Penicillamine

ESCA: For the treatment of rheumatoid arthritis

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of penicillamine for rheumatoid arthritis can be shared between the specialist and general practitioner (GP). You are **invited** to participate however, if you do not feel confident to undertake this role, then you are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care will be explained to the patient by the specialist initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with rheumatoid arthritis are usually under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

RESPONSIBILITIES and ROLES

Specialist responsibilities
1. Confirm the diagnosis of rheumatoid arthritis.
2. Discuss the potential benefits, treatment side effects, and possible drug interactions with the patient.
3. Ask the GP whether he or she is willing to participate in shared care before initiating therapy so that appropriate follow on prescribing arrangements can be made.
4. Do baseline monitoring prior to initiation of penicillamine.
5. Initiate treatment and stabilise dose of penicillamine.
6. Review the patient's condition and monitor response to treatment regularly.
7. A written summary to be sent promptly to the GP i.e. within 10 working days of a hospital outpatient review or inpatient stay.
8. Report serious adverse events to the MHRA.
9. Ensure clear backup arrangements exist for GPs, for advice and support (Please complete details below).

General Practitioner responsibilities						
1. Reply to the request for shared care as soon as practicable i.e. within 10 working days.						
2. Prescribe penicillamine at the dose recommended.						
3. In the patient's notes, using the appropriate Read Code listed below, denote that the patient is receiving treatment under a shared care agreement						
GP Prescribing System	**Read Code**	**Description**		**GP Prescribing System**	**Read Code**	**Description**
EMIS and Vision	8BM5.00	Shared care prescribing		SystmOne	XaB58	Shared care
4. Monitor patient's response to treatment; make dosage adjustments if agreed with specialist						
5. Report to and seek advice from the specialist or clinical nurse specialist on any aspect of patient care that is of concern to the GP, patient or carer and may affect treatment.						
6. Refer back to specialist if condition deteriorates.						
7. Report serious adverse events to specialist and MHRA.						
8. Stop treatment on advice of specialist.						

Patient's role
1. Report to the specialist, clinical nurse specialist or GP if he or she does not have a clear understanding of the treatment.
2. Share any concerns in relation to treatment with penicillamine with the specialist, clinical nurse specialist or GP.
3. Report any adverse effects to the specialist or GP whilst taking penicillamine.
4. Attend regular outpatient appointments with the specialist.

BACK-UP ADVICE AND SUPPORT

Trust	Contact details	Telephone No.	Email address:
	Consultant:-		
	Specialist Nurse		

Based on MTRAC template
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SUPPORTING INFORMATION

Indication	Severe active rheumatoid arthritis, including juvenile forms
Dosage and Administration BSR Recommendation	Typical regimen: 125–250 mg/day increasing by 125 mg every 4 weeks to 500 mg/day. If no response in 3 months consider an increase in dose to 750 mg/day. Maximum dose is 1–1.5 g/day but there appears to be no clear advantage in using doses greater than 500 mg/day Inadequate response to 750 mg/day should prompt a review of the patient's DMARD therapy
Renal Impairment	Penicillamine should be initiated at a low dose with intervals between dose increase of at least twelve weeks. Fortnightly monitoring for toxicity is mandatory throughout treatment for rheumatoid arthritis.
Contra-indications / Special precautions	**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. **Cautions** Full blood and platelet counts should be performed and renal function should be assessed prior to treatment with penicillamine. Monitoring of blood and platelet counts should be carried out at appropriate intervals, together with urinalysis for detection of haematuria and proteinuria. Urinalysis should be carried out weekly at first, and following each increase in dose, then monthly, although longer intervals may be adequate for cystinuria and Wilson's disease. Increasing or persistent proteinuria may necessitate withdrawal of therapy. During the first eight weeks of therapy full blood counts should be carried out weekly or fortnightly and also in the week after any increase in dose, otherwise monthly thereafter. In cystinuria or Wilson's disease, longer intervals may be adequate. Withdrawal of treatment should be considered if platelets fall below 120,000/mm^3 or white blood cells below 2,500/mm^3, or if three successive falls are noted within the normal range. Treatment may be restarted at a reduced dose when counts return to normal, but should be permanently withdrawn on recurrence of leucopenia or thrombocytopenia. Penicillamine may potentiate the bone marrow suppression caused by clozapine. 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. Concomitant use of NSAIDs and other nephrotoxic drugs may increase the risk of renal damage. Penicillamine should be used with caution in patients who have had adverse reactions to gold. 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 and concomitant treatment with gold should be avoided. If concomitant oral iron, digoxin or antacid therapy is indicated, this should not be given within two hours of taking penicillamine. Antihistamines, steroid cover, or temporary reduction of dose will control urticarial reactions. Reversible loss of taste may occur. Mineral supplements to overcome this are not recommended. Haematuria is rare, but if it occurs in the absence of renal stones or other known cause, treatment should be stopped immediately. A late rash, described as acquired epidermolysis bullosa and penicillamine dermopathy, may occur after several months or years of therapy. This may necessitate a reduction in dosage. Breast enlargement has been reported as a rare complication of penicillamine therapy in both women and men Danazol has been used successfully to treat breast enlargement which does not regress on drug discontinuation. The use of DMARDs, including penicillamine, has been linked to the development of septic arthritis in patients with rheumatoid arthritis, although rheumatoid arthritis is a stronger predictor for the development of septic arthritis than the use of a DMARD. Deterioration of the neurological symptoms of Wilson's disease (dystonia, rigidity, tremor, dysarthria) have been reported following introduction of penicillamine in patients treated for this condition. This may be a consequence of mobilisation and redistribution of copper from the liver to the brain. 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

Side Effects	• Nausea • Anorexia • Mouth ulcers • Loss of taste or metallic taste (resolves after six weeks and treatment can be continued) • Rashes • Leucopaenia • Thrombocytopaenia • Proteinuria • Haematuria	
Monitoring BSR Recommendations	Pre-treatment Assessment	• FBC, U&E and LFTs • Urinalysis dipstick
	After commencing treatment	• FBC, U&E, LFTs and urinalysis every two weeks for three months. • Then monthly for four months • Then every six to eight weeks • Patient should be asked about the presence of rash or oral ulceration at each visit.
	Disease monitoring	Occasional ESR/CRP helps assessment
	Actions to be taken:	
	WBC<3.5x10^9/l	Withhold until discussed with specialist team.
	Neutrophils<2.0x10^9/l	Withhold until discussed with specialist team.
	Platelets<150x10^9/l	Withhold until discussed with 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 specialist team.
	Severe rash or oral ulceration. Late rashes are more serious than early ones	Withhold until discussed with specialist team
	Nausea	Taking medication before bed may reduce nausea
	Alteration of taste	Continue treatment (may settle spontaneously).
	Abnormal bruising or severe sore throat	Check FBC immediately and withhold until results are available
	Dose reduction	For side effects, e.g.: • Mouth ulcers • Metallic taste • GI upset • Rash

Drug Interactions

Penicillamine has the following interaction information:

Antacids	absorption of penicillamine reduced byantacids **Note:** antacids should preferably not be taken at the same time as other drugs since they may impair absorption
Clozapine	avoid concomitant use of penicillamine with clozapine (increased risk of agranulocytosis) **Note:** Avoid concomitant use of clozapine with drugs that have a substantial potential for causing agranulocytosis
Digoxin	penicillamine possibly reduces plasma concentration of digoxin
Iron Salts	absorption of penicillamine reduced by *oral* iron salts
NSAIDs	possible increased risk of nephrotoxicity when penicillamine given with NSAIDs **Note:***See also* Aspirin. Interactions do not generally apply to topical NSAIDs
Sodium Aurothiomalate	manufacturer of penicillamine advises avoid concomitant use with sodium aurothiomalate (increased risk of toxicity)
Zinc	penicillamine reduces absorption of zinc , also absorption of penicillamine reduced by zinc

References

- British Society for Rheumatology (BSR) guidelines
- Distamine tablets SmPC
- Penicillamine BNF

I agree to participate in this shared care agreement for the treatment of the below named patient with penicillamine for rheumatoid arthritis

General Practitioner
Name (please print)_____Signature _____Date_____

Hospital Specialist/Consultant
Name (please print)_____Signature_____Date_____

Patient's name	Date of birth	Sex	Home Address	Hospital Number
				NHS Number

Please keep a copy of this agreement for your own records and forward the original to the above named Consultant at: