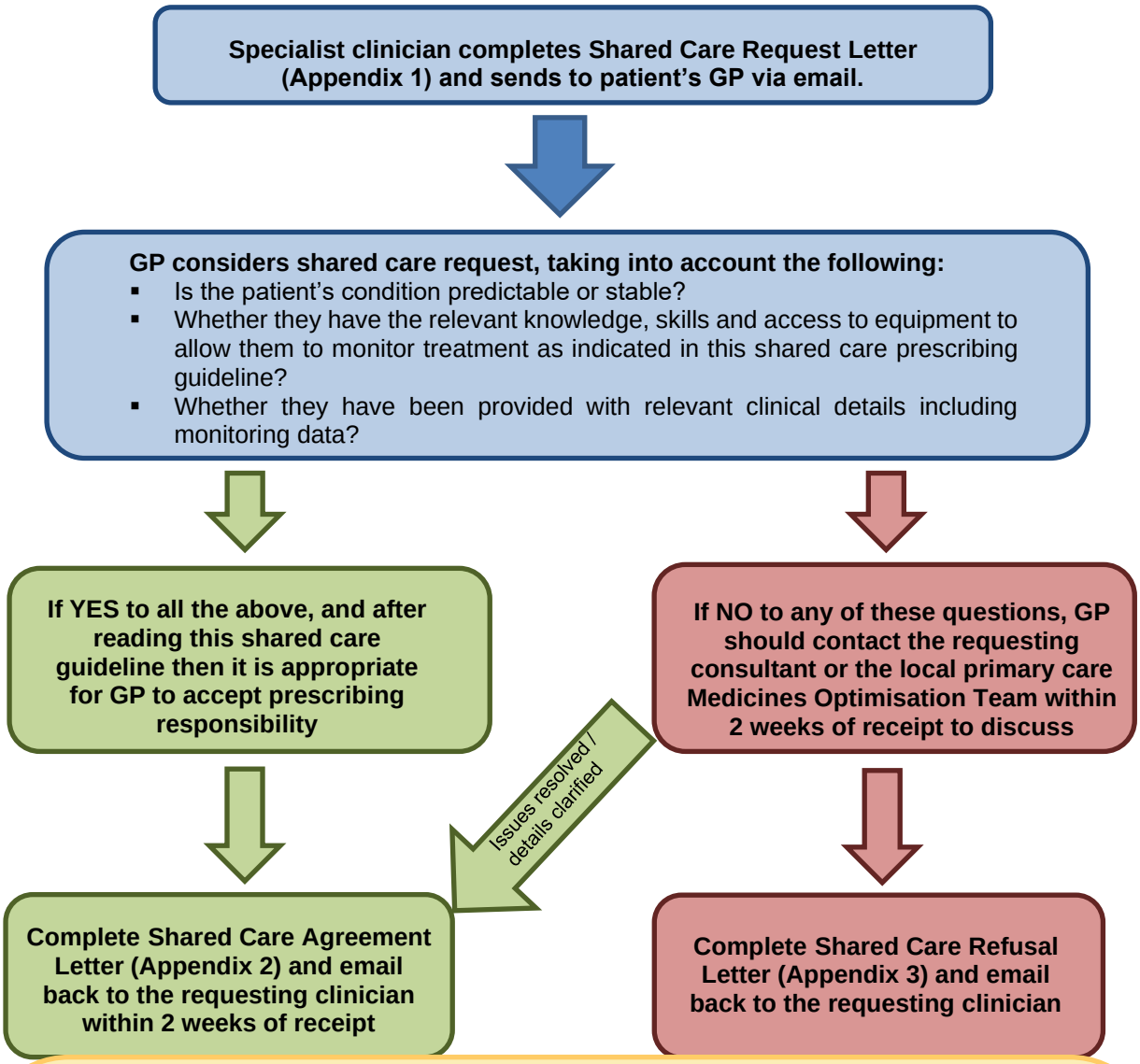
SHARED CARE PRESCRIBING GUIDELINE

Penicillamine for the treatment of Wilson's disease in ADULTS & PAEDIATRICS

South East London Integrated Medicines Optimisation Committee (SEL IMOC). A partnership between NHS organisations in South East London Integrated Care System: NHS South East London (covering the boroughs of Bexley/Bromley/Greenwich/ Lambeth/Lewisham and Southwark) and GSTFT/KCH /SLaM/ Oxleas NHS Foundation Trusts and Lewisham & Greenwich NHS Trust

SHARED CARE PROCESS FLOWCHART



NOTES

There may be implications for the patient where invitation to share care is declined. For example, the patient may need to be changed to an alternative treatment regimen. It would not normally be expected that shared care prescribing would be declined on the basis of cost.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. **It is important that patients are consulted about treatment and are in agreement with it**.

Prescribing should follow requirements in the South East London Interface Prescribing Policy.
The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use. The patient's best interests are always paramount.

If the GP is not confident to undertake these roles, then he or she is 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. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

1. AREAS OF RESPONSIBILITY

Consultant / Specialist team responsibilities

- Ensuring patient fits criteria for use of this drug (e.g. no contraindications, cautions, fits local agreement for use of the drug)
- Baseline monitoring tests (to be listed)
- To initiate, stabilise and supply treatment over the initial stabilisation period (12 months)
- To inform patients of practical issues related to the use of penicillamine, such as administration, storage and maximum dose – see "Information provided to patient" section on page 2
- At the time of initiating, notify GP in writing that penicillamine has been prescribed. The GP should be invited to share care once the patient is stable. Information provided to the GP should include:
  - A copy of the shared care guidelines
  - That a prescription for the next 3 months' supply has been given
  - Information on when the patient will next be reviewed and by whom.
  - A request that the GP continue prescribing after the initial stabilisation period (12 months).
- Any continuous monitoring that will remain under the consultant's responsibility
- To review patient every 6 months as a minimum
- To review patient at the request of GP should any problems arise (side-effects / lack of efficacy) within 2 weeks
- To communicate promptly with the GP if treatment is changed, within 2 weeks
- Inform GP of patients who do not attend clinic appointments
- To report any suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk
- To provide an advice to the patient/carer when requested

General Practitioner responsibilities

- To consider shared care proposal within 2 weeks of receipt. If agree to request to continue prescribing as detailed in shared care guideline. Confirmation to the requesting consultant is required **within 2 weeks** of receipt of this guideline by completing and returning the agreement on page 3
- If do not agree to shared care discuss with requesting consultant or local primary care medicines management team within 2 weeks of receipt of shared care request
- To provide ongoing prescriptions for penicillamine after the initial stabilisation period (12 months)
- To adjust the dose as advised by the specialist.
- To agree monitoring requirements with specialist – see page 2 of this document for GP monitoring requirements.
- To report and seek advice regarding any concerns, for example: side-effects, co-morbidities, pregnancy, or lack of efficacy to the specialist team
- To advise the specialist if non-compliance is suspected
- To refer back to specialist if the patient's condition deteriorates.
- To stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
- To report any suspected adverse effects to the MHRA via the Yellow Card scheme: http://www.yellowcard.gov.uk
- Request advice from the hospital specialist when necessary

Patient's / Carer's responsibilities

- To contact the specialist or GP if he or she does not have a clear understanding of any aspect of the treatment.
- To inform prescribing specialist, GP and other healthcare professionals of any other medication being taken, including over the counter products, alternative therapies or recreational drugs.
- To inform community pharmacists that they are using penicillamine before purchasing medication over-the-counter
- To attend all hospital and GP appointments
- To take medicines as agreed and take steps to ensure that no doses are missed and not to share medicines with others
- To read the patient information leaflet included with the medication.
- To report any adverse effects or warning symptoms (e.g. sore throat, fever) to GP or hospital specialist
- To report to GP and Hepatology team if pregnant or breastfeeding.
- To inform GP and hospital of any changes in addresses or telephone contact numbers.
- Patients must not exceed the recommended dose

2. CLINICAL INFORMATION

NOTE: The information here is not exhaustive. Please also consult the current Summary of Product Characteristics (SPC) for **Penicillamine** prior to prescribing for up to date prescribing information, including detailed information on adverse effects, drug interactions, cautions and contraindications (available via www.medicines.org.uk)

Background	Penicillamine has historically been initiated in secondary care with continuation by the GP. Penicillamine is an effective chelator of copper & is used to promote copper excretion in the urine, reducing copper deposition in the liver and other organs. It is potentially toxic and therefore the drug must be monitored.	
Indications Note if indication is unlicensed or not	Licensed indication: Wilson's disease (hepatolenticular degeneration) in adults and children (0 to 18 years).	
Place in Therapy Indicate what drugs should have been tried before this drug is considered	Penicillamine is first line for the treatment of Wilson's disease.	
Locally agreed off-label use Including supporting information	N/A	
Initiation and ongoing dose regime **Note:** • Transfer of monitoring and prescribing to primary care is normally after the patient's dose has been optimized and with satisfactory investigation results for at least 3 months. • The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability. • All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician. • Any changes in treatment will be the responsibility of the specialist.	**Initial stabilisation:** **(The loading period must be prescribed by the initiating specialist)** • Adults: Started with 250mg daily, increasing to 250mg BD after one week and then adjusted to response. • Paediatrics: 2.5mg/kg twice daily, increase over 1-2 weeks up to 10mg/kg twice daily, max 2g/day. Doses over 1g are off label in paediatrics. **Maintenance dose (following initial stabilisation):** **(The initial maintenance dose must be prescribed by the initiating specialist)** • Adults: Maintenance dose should be approximately 0.75-1.5g daily. The maximum recommended dose is 2g daily. • Paediatrics: 2.5mg/kg twice daily, increase over 1-2 weeks up to 10mg/kg twice daily, max 2g/day. Doses adjusted on chelation. **Conditions requiring dose adjustment** • Dosing in the elderly is recommended at maximum 20mg/kg daily. Careful monitoring is necessary since increased toxicity has been observed in this patient population regardless of renal function. • Care should be exercised in patients with renal insufficiency; modification of dosage may be necessary as guided by the specialist. **Duration of treatment** • Lifelong • Pyridoxine 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: ▪ **Paediatrics Pyridoxine dosing** (unlicensed/off label): 50mg weekly for prevention of penicillamine induced neuropathy. The licensed dose of pyridoxine in this indication can also be used, 5-10mg daily in children aged 1-11 years old and 10mg daily in children aged 12 years, however 50mg weekly is preferred to aid compliance and reduce pill burden. ▪ **Adults Pyridoxine dosing**: 20mg daily	
Pharmaceutical aspects	Route of administration	Oral
	Formulation	125mg & 250mg Tablets

<table>
<tr><td rowspan="2"></td><td>Administration details</td><td>Penicillamine should be taken on an empty stomach at least one hour before meals.
For paediatrics: 125mg/250mg tablets/capsules can be crushed/opened and dissolved in 5mls water to give 125mg/5ml or 250mg/5ml solution. For example for a child weighing 30kg at a dose of 300mg – 2x250mg tablets can be dissolved in 10ml to give a 6ml dose.

However, If the child can swallow tablets, the dose is rounded to the nearest 125mg e.g. for the 30kg example, the dose of 300mg would be rounded down to 250mg.</td></tr>
<tr><td>Other important information</td><td>Please see Summary of products characteristics (SmPC)</td></tr>
<tr><td>**Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist**</td><td colspan="2">**Baseline investigations:**
• Full blood count (FBC) prior to initiation – including platelets and urea & electrolytes (U&E's)
• Urinalysis (24 hour copper excretion) – for monitoring of response

Initial monitoring
Monitoring at baseline and during initiation is the responsibility of the specialist, only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to the GP.
• FBC, U&Es, Creatinine and urinalysis every 2 weeks until dose and monitoring stable for 12 months, completed by the specialist team. Then every 3-6 months as advised by specialist clinician.

Ongoing monitoring:
• Response and bloods as below:</td></tr>
<tr><td rowspan="5">**Ongoing monitoring requirements to be undertaken by primary care**</td><td>**Monitoring**</td><td>**Frequency**</td></tr>
<tr><td>**FBC**</td><td>3-6 monthly. FBC should also be carried out within 4 weeks of any dose increase.</td></tr>
<tr><td>**Renal function (creatinine and U&Es)**</td><td>3 - 6 monthly as advised by specialist clinician. Consider checking renal function if change to clinical status.</td></tr>
<tr><td>**Urgent FBC**</td><td>For patients developing significant infection - looking for leucopoenia.</td></tr>
<tr><td>**Urinalysis and Protein: Creatinine Ratio (PCR)**</td><td>3 monthly. They should also be carried out a month after any dose increase.</td></tr>
<tr><td rowspan="5">**Adverse effects and management**

Any serious adverse reactions should be reported to the MHRA via the Yellow Care scheme www.mhra.gov.uk/yellowcard</td><td>**Result**</td><td>**Action for GP**</td></tr>
<tr><td>**Proteinuria 2+ (on dipstick analysis/urinalysis) or Haematuria**</td><td>Check MSU and treat if evidence of infection. If sterile and 2+ withhold drug and inform hepatology team.
See section 4 for contact numbers.</td></tr>
<tr><td>**WBC < 3.5 x109/l or neutrophils <2 x109/l**</td><td rowspan="2">Inform hepatology team.
See section 4 for contact numbers.</td></tr>
<tr><td>**Decline in platelet count from baseline or less than 50x109/l**</td></tr>
<tr><td>**Sore throat, abnormal bleeding or bruising, haemoptysis, unexplained rash, oral ulceration, infection, fever**</td><td>Check FBC; **if abnormal STOP penicillamine** and inform hepatology team.
See section 4 for contact numbers.</td></tr>
</table>

	Taste loss	Reassure (may settle spontaneously after approx. 6 weeks) & continue drug. Discuss with specialist if persists and troublesome.
	Decline in renal function from baseline	Please refer to section 'Criteria for stopping treatment' .Check if prescribed concurrent renal toxic drugs & refer back to specialist.
Advice to patients and carers The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.	**The patient/carer should be advised to report any of the following signs or symptoms to their GP without delay:** • sore throat • abnormal bleeding/ bruising • rashes • mouth ulcer • cough • haemoptysis	
Criteria for stopping treatment e.g. poor response, adverse effects requiring cessation	• Hypersensitivity reaction to penicillamine or any of the ingredients. • Agranulocytosis, aplastic anaemia or development of thrombocytopenia due to penicillamine • Patients with moderate or severe renal insufficiency – i.e.. A rise in serum creatinine of 50% from baseline or fall in eGFR by >25%.	
Follow up arrangements e.g. frequency of specialist clinic attendance	Every 6 months once stable	
Pregnancy, paternal exposure and breast feeding It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both the GP and the specialist.	**Pregnancy:** Referral back to specialist centre for advice and more frequent monitoring. **Breastfeeding:** If recommended by specialist penicillamine can be taken whilst breastfeeding, the infant should be monitored for epigastric pain, nausea, vomiting and low amounts of copper and zinc during therapy.	
Additional information	**Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.** Patients who are allergic to penicillin may react similarly to penicillamine, but cross sensitivity appears to be rare. **Interactions** • Concomitant use of antipsychotics such as clozapine should be avoided – increased risk of agranulocytosis. • Concomitant use of NSAIDs and other nephrotoxic drugs may increase the risk of renal damage. • Iron supplements, zinc supplements and antacids may reduce absorption of penicillamine – do not take within two hours of penicillamine. • Digoxin – levels can be reduced by concurrent use of penicillamine *Please note this is not an exhaustive list- please refer to current BNF and SPC for further drug interactions	
Evidence base for treatment and key references Include hyperlinks to original sources and access dates	• EASL Clinical Practice Guidelines: Wilson's disease - Journal of Hepatology (journal-of-hepatology.eu) • NHS England » Trientine for Wilson disease (all ages) • Wilson Disease - NORD (National Organization for Rare Disorders) (rarediseases.org)	

To be read in conjunction with the following documents	Further information can be found in the SPC: https://www.medicines.org.uk/emc/medicine/33539#gref
Local arrangements for referral Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.	Through electronic correspondence

3. COMMUNICATION AND SUPPORT

King's College and Princess Royal Hospitals switchboard: 0203 299 9000	
Consultant/specialist team Adults: Dr Adrian Bomford & Prof Aftab Ala Paediatrics: Prof Anil Dhawan. Paediatric CNS:	Tel: 020 3299 3366 Email: kch-tr.LiverSecretary@nhs.net Tel: 0203299 4448 Email: anil.dhawan@nhs.net Tel: 0203299 4646 Email: kch-tr.LiverCns@nhs.net
Medication – Prescribing advice, interactions, availability of medicines Kings Adult Liver pharmacy team Paediatrics team	Tel: 0203 299 9000 (Ext. 35714) Email: kch-tr.liverpharmacy@nhs.net Tel: 0203 299 9000 (Ext. 35723) Email: kch-tr.PaediatricLiverPharmacists@nhs.net
Guy's and St. Thomas' Hospital switchboard: 0207 188 7188	
Consultant/specialist team Terry Wong – Lead clinician	Email: LiverHelpline@gstt.nhs.uk
Medication – Prescribing advice, interactions, availability of medicines Lead Hepatology pharmacist/gastroenterology pharmacy team Medicines Information	Tel: 020 718 85005 Email: gst-tr.gastro-pharmacists@nhs.net Tel: 020 7188 8748 Email: medinfo@gstt.nhs.net

Appendix 1: Shared Care Request letter (Specialist to Primary Care Prescriber)

Dear *[insert Primary Care Prescriber's name]*

Patient name: *[insert patient's name]*
Date of birth: *[insert date of birth]*
NHS Number*:* *[insert NHS Number]*
Diagnosis: *[insert diagnosis]*

As per the agreed South East London shared care prescribing guideline for *[insert medicine name]* for the treatment of *[insert indication],* this patient is now suitable for prescribing to move to primary care.

The patient fulfils criteria for shared care and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out.

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*
For patients of child-bearing potential: The patient has agreed to use appropriate contraception for the duration of treatment and will inform the GP and specialist team in the event of family planning.	*Yes/No /Not applicable*
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 timeframe e.g. within 3 months / 6 months (please specify)	

Treatment was started on *[insert date started]* and the current dose is *[insert dose and frequency]*.

If you are in agreement, please undertake monitoring and treatment from *[insert date]* NB: date must be at least 3 months from initiation of treatment.

The next blood monitoring is due on *[insert date]* and should be continued in line with the shared care guideline.

Please could you reply to this request for shared care and initiation of the suggested medication to either accept or decline within 14 days.

Appendix 2: Shared Care Agreement Letter (Primary Care Prescriber to Specialist)

Primary Care Prescriber Response

Dear *[insert Doctor's name]*

Patient *[insert Patient's name]*

NHS Number *[insert NHS Number]*

Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment

Medicine	Route	Dose & frequency

I can confirm that I am willing to take on this responsibility from *[insert date]* and will complete the monitoring as set out in the shared care protocol for this medicine/condition.

Primary Care Prescriber signature: _____ Date: _____

Primary Care Prescriber address/practice stamp:

Appendix 3: Shared Care Refusal Letter (Primary Care Prescriber to Specialist)

Re*:*

Patient *[insert Patient's name]*

NHS Number *[insert NHS Number]*

Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient.

In the interest of patient safety, the local NHS in South East London have classified *[insert medicine name]* as a Shared Care medicine, and requires a number of conditions to be met before transfer can be made to primary care.

I regret to inform you that in this instance I am unable to take on responsibility due to the following:

		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 (Regional Medicines Optimisation Committees) 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. NB: Capacity issues to be discussed with local primary care Medicines Optimisation Team prior to returning this form)**	

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs." In this case we would also see the term GP being interchangeable with the term Primary Care Prescriber.

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

Primary Care Prescriber signature: _____ Date: _____

Primary Care Prescriber address/practice stamp: