

Shared Care Guideline

**Penicillamine for rheumatoid arthritis and other rheumatological diseases
(Adults)**

It is vital for safe and appropriate patient care that there is a clear understanding of where clinical and prescribing responsibility rests between consultants and general practitioners (GPs).

This guideline reinforces the basic premise that:

When clinical and / or prescribing responsibility for a patient is transferred from hospital to GP, the GP should have full confidence to prescribe the necessary medicines. Therefore, it is essential that a transfer of care involving medicines that a GP would not normally be familiar with, should not take place without the “sharing of information with the individual GP and their mutual agreement to the transfer of care.”

These are not rigid guidelines. On occasions, consultants and GPs may agree to work outside of this guidance. As always, the doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

Indications:

Penicillamine is used for the management of severe active rheumatoid arthritis.

Dosage and administration:

The usual starting dose is 125-250mg daily, increasing by 125mg every 4 weeks to usual maintenance dose of 500mg – 750mg daily in divided doses. Maximum 1.5g daily
Elderly: up to 125 mg daily for 1 month increased by similar amounts at intervals of not less than 4 weeks; max. 1 g daily

Dosage in renal impairment:

eGFR 20-50ml/min: avoid if possible or reduce dose. 125 mg for first 12 weeks. Increase by same amount every 12 weeks.
eGFR <20ml/min: avoid – nephrotoxic.

Penicillamine should be taken on an empty stomach at least half an hour before meals, or at bedtime.

Patients should be warned not to expect improvement for at least 6 – 12 weeks after initiation and penicillamine should be discontinued if there is not improvement within 1 year.

Additional Information

- Reversible loss of taste may occur. Mineral supplements to overcome this are not recommended
- Pyridoxine daily may be given to patients on long term therapy, especially if they are on a restricted diet, since penicillamine increases the requirement for this vitamin
- Breast enlargement has been reported as a rare complication of penicillamine therapy in both women and men

Monitoring requirements:

Before treatment:

- Full blood count (FBC) including platelets, urea and electrolytes (U&Es), creatinine and urinalysis for detection of haematuria and proteinuria

During treatment:

- FBC, LFTs, U/Es, creatinine and urinalysis weekly for the first month then monthly thereafter if stable EXCEPT in renal impairment, when monitoring should be fortnightly throughout

treatment

- Repeat FBC and LFTs in the week after any increase in dose and then return to monthly.
- Patients should be asked about a rash or oral ulceration at each visit.
- Annual fasting lipids (HDL, Cholesterol, HDL/Cholesterol ratio)
- ESR monthly for disease monitoring purposes

Responsibility for monitoring, once stable, rests with the GP

Action to be taken if abnormal results/adverse effects:

- WBC < 3.5 x 10⁹/l Check neutrophil count
- Neutrophils < 2.0 x 10⁹/l Monitor weekly. If it falls below 1.5 x 10⁹/l STOP DRUG and contact helpline.
- Platelets < 150 x 10⁹/l Monitor weekly. If drop below 100 x 10⁹/l contact helpline
- Rash Mild: drug can be continued at reduced dose if necessary.
Severe: STOP DRUG and contact helpline (late rashes are more serious than early ones)
- Oral ulceration Repeat FBC and act on results as above
Mild: salt water mouth wash
Moderate: Hydrocortisone (Corlan) pellets (1 applied to affected area qds)
Severe: Hydrocortisone (Corlan) pellets and contact helpline
- MCV > 100fl Check B12, Folate and TSH and if low, start appropriate supplements.
- Abnormal bruising Repeat FBC and act on results as above
- Sore throat Repeat FBC and act on results as above
- Muscle weakness Withhold and contact helpline
- Proteinuria 2+ or more Check MSSU: If evidence of infection - treat appropriately.
If sterile and proteinuria persists, withhold until discussed with specialist team
- Haematuria Withhold and contact helpline

Please note that in addition to absolute values for haematological indices, a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Contraindications:

- Penicillamine should not be given to women who are pregnant or breastfeeding, unless considered to be absolutely essential
- Hypersensitivity to penicillamine or any of the ingredients.
- Agranulocytosis, aplastic anaemia or severe thrombocytopenia due to penicillamine.
- Lupus erythematosus.
- Moderate or severe renal impairment

Drug interactions: see appendix 1 of current BNF for full list of interactions, avoid concomitant use of nephrotoxic drugs

- Oral absorption of penicillamine may be reduced by concomitant administration of iron or antacids – do not give iron or antacids within two hours of taking penicillamine
- Oral absorption of digoxin may be reduced by concomitant administration of penicillamine – do not give digoxin within two hours of taking penicillamine
- Concomitant use of NSAIDs and other nephrotoxic drugs may increase the risk of renal damage
- Concomitant use of clozapine: penicillamine may potentiate the blood dyscrasias seen with clozapine

- Concomitant use of zinc: oral absorption of penicillamine may be reduced by concomitant administration of zinc; absorption of zinc may also be reduced by penicillamine.
- Sodium Aurothiomalate: manufacturer of penicillamine advises avoid concomitant use, (increased risk of toxicity)

Cautions:

- Concomitant or previous treatment with gold may increase the risk of side effects with penicillamine treatment. Therefore penicillamine should be used with caution in patients who have previously had adverse reactions to gold
- Elderly: Increased toxicity has been observed regardless of renal function.
- Patients who are hypersensitive to penicillin may react rarely to penicillamine

Adverse Effects:

Initially nausea, anorexia, fever; proteinuria, thrombocytopenia; rarely mouth ulceration, stomatitis, male and female breast enlargement, haematuria (withdraw immediately if cause unknown), alopecia, pseudoxanthoma elasticum, elastosis perforans, skin laxity; also reported pancreatitis, vomiting, cholestatic jaundice, pulmonary haemorrhage, bronchiolitis, pneumonitis, blood disorders including neutropenia, agranulocytosis, aplastic anaemia, haemolytic anaemia and leucopenia, nephrotic syndrome, glomerulonephritis, Goodpasture's syndrome, septic arthritis in patients with rheumatoid arthritis, lupus erythematosus, myasthenia gravis, polymyositis, rheumatoid arthritis, urticaria, dermatomyositis, pemphigus, Stevens-Johnson syndrome, late rashes (consider dose reduction)

Specialist responsibilities:

- Confirm the diagnosis of rheumatoid arthritis
- Discuss with the patient the benefits and side effects of treatment with penicillamine
- If the patient is a woman of child bearing potential – ensure that they are aware of the importance of effective contraception and the need to discuss with their consultant if they wish to become pregnant
- Ensure that the patient understands and accepts their responsibilities (see section below)
- Seek consent for treatment and document in the patient's notes.
- Ensure baseline monitoring of full blood count and biochemical profile
- Discuss how the patient/carer can be aware of possible signs penicillamine toxicity or intolerance
- Provide written instruction to the GP for initiation and escalation of penicillamine.
- Provide the patient with a monitoring booklet and enter the blood results into the booklet.
- Review the patient at the intervals specified below to monitor the patient's disease activity, the efficacy of the treatment and the ability to tolerate it, and consider whether continuation of treatment is appropriate.
- Discontinue if no response or patient has a significant adverse effect.
- Promptly communicate with the GP via a clinic letter any changes in treatment, results of monitoring undertaken, and assessment of adverse events. The clinic letter should clearly state if the dose has remained the same or if a dose adjustment had been made – specifically highlighting the new dose in comparison with the preceding one.
- Advise GPs when to stop treatment.
- Provide clear arrangements for back-up, advice and support.
- Report serious adverse events at <https://yellowcard.mhra.gov.uk/>

GP's responsibilities:

- Initial referral to Consultant Rheumatologist raising the possibility of rheumatoid arthritis.
- Provide the patient with monthly repeat prescriptions of medication following written instructions for initiation and escalation by the specialist. The patient should allow at least 48 hours for the prescription from the GP to be generated.
- Continue monitoring as outlined on the first page and document the results in the shared care booklet.
- Ensure patient's monitoring booklet and practice computer system are updated with any dose changes.
- Refer promptly to the specialist if there is a change in the patient's status or concerns regarding compliance. In most cases, do not stop treatment without discussion with the Rheumatology Helpline.
- If patient fails to attend more than 2 monitoring visits it is not safe to continue treatment – contact the Rheumatology Helpline for advice.
- Report serious adverse events to the specialist and at <https://yellowcard.mhra.gov.uk/>
- Administer Pneumococcal Vaccine/ Pneumovax® II and annual influenza vaccines.
- Consider passive immunisation with Varicella zoster immunoglobulin in non-immune patients exposed to chicken pox or shingles.

Patient responsibilities:

- Read the written patient information provided about the drug and have a clear understanding of the risks/benefits of oral penicillamine treatment.
- Attend for blood tests.
- Report any adverse effects to their GP and/or specialist whilst treated with penicillamine.
- Limit alcohol to national safe weekly limits
- Take monitoring booklet every time the patient sees the GP, has a hospital appointment or visits the pharmacist.

Secondary care review: During initiation: 4 – 6 weekly until controlled

Once disease controlled: Annual review by consultant

Availability: 125mg tablet: 56 = £37.33 250mg tablet: 56 = £75.00

Prices from Online Drug Tariff February 2016

Back up advice and support:

Rheumatology Helpline

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