitoring standard	**When/how often**
FBC + LFT	Prior to initiation and every 2 weeks for the first 12 weeks
Urinalysis (24-hour copper excretion and proteinuria)	Prior to initiation and every 2 weeks for the first 12 weeks. Then annually when stable.
Ask patient about any sore throat, fever, infection, non-specific illness, unexplained bleeding and bruising, purpura, mouth ulcers or rashes.	At each encounter with patient.

b) Primary Care

Monitoring standard	**When/how often**
FBC + LFT	• After initiation or dose change: Every month for the first 12 months, then every 3 months. • As required if patients develop a significant infection - looking for leucopoenia.
Urinalysis/ dipstick test for proteinuria	To be carried out when requested by secondary care as required, such as 1 week after a dose change.
Ask patient about any sore throat, fever, infection, non-specific illness, unexplained bleeding and bruising, purpura, mouth ulcers or rashes.	At each encounter with patient.

Abnormal test result/ symptoms	**Action by** Primary care clinician
Proteinuria 2+	Check MSU and treat if evidence of infection. If sterile and 2+ withhold drug and inform hepatology team or specialist nurse. See section 12 for contact numbers.
WBC < 3.5 $x10^9$/l or neutrophils <2 $x10^9$/l	**Stop penicillamine** and inform hepatology team or nurse practitioner. See section 12 for contact numbers.
Platelets < 150 $x10^9$/l	**Stop penicillamine** and inform hepatology team or nurse practitioner. See section 12 for contact numbers.
AST or ALT increase of over 50% of baseline values	Inform hepatology team or nurse practitioner. See section 12 for contact numbers.
Sore throat, abnormal bleeding or bruising, unexplained rash, oral ulceration, infection, fever	Check FBC; **if abnormal stop penicillamine** and inform hepatology team or specialist nurse. See section 12 for contact numbers.

11. Shared care responsibilities

a) Hospital specialist:

- Initiate penicillamine and inform primary care clinician of dose.
- Send a letter to the primary care clinician requesting shared care for the patient, enclosing a copy of the blood test results.
- Inform the primary care clinician after each clinic attendance if there is any change to treatment or monitoring.
- Inform primary care clinician of patients who do not attend clinic appointments and advise regarding arrangements for further follow up.
- To provide any advice to the patient/ carer when requested.

b) General practitioner:

- Agreement to shared care guideline by the primary care clinician.
- Prescribe penicillamine as directed by hospital specialist.
- Monitor patients on penicillamine as described in section 10.
- Report any adverse events to the hospital specialist, where appropriate, and as described in section 9.
- Request advice from the hospital specialist when necessary.

c) Patient or parent/ carer:

- Patients are strongly encouraged to sign up and have access to EPIC MyChart and the NHS App to access their personal medical information (drug information, test results, appointments and letters).
- Report to the hospital specialist or primary care clinician if they do not have a clear understanding of their treatment.
- Take penicillamine as prescribed and do not stop taking it without speaking to their primary care prescriber or specialist.
- Patients must attend their scheduled clinic and blood test appointments (where relevant).
- Must inform other clinical staff that they are receiving treatment.
- Report any adverse effects to the hospital specialist or primary care clinician.

12. Contact numbers for advice and support

Cambridge University Hospitals NHS Foundation Trust

Specialist	**Post**	***Telephone***
Dr Bill Griffiths	Consultant Hepatologist	01223 586891 (secretary)
Fiona Smith	Hepatology clinical nurse specialist	01223 256529 Option 2 or via hospital switchboard 01223 245151
Leslie Wong	Advanced Clinical Pharmacist – Hepatology and the Eastern Liver Network	01223 217611
Patients' medicines helpline: Mon-Fri: 09:00 to 17:00 hrs medinfo@addenbrookes.nhs.uk	-	01223 217502

13. Equality and diversity statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service equality and diversity statement.

14. Disclaimer

It is **your** responsibility to check that this printed out copy is the most recent issue of this document.

15. Document management

Ratification Process	**Details**
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The information contained in this guideline is issued on the understanding that it is accurate based on the resources at the time of issue. For further information please refer to the most recent Summary of Product Characteristics.