NHS Shropshire Clinical Commissioning Group

The Robert Jones and Agnes Hunt NHS Orthopaedic Hospital NHS Foundation Trust

D-Penicillamine
Rheumatology Local Safety Monitoring Schedule

This local safety monitoring schedule supports clinicians under the Local Enhanced Service for High Risk Drug Monitoring (formerly Near Patient Testing). Aligning clinical and prescribing responsibility enhances patient safety because the individual signing the prescription will also be responsible for ensuring that any necessary monitoring has been undertaken and will have access to the results of this.

The prescriber and specialist assume joint clinical responsibility for the drug and the consequences of its use.

Specialist details	GP details	Patient details
Name:	Name:	Name:
Address:	Address:	Contact number:
Email:	Email:	
Contact number:	Contact number:	

Introduction

D-Penicillamine is a chelating agent used as an immunomodulator.
Despite its namesake, D-penicillamine is **not** contraindicated in patients with penicillin allergy.
Licensed indication: severe active rheumatoid arthritis

Adult dosage and administration

A typical dose regimen may be: 125-250mg/day increasing by 125mg every 4 weeks to 500mg/day. If no response in 3 months consider an increase in dose to 750mg/day.

Available as: 125mg and 250mg tablets

It may take up to 3 months for significant response to be achieved.

Specialist responsibilities

- Provide GP with clear written advice on required dosage and frequency of D-penicillamine, written monitoring guidelines and drug information. Check for interactions with other medicines.
- Provide the patient/carer with relevant (written) information on use, side-effects and need for monitoring of infection.
- **Advise on need for adequate contraception.**
- Provide monitoring record booklet and record baseline results
- Arrange pre-treatment baseline investigations in primary or secondary care.
- Baseline tests
    - **FBC**
    - **U&Es + creatinine**
    - **Urinary dipstick for protein**
- Review results of safety monitoring and request additional tests as required.
- Monitor disease response to treatment and need to continue therapy.
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed.
- Identify and report adverse events to the GP and the MHRA (via yellow card).
- Provide any other advice or information for the GP if required

Authors: C Daly/S Lyttle, Shropshire CCG Dr M Garton, Sr S Bird, RJAH Rheumatology Dept
Date prepared: March 2015 Date for review: March2018

Primary Care responsibilities

- Prescribe D-penicillamine at the dose recommended if patient is having appropriate regular monitoring and monitoring results are within acceptable range.
- Repeat prescriptions should be removed from the surgery repeats pile and retained separately for prescribers to review prior to signing. Maximum 28 days supply.
- Arrange and record ongoing monitoring **every 2 weeks until dose stable for 3 months, then monthly thereafter**:
  - **FBC**
  - **Urinalysis**
  - **U&E**
- Report any adverse drug reactions to the initiating specialist and the usual bodies (e.g. MHRA).
- Patients on combination DMARD therapy may need more frequent monitoring. Please check the Local Safety Monitoring Schedule for each drug.
- Ensure no drug interactions with other medicines
- Ask about unexplained rash, oral ulceration/sore throat or unusual bruising at every consultation
- Ensure a clinician updates the patient's record following specialist review.
- If patient develops symptoms/signs of systemic infection, check FBC. D-penicillamine can normally be continued unless there is leucopenia

Withhold D-Penicillamine and contact specialist if:

- WBC $< 3.5 \times 10^9$/L
- Neutrophils $< 2 \times 10^9$/L
- Platelets $< 150 \times 10^9$/L
- Proteinuria ++ or more (see adverse effects)
- Severe rash or oral ulceration – late rashes are more serious than early ones
- Unusual bruising / severe sore throat – check FBC immediately and re-start therapy only if results normal

Please note: A rapidly increasing or decreasing trend in values should prompt caution and extra vigilance.

Results should be recorded in the patient's shared care monitoring record

Adverse effects, Precautions and Contra-indications

Leucopenia/thrombocytopenia – reductions of the white cell count or platelet count below the thresholds indicated, or three successive falls within the normal range should prompt drug withdrawal, and monitoring of the blood count. Discuss with specialist the re-introduction of D- penicillamine treatment at a lower dose AFTER the blood count has recovered (early blood dyscrasias only). Withdraw drug permanently if problem recurs.

Proteinuria / haematuria: Transient mild proteinuria is common. If urinalysis reveals protein ++ or more, perform MSSU. If no infection present, request albumin creatinine ratio (in plain sterile bottle) and if >30mg/mmol creatinine discontinue penicillamine and refer to initiating specialist. Haematuria is a rare sign of toxicity – discuss with specialist and suspend treatment.

Rash: may be pruritic, erythematous, maculopapular or urticarial. Stop D-penicillamine and consider re-introduction at lower dose once settled. Late rashes are more likely to recur on re-challenge. – stop D-penicIllamine permanently if rashes are recurrent

Loss/alteration of taste: can occur but occasionally settles spontaneously.

Stomatitis: if persistent or severe refer to specialist

Gold: Use penicillamine with caution in patients who have had an adverse reaction to gold.

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Contraindications include:

- Hypersensitivity to penicillamine
- Systemic lupus erythematosus
- Moderate or severe renal impairment (avoid if eGFR < 50 ml/min)
- Pregnancy: penicillamine should not be administered to patients who are pregnant and therapy should be stopped when pregnancy is confirmed or suspected, unless considered absolutely essential by the specialist
- Breastfeeding

NOTE: **Allergy to penicillin is NOT a contraindication to penicillamine therapy.**

Common Drug Interactions

Iron: decreases absorption of penicillamine (do not give within 2 hours if prescribing is necessary, recommend that iron is taken at least 8 hours AFTER penicillamine)
Antacids: decreases absorption of penicillamine (do not give within 2 hours)
Zinc: decreases absorption of penicillamine (do not give within 2 hours)
Digoxin: digoxin levels can be reduced by concurrent use of penicillamine
Gold: concomitant use not recommended.
Antipsychotics: avoid due to increased risk of agranulocytosis.

Communication

For any queries relating to this patient's treatment with penicillamine, please contact the consultant named at the top of this document.

This information is not inclusive of all prescribing information, potential adverse effects and drug interactions

Please refer to full prescribing data in the SPC or the BNF

References

GMC: Prescribing guidance: Shared care www.gmc-uk.org/guidance/ethical_guidance/14321.asp(accessed 20/10/2014)

NMC : Standards of proficiency for nurse and midwife prescribers http://www.nmc-uk.org/Documents/NMC-Publications/NMC-Standards-proficiency-nurse-and-midwife-prescribers.pdf (accessed 3/11/2014)

SPC Distamine : http://www.medicines.org.uk/emc/medicine/9211

Chakravarty, K., McDonald, H., Pullar, T. et al. (2008) BSR/BHPR guideline for disease-modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatologists. *Rheumatology* **47**(6), 924-925.