Penicillamine

Traffic light classification- Amber 1
Information sheet for Primary Care Prescribers
Part of the Shared Care Protocol: Management of Rheumatological Conditions with Disease-Modifying Anti Rheumatic Drugs in Adults

Indications[1,2]
Rheumatoid Arthritis - licensed.

Therapeutic Summary
Penicillamine is an established treatment used to suppress the disease process in rheumatological conditions. Clinical improvement may take up to 6 months. Simple analgesics and NSAIDs may need to be continued. Patient reported adverse effects usually occur early in therapy, but please see explicit criteria for review below. This medicine is now rarely used

Products available
125mg and 250mg tablets.

Dosages and route of administration[1,2]
The usual dose is 250 - 750mg / day. A few patients may require up to 1500mg daily to obtain benefit.

Duration of treatment[3]
All DMARDs are long term treatments. Penicillamine has a cumulative action and a clinical improvement is normally seen within 3 - 6 months after starting treatment.

Monitoring Requirements and Responsibilities[3]
Pre-treatment assessment to be performed by the specialist and will include:

- FBC, U&Es and urinary dipstick for protein.

Ongoing monitoring:

Time period in treatment	Frequency of monitoring	Tests to be done		
		FBC	LFTs	U&Es
0-6 weeks	Fortnightly	✓	✓	✓
6 weeks – 3 months	Monthly	✓	✓	✓
>3 months and stable dose for 6 weeks	3 monthly*	✓	✓	✓
Any dose increase	2 weeks post dose increase then revert to above protocol	✓	✓	✓

- Patient should report any rash, oral ulceration, sore throat, abnormal bruising or bleeding. GP to ask about skin rash or oral ulceration at every visit.
- GP to assess and manage cardiovascular risk factors – patient at higher risk of cardiovascular events due to rheumatological disease activity.
- No additional monitoring requirements are required in primary care for patients receiving additional biological therapy including anti -TNF therapy.
- Routine influenza and pneumococcal vaccines are highly recommended.

Explicit criteria for review and discontinuation of the medicine- Other benchmark values may be set by secondary care in specific clinical circumstances.
This will be communicated by secondary care.

Adverse Event	Action
WBC <3.5x10^9/l	Withhold until discussed with rheumatology specialist team.
Neutrophils <2x10^9/l	Withhold until discussed with rheumatology specialist team.
Platelets <150x10^9/l	Withhold until discussed with rheumatology specialist team.
If proteinuria is 2+ or more	Check MSSU: If evidence of infection treat appropriately. If sterile and 2+ proteinuria or more persists, withhold until discussed with rheumatology specialist team.
Haematuria	In the absence of renal stones or other known cause, treatment should be stopped immediately.
Severe rash or oral ulceration. Late rashes are more serious than early ones.	Withhold until discussed with rheumatology specialist team.
Urticarial reactions	Antihistamines, steroid cover, or temporary reduction of dose.
Alteration of taste	Continue treatment (may settle spontaneously).
Nausea	Taking medication before bed may reduce nausea.
Abnormal bruising or severe sore throat	Check FBC immediately and withhold until results are available.

In addition to absolute values for haematological or biochemical indices a rapid fall or rise or consistent downward or upward trend in any value should prompt caution and extra vigilance.

For a full list of side effects refer to the BNF or Summary of Product Characteristics

IF YOU ARE IN ANY DOUBT ABOUT ANY POTENTIAL ADVERSE REACTION, PLEASE CONTACT THE RHEUMATOLOGY SPECIALIST TEAM.

Relevant contraindications[1,2]

- Hypersensitivity to penicillamine or any of the ingredients.
- Moderate or severe renal impairment.
- Pregnancy and lactation.

Relevant precautions[1,2]

- Renal impairment (contraindicated in moderate or severe impairment) – Fortnightly monitoring is necessary.
- Elderly patients – increased toxicity unrelated to renal function.

Clinically relevant medicine interactions and their management[1,2,4,5]

- If concomitant oral iron, zinc or antacid therapy is indicated, this should not be given within two hours of taking penicillamine.
- Concomitant use of NSAIDs and other nephrotoxic medicines may increase the risk of renal damage- caution in use.
- Clozapine - Penicillamine may potentiate the blood dyscrasias seen with clozapine, avoid concomitant use.
- Levodopa – may result in elevated levodopa levels

For a full list of drug interactions refer to the BNF or Summary of Product Characteristics

Information given to patient[1,2,4,5]

- Patients should be advised to tell doctor promptly if sore throat, fever, infection, non- specific illness, unexplained bleeding and bruising, purpura, mouth ulcers or rashes develop.
- The patient should be advised to take the dose at least 30 minutes before food (if taken with food the amount of penicillamine absorbed can be reduced by 50%).
- The patient will also be given an approved drug information leaflet from Arthritis Research UK. Further copies available at www.arthritisresearchuk.org.

Patient's roles and responsibilities

The patient will:

- Take their medication as agreed, unless otherwise instructed by an appropriate healthcare professional.
- Attend for all regular blood tests and all follow-up appointments with GP and specialist. If they are unable to attend any appointments they should inform the relevant practitioner as soon as possible and arrange an alternative appointment.
- Inform all healthcare professionals of their current medication prior to receiving any new prescribed or over-the-counter medication.
- Report all suspected adverse reactions (as above) to medicines to their GP.
- Store their medication securely away from children.
- Read the information supplied by their GP, specialist and pharmacist and contact the relevant practitioner if they do not understand any of the information given.

References

1. Penicillamine film-coated tablets – Mylan. Summary of Product Characteristics 125mg and 250mg [22/06/2017] on Electronic Medicines Compendium: (accessed on 22/06/2020) via www.medicines.org.uk/emc.
2. Penicillamine 125mg and 250mg tablets – Kent Pharmaceuticals Ltd. Summary of Product Characteristics [21/06/2016] on Electronic Medicines Compendium: (accessed on 22/06/2020) via www.medicines.org.uk/emc.
3. Ledingham J, Gillick N, Irving K. et al. (2017) BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. Rheumatology doi:10.1093/rheumatology/kew149
4. BNF [online] via www.medicinescomplete.com [accessed 22/06/2020]
5. Baxter K (ed), Stockley's Drug Interactions. [online] London: Pharmaceutical Press accessed via www.medicinescomplete.com (accessed on 22/06/2020)