DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE
SHARED CARE AGREEMENT

PENICILLAMINE for adult patients

1. REFERRAL CRITERIA

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patient's GP and the patient's condition is stable or predictable.
- Safe prescribing must be accompanied by effective monitoring.
- When transfer agreed the patient will be given a supply of penicillamine sufficient for 4 weeks maintenance therapy.

2. AREAS OF RESPONSIBILITY

GP responsibilities	Consultant responsibilities
1. If NOT participating in shared care reply to the request from the consultant/specialist as soon as practicable (see appendix 1) **2.** Ensure compatibility with other concomitant medication. **3.** Prescribe at the dose recommended. **4.** Perform monitoring tests as specified in section vii **5.** Adjust the dose as advised by the specialist. **6.** Stop treatment on the advice of the specialist or immediately if any urgent need to stop treatment arise **7.** Manage adverse effects as detailed in section vi. and discuss with specialist team when required. Report adverse effects to the referring specialist and the MHRA yellow card scheme. **8.** Ensure the patient is offered an annual flu vaccination and a one off pneumococcal vaccination.	**1.** Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol and communicated to primary care. Assess for contraindications and cautions and interactions. **2.** Use a shared decision making approach; discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling to enable the patient to reach an informed decision. **3.** Perform baseline tests as recommended in section vi and provide results of baseline tests. **4.** Prescribe penicillamine for the first three months or until the drug monitoring is stable. **5.** To contact patient's GP to request prescribing under shared care and send a link to or copy of the shared care protocol. **6.** Recommend dose of the drug and frequency of monitoring as per section 4vi. **7.** Periodically review the patient and advise the GP promptly on when to adjust the dose, stop treatment or consult with the specialist. **8.** Ensure that clear backup arrangements exist for GPs to obtain advice and support. **9.** Communicate any dose increase to the GP and transfer monitoring to GP when the patient's condition is stable or predictable. **10.** Advise on the suitability for live vaccinations (e.g. herpes zoster vaccination) in accordance with national screening programme **11.** Report any adverse effects to the MHRA yellow card scheme and GP.

Patient responsibilities

1. Report to the specialist or GP if there is not a clear understanding of the treatment and share any concerns in relation to treatment.
2. Take penicillamine as prescribed and avoid abrupt withdrawal unless advised by the primary care prescriber or specialist.
3. Attend regularly for monitoring and review appointments with primary care and specialist, and keep contact details up to date with both prescribers. Be aware that medicines may be stopped if they do not attend.
4. Inform specialist or GP of any other medication being taken including over-the-counter products.
5. Report any adverse effects or warning symptoms of blood disorders (e.g. sore throat, fever, unexplained bleeding) to the specialist or GP whilst taking penicillamine.

3. COMMUNICATION AND SUPPORT

i. Hospital contacts:	ii. Out of hours contacts and procedures:
University Hospital of Derby and Burton NHS Foundation Trust **Derby Hospitals** Rheumatology helpline: 01332 787710 **Queens Burton Hospital** 01283 511511/566333	**Derby** Pharmacy, ask for on-call pharmacist via switchboard: 01332 340131 Messages can be left on the Derby Rheumatology nurse advice line: 01332 787710 The aim is to address these next working day

Rheumatology Consultants; Dr R Laximinarayan ext 3167 Dr S Das/ Dr D Ray ext 3211/3247 Clinical Rheumatology Nurse Specialist ext 4112 Bhft.rheumatologynurses@nhs.net **Chesterfield Royal Hospital NHS Foundation Trust** Contact the referring consultant/nurse via switchboard: 01246 277271	**Burton** 01283 511511 / 566333 ask for on-call pharmacist via switchboard Messages can be left on the nurse advice line out of hours. 01283 511511 ext 4112. If the advice line is not staffed, messages may be left 24 hours a day. The team aim to respond at latest within two working days. The specialist nurses may also be bleeped via switchboard for urgent enquiries. **Chesterfield** Contact the on-call Medic for the relevant speciality via switchboard: 01246 277271
iii. Specialist support/resources available to GP including patient information: Patient information leaflet: https://www.medicines.org.uk/emc/files/pil.2712.pdf **Rheumatology** British Society of Rheumatology Specialist website: http://www.rheumatology.org.uk/ Versus Arthritis https://www.versusarthritis.org/	

4. CLINICAL INFORMATION

i. Prescribed indications	**Licensed** Rheumatoid arthritis Wilson's disease
ii. Therapeutic summary	Penicillamine is a potent heavy metal chelator probably having an effect on free radical scavenging. The precise mode of action is unknown. In the treatment of rheumatoid arthritis, response to Penicillamine is often slow and improvement may not occur for 3-6 months, The use of existing analgesics, anti-inflammatories or steroids should be continued and later gradually withdrawn, subject to patient improvement.
iii. Dose & Route of administration	**Rheumatoid Arthritis** 125-250 mg/day for the initial 4 week period. Increasing by the same amount every 4 to 12 weeks until remission occurs (e.g. to 500mg/day in 2 divided doses; if no response in 3 months increase the dose to 750mg/day.) Usual maintenance dose is 500-750mg daily in divided dosages. Maximum dose is 1-1.5gm/day but there appears to be no clear advantage in using doses greater than 500 mg/day. Inadequate response to 750mg/day should prompt *a review* of the patient's DMARD therapy. The daily dosage may be reduced by 125mg to 250mg every 12 weeks when patient has shown remission for 6 months Elderly Initial dose should not exceed 125mg daily for the first month, increasing by similar increments every four to twelve weeks until the minimum maintenance dose to suppress symptoms is reached. Renal Insufficiency Penicillamine therapy should be initiated at a low dose with intervals between dose increases of at least 12 weeks. Ongoing fortnightly monitoring may be required in certain at-risk patients. **Wilson's Disease** 1500 mg to 2000 mg daily in divided doses. Dose reduction to 750-1000mg daily may be attempted when remission occurs. BNF states a dose of 2g daily should not be continued for more than one year. Penicillamine should be taken orally on an empty stomach at least half an hour before meals (or indigestion remedies or medicines containing iron or zinc), or on retiring.
iv. Duration of treatment	Medium to long term: depends on response to treatment, side effects and level of disease activity

v. Adverse effects
For further detail see BNF and SPC

Common/very common:

- Proteinuria – occurs in up to 30% of patients and is partially dose-related. Discontinue if nephrotoxicity occurs
- Thrombocytopenia- may occur at any time during treatment and is usually reversible.

Others include: nausea, anorexia, fever, rash; haematuria.

Adverse effect	Action for primary care
Abnormal bruising or severe sore throat	Check **FBC immediately** and **withhold until** results are available and discuss *with specialist team if necessary.*
Haematuria (rare)	Withhold **until discussed** *with specialist team if cause unknown*
Skin rash or oral ulceration	Rashes may occur with treatment and early rashes are more common when full doses are given from the start, but late rashes are more serious than the early ones. Severe rash- Withhold **until discussed** *with specialist team*. Temporary withdrawal or reduction in dosage may control the rashes but occasionally antihistamines or steroid cover may be necessary for acute urticarial rashes.
Nausea and anorexia	Generally improves with time Taking medication before bed may reduce nausea.
Alteration of taste	Continue treatment (may settle spontaneously after approx. 6 weeks) Discuss with specialist if persist and troublesome.

vi. Monitoring requirements

<u>Consultant/ specialist monitoring schedule</u>

Baseline and 2 weekly until on a stable dose for at least 6 weeks

- FBC
- ALT and/or AST and albumin
- U&E including creatinine/CrCl
- Urinalysis

Periodically review the patient and advise the GP promptly on when to adjust the dose, stop treatment or consult with the specialist**.**

<u>GP responsibility monitoring schedule</u>

In patients following the 6 weeks of dose stability conduct **monthly** monitoring:

- FBC
- ALT and/or AST and albumin
- U&E including creatinine/ CrCl
- urinalysis (blood and protein)

Patients who have been stable for 12 months can be considered for reduced monitoring frequency (every 3 months) on an individual basis.

Patient should be **asked** about the presence of **rash or oral ulceration** at each visit.

For rheumatic patients CRP/ESR may be done every 3 months (this is not done for dermatology patients). These tests are part of the assessment of the underlying rheumatic disease rather than a requirement for monitoring of immunomodulating therapy. The monitoring CRP/ESR may be coordinated between secondary and primary care on an individual basis.

Patients with Renal impairment- Fortnightly monitoring throughout treatment for rheumatoid arthritis. Follow consultant advice.

<u>Dosage increase</u>

For dose **increase**, monitor 2 weekly until stable for 6 weeks. Dose and monitoring to be agreed with consultant. GP's to then continue monthly monitoring.

- FBC
- ALT and/or AST and albumin
- U&E including creatinine/ CrCl
- urinalysis (blood and protein)

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<u>Actions to be taken</u>
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In addition to responding to absolute values in laboratory tests, it is also relevant to observe trends in results (e.g gradual decreases in white blood cells (WBC) or albumin, or increasing liver enzymes)
NB – a rapidly increasing or decreasing trend in any value should prompt caution irrespective of actual value.
Parameters below are to be used as a guide for clinicians rather than absolute values, where monitoring should be based on individualised basis. It is important to consider alternative explanations other than the immunomodulation agents, especially in patients who have been stable for prolonged periods

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<tr><td>WBC < 3.5 x 10^9/l
Lymphocytes < 0.5x10^9/L
Neutrophils < 1.6 x 10^9/l
Platelets < 140 x 10^9/l
Eosinophilia >0.5x10^9/L</td><td>Discuss urgently with specialist team and consider interruption.
Isolated low lymphocytes more likely to be due to disease or other factors- GP to consider non-drug related causes (contact specialist for advice if unsure). The specialist may advise on individual cases if the abnormality is thought to be due to other factors and in this instance may set differential parameters which can be communicated to the GP.</td></tr>
<tr><td>Mean cell volume>105 f/l</td><td>Check serum B12, folate & TFT Discuss urgently with specialist team and consider interruption.</td></tr>
<tr><td>ALT and/or AST>3x upper limit of normal (ULN) or >100 units/ml (local consensus), or any sudden increases (e.g. double of baseline); or unexplained fall in albumin <30g/l</td><td>Contact Specialist urgently and consider interruption. Assess for other causes of hepatic dysfunction such as alcohol history and drug interactions, including OTC or complementary medication.</td></tr>
<tr><td>Creatinine increase for example >30% over 12 months and/or CrCl <60ml/min</td><td>Contact Specialist urgently and consider interruption</td></tr>
<tr><td>Greater than 2 proteinuria on urinary dipstick (see adverse effects section above)</td><td>check check mid-stream sample of urine
If evidence of infection, treat appropriately
If sterile and persists, discuss with specialist.</td></tr>
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<tr><td>vii. Contraindications and cautions</td><td>
Contraindications
Agranulocytosis, aplastic anaemia or severe thrombocytopenia due to penicillamine.
Lupus erythematosus
Moderate or severe renal impairment.

Cautions

Renal impairment- concomitant nephrotoxic drugs including gold treatment (manufacturer states concomitant use with gold not recommended)
Older people- Especially careful monitoring is necessary since increased toxicity has been observed in this patient population regardless of renal function
Patients who are allergic to penicillin may react similarly to penicillamine, but cross-sensitivity appears to be rare.

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<tr><td>viii. Clinically relevant drug interactions

For a full list of interactions please refer to the BNF</td><td>

Antacids, iron or zinc sulphate: Do not give within 2 hours as reduces absorption of Penicillamine
Clozapine: penicillamine may potentiate the blood dyscrasias seen with clozapine
Digoxin: Levels of digoxin can be reduced by concurrent use of D-Penicillamine. Do not give within 2 hours
Gold: avoid concomitant use if adverse reactions to gold. Manufacturer states concomitant use not recommended.
NSAID: Concomitant use of NSAIDs and other nephrotoxic drugs may increase the risk of renal damage

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<tr><td>ix. Pregnancy, paternal exposure and breastfeeding</td><td>
Pregnancy & lactation:
The safety of penicillamine for use during pregnancy & lactation has not been established. D-Penicillamine should not be administered to patients with suspected or confirmed pregnancy unless the benefit is considered to outweigh the risk according to the specialist team.
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<tr><td>x. Additional information</td><td>
Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed

To be read in conjunction with the following documents

RMOC Shared Care Guidance
NHSE/NHSCC guidance – items which should not be routinely prescribed in primary

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	care: guidance for CCGs • NHSE policy- Responsibility for prescribing between Primary & Secondary/Tertiary Care
xi. Supply of ancillary equipment	Not applicable
xii. Supply, storage and reconstitution instructions	Not applicable
Prepared by **Reviewed (2019, 2023)** **In consultation with**	The Shared Care Guidelines Group Derby Hospitals NHS Foundation Trust Chesterfield Royal Hospital NHS Foundation Trust Derbyshire Medicines Management Clinical Policies & DecisionsThe Derbyshire Medicines Management Shared Care and Guidelines Group

This does not replace the SPC, which should be read in conjunction with it

Date Prepared: October 2011 **Reviewed:** June 2023 **Review Date:** Currently under review

Sample Transfer Letter

Hospital No: «HOSPITAL_NUMBER»
NHS No: «NHS_NUMBER»

{Insert date}

PRIVATE & CONFIDENTIAL
«GP_TITLE» «GP_INITIALS» «GP_SURNAME»
«GP_ADDRESS_1»
«GP_ADDRESS_2»
«GP_POSTCODE»

DERBYSHIRE JAPC SHARED CARE AGREEMENT LETTER

Dear «GP_TITLE» «GP_SURNAME»

«FORENAME_1» «SURNAME» «DATE_OF_BIRTH»
«CURRENT_ADDRESS_1» «CURRENT_ADDRESS_2» «CURRENT_POSTCODE»

Your patient was seen on ***{Insert date}*** with a diagnosis of ***{Insert diagnosis}***. I have initiated the following medication ***{Insert drug name}*** and am writing to ask you to participate in the shared care for this patient.

This medication has been accepted as suitable for shared care by the Derbyshire Joint Area Prescribing Committee (JAPC). I agree to the secondary care responsibilities set out in the shared care agreement for this medication (available from www.derbyshiremedicinesmanagement.nhs.uk/clinical_guidelines/shared_care_guidelines). I am therefore requesting your agreement to share the care of this patient. Where preliminary tests are set out in the agreement I have carried these out and results are below.

Dose Regimen	Date ***{Insert medicine name}*** started	Date for GP to start prescribing ***{Insert medicine name}*** from
The baseline test results are (if applicable): **See overleaf for initiation criteria.**		

I can confirm that the following has happened with regard to this treatment:

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	*Yes / No*
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	*Yes / No*
The risks and benefits of treatment have been explained to the patient	*Yes / No*
The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been explained and agreed	*Yes / No*
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	*Yes / No*
I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)	*Yes / No*
I have included with the letter copies of the information the patient has received	*Yes / No*
I have provided the patient with sufficient medication to last until	
I have arranged a follow up with this patient in the following timescale	

If you do **NOT** wish to participate in shared care for this patient, usually under clinical grounds, please complete the attached form.

Yours sincerely

{Consultant name}

GP RESPONSE TO SHARED CARE (only complete & send if **NOT** participating in shared care*)
* For completeness please record medication on GP clinical system as per guidance- 'Recording medicines prescribed and issued by other Healthcare Providers'

Shared care is produced by GPs and specialists knowledgeable in the field of that drug usage. The shared care has been approved by the JAPC. This allows a more convenient service to the patient and cost effective use of NHS resources.

Patient:	NHS No:
Consultant:	Medicine requested for shared care:

I will **NOT** be undertaking the GP responsibilities as described in the agreed shared care guideline. My clinical reasons for declining shared care for this patient are listed in the box below:

		Tick which apply
1.	**The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care** As the patients primary care prescriber I do not feel clinically confident to manage this patient's condition because *[insert reason]*. I have consulted with other primary care prescribers in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice. **I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given above.**	
2.	**The medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement** As the medicine requested to be prescribed is not included on the national list of shared care drugs as identified by RMOC or is not a locally agreed shared care medicine I am unable to accept clinical responsibility for prescribing this medication at this time. **Until this medicine is identified either nationally or locally as requiring shared care the responsibility for providing this patient with their medication remains with you**	
3.	**A minimum duration of supply by the initiating clinician** As the patient has not had the minimum supply of medication to be provided by the initiating specialist I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.***	
4.	**Initiation and optimisation by the initiating specialist** As the patient has not been optimised on this medication I am unable to take clinical responsibility for prescribing this medication at this time. Therefore can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.***	
5.	**Shared Care Protocol not received** As legal responsibility for clinical care lies with the clinician who signs the prescription, I need to ensure that I am in possession of sufficient clinical information for me to be confident to prescribe this treatment for my patient and it is clear where each of our responsibilities lie to ensure the patient is safely managed. For this reason I am unable to take clinical responsibility for prescribing this medication at this time, therefore would you please contact the patient as soon as possible in order to provide them with the	

	medication that you have recommended. ***Until I receive the appropriate SCP, responsibility for providing the patient with their medication remains with you.***	
6.	**Other (Primary Care Prescriber to complete if there are other reasons why shared care cannot be accepted)**	

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible

Yours sincerely

{GP name}
{Surgery}

Please send a copy of this response to the specialist/consultant requesting shared care