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National shared care protocol:

Riluzole for patients within adult services

4 July 2022, Version 1

Review date – September 2025

The content of this shared care protocol was correct as of January 2022. As well these protocols, please ensure that summaries of product characteristics (SPCs), British national formulary (BNF) or the Medicines and Healthcare products Regulatory Agency (MHRA) or NICE websites are reviewed for up-to-date information on any medicine.

Specialist responsibilities

- Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol (section 2) and communicated to primary care.
- 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 (see section 11) to enable the patient to reach an informed decision. Obtain and document patient consent. Provide an appropriate patient information leaflet.
- Assess for contraindications and cautions (see section 4) and interactions (see section 7).
- Conduct required baseline investigations and initial monitoring (see section 8).
- Initiate treatment as outlined in section 5. Prescribe the maintenance treatment for at least 4 weeks; transfer to primary care will usually be after around 12 weeks.
- When transfer to primary care is appropriate complete the shared care documentation and send to patient's GP practice detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required. Include contact information (section 13).
- Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care.
- Conduct the scheduled reviews and monitoring in section 8 and communicate the results to primary care. After each review, advise primary care whether treatment should be continued,

confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.

- Reassume prescribing responsibilities if a woman becomes or wishes to become pregnant.
- Provide advice to primary care on the management of adverse effects if required.
- Advise primary care if treatment should be discontinued.

Primary care responsibilities

- Respond to the request from the specialist for shared care in writing. It is asked that this be undertaken within 14 days of the request being made, where possible.
- If accepted, prescribe ongoing treatment as detailed in the specialists request and as per section 5, taking into any account potential drug interactions in section 7. Conduct the required monitoring as outlined in section 9. Communicate any abnormal results to the specialist.
- Manage adverse effects as detailed in section 10 and discuss with specialist team when required.
- Stop riluzole if neutropenia develops. Arrange for immediate hospital assessment if neutropenic sepsis is suspected.
- Stop riluzole and make an urgent referral to the specialist if ALT rises to 5 times the ULN or if chest x-ray finding are suggestive of interstitial lung disease.
- Refer the management back to the specialist if the patient becomes or plans to become pregnant.
- Stop treatment as advised by the specialist.

Patient and/or carer responsibilities

- Take riluzole as prescribed and avoid abrupt withdrawal unless advised by the prescriber.
- 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.
- Report adverse effects to their prescriber. Seek immediate medical attention if they develop any symptoms as detailed in section 11, particularly if signs of febrile illness.
- Report the use of any over the counter (OTC) medications to their prescriber and be aware they should discuss the use of riluzole with their pharmacist before purchasing any OTC medicines.
- Not to drive or operate heavy machinery if riluzole affects their ability to do so safely.

- Patients of childbearing potential should take a pregnancy test if they think they could be pregnant, and inform the specialist or GP immediately if they become pregnant or wish to become pregnant.

1. Background

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Riluzole is indicated for extending life or the time to mechanical ventilation for patients with the amyotrophic lateral sclerosis (ALS) variant of motor neurone disease (MND). ALS is a progressive neurodegenerative disease that causes the loss of motor neurones resulting in a gradual increase in muscle weakness and muscle wasting.

Riluzole is recommended by NICE technology appraisal guidance (TA20: Guidance on the use of Riluzole (Rilutek) for the treatment of Motor Neurone Disease) as an option for treatment of people with ALS. It should be initiated by a neurological specialist with expertise in the management of MND.

Clinical trials have demonstrated that riluzole extends survival for patients with ALS, but only in the early stages of the disease. Further studies have not shown that riluzole is effective in the late stages of ALS. Patients in later stages of disease should be reviewed and given the opportunity to stop riluzole, if they consider it appropriate.

The safety and efficacy of riluzole has only been studied in ALS, therefore riluzole should not be use in any other form of MND.

Riluzole is not recommended for use in children.

2. Indications

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Licensed indication: to extend life or the time to mechanical ventilation for patients with amyotrophic lateral sclerosis (ALS).

3. Locally agreed off-label use

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National scoping did not identify any additional appropriate off-label indications

4. Contraindications and cautions

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This information does not replace the Summary of Product Characteristics (SPC), and should be read in conjunction with it. Please see BNF & SPC for comprehensive information.

Contraindications:

- Hypersensitivity to the active substance or to any of the excipients.
- Hepatic disease or baseline transaminases greater than 3 times the upper limit of normal (ULN).
- Pregnancy or breast-feeding.
- Acute porphyrias.

Cautions:

- Liver impairment: riluzole should be prescribed with care in patients with:
- a history of abnormal liver function
- slightly elevated serum transaminases (up to 3 times ULN), bilirubin and/or gamma-glutamyl transferase (GGT) levels
- baseline elevations of several liver function tests (especially elevated bilirubin) should preclude the use of riluzole
- Interstitial lung disease has been reported in patients treated with riluzole.
- Neutropenia or febrile illness.
- Renal Impairment (due to lack of data).

5. Initiation and ongoing dose regimen

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- Transfer of monitoring and prescribing to primary care is normally after the patient has been treated for around 12 weeks, and with satisfactory investigation results for at least 4 weeks
- 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.
- Termination of treatment will be the responsibility of the specialist.

Usual dose:

50mg twice daily

The initial maintenance dose must be prescribed by the initiating specialist.

Conditions requiring dose adjustment:

None

6. Pharmaceutical aspects

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Route of administration:	Oral
Formulation:	50mg tablets 5mg/mL oral suspension
Administration details:	Riluzole tablets can be crushed and dispersed in water for enteral tube administration or mixed with soft food e.g. yoghurt or puree. Give immediately or within 15 minutes. Riluzole may block enteral feeding tubes, so ensure that the tube is flushed well after each dose. Crushed tablets may have a local anaesthetic effect in the mouth. Crushing or splitting riluzole tablets is unlicensed. The oral suspension is suitable for administration via enteral feeding tubes. The suspension must be manually gently shaken for at least 30 seconds by rotating the bottle by 180° and the homogeneity should be visually verified.
Other important information:	Patients should be warned about the potential for dizziness or vertigo, and advised not to drive or operate machinery if these symptoms occur.

7. Significant medicine interactions

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The following list is not exhaustive. Please see BNF or SPC for comprehensive information and recommended management.

Riluzole is metabolised by cytochrome P450 isoform 1A2 (CYP1A2), and has the potential to interact with drugs which inhibit or induce CYP1A2. The clinical relevance of these interactions

has not been established, and some of these medicines are frequently used with riluzole without incident. Discuss with specialist team if there are any concerns.

- CYP1A2 inhibitors include caffeine, diclofenac, diazepam, clomipramine, imipramine, fluvoxamine, phenacetin, theophylline, amitriptyline, quinolones, mexiletine, nicergoline, rucaparib, vemurafenib, combined hormonal contraceptives
- CYP1A2 inducers include cigarette smoke, charcoal-grilled food, rifampicin, omeprazole

8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist

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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 primary care.

Baseline investigations:

- Liver function tests (LFTs), including serum transaminases, bilirubin and/or gamma-glutamyl transferase.
- Full blood count (FBC) including a differential white cell count (WCC).
- Urea and electrolytes.

Initial monitoring:

- LFTs, including alanine aminotransferase (ALT), should be measured every month during the first 3 months of treatment, every 3 months during the remainder of the first year, or until transferred to primary care.
- FBC and WCC every month during the first 3 months of treatment and every 3 months during the remainder of the first yearuntil transferred to primary care.

Ongoing monitoring:

Routine review to assess effectiveness and ongoing appropriateness of treatment every 6 months, or as clinically indicated.

After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.

9. Ongoing monitoring requirements to be undertaken by primary care

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See section 10 for further guidance on management of adverse effects/responding to monitoring results.

Monitoring and advice	Frequency
• LFTs, FBC & WCC	Every month during the first 3 months of treatment, then every 3 months for the remainder of the first year. NB: where monthly or quarterly monitoring is performed in secondary care prior to transfer, there is no need to repeat individual tests. Annually after the first year.
(If relevant) If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.	

10. Adverse effects and other management

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Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme. Visit www.mhra.gov.uk/yellowcard

For information on incidence of ADRs see relevant summaries of product characteristics

Result	Action for primary care
As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance.	
Altered LFTs Elevated LFTs up to 5 times ULN	Continue riluzole and discuss with specialist. Increase monitoring frequency if ALT is elevated.
ALT rises to 5 times ULN	Stop riluzole and inform specialist. Riluzole should not normally be re-started.
Respiratory function	

Dry cough or dyspnoea	Order chest x-ray. Stop riluzole immediately if findings are suggestive of interstitial lung disease. Inform specialist of findings.
Haematological parameters Febrile illness	Check WCC. Treat febrile illness according to local pathways. Arrange for immediate hospital assessment if neutropenic sepsis is suspected.
Confirmed neutropenia	Stop riluzole and inform specialist. Review patient for signs and symptoms of infection and treat or refer according to local pathways, as appropriate. Arrange for immediate hospital assessment if neutropenic sepsis is suspected.
Decreased WCC to below lower limit of local reference range	If clinical evidence of febrile illness/neutropenia, stop riluzole and treat or refer according to local pathways, as appropriate. Arrange for immediate hospital assessment if neutropenic sepsis is suspected. In the absence of febrile illness or clinical signs of neutropenia, seek advice from specialist.

11. Advice to patients and carers

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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 should be advised to report any of the following signs or symptoms to their primary care prescriber without delay:

- Signs or symptoms of infection, such as fever, chills or shivering, flu-like symptoms, sore throat, rashes, or mouth ulcers.
- Dry cough and/or dyspnoea.
- Signs or symptoms of liver problems, such as yellow skin or eyes (jaundice), itching all over, nausea or vomiting.

The patient should be advised:

- Not to stop taking riluzole without talking to their doctor and not to share their medicines with anyone else.
- Tell their prescriber if their smoking status changes, since this may affect their medicine
- Not to drive or operate machines if riluzole affects their ability to do so safely, e.g. by causing dizziness or drowsiness, and to inform the DVLA if their ability to drive safely is affected. See https://www.gov.uk/driving-medical-conditions and https://www.gov.uk/motor-neurone-disease-and-driving.

Patient information

- MND association riluzole information leaflet https://www.mndassociation.org/app/uploads/2015/07/5A-Riluzole.pdf
- MND Scotland riluzole fact sheet https://www.mndscotland.org.uk/media/1824/22-riluzole-2017.pdf
- NHS.uk. Low white blood cell count https://www.nhs.uk/conditions/low-white-blood-cell-count/

Patient information leaflets are also available from https://www.medicines.org.uk/emc/search?q=riluzole

12. Pregnancy, paternal exposure and breast feeding

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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 primary care prescriber and the specialist.

Pregnancy:

Riluzole is contraindicated in pregnancy.

Breastfeeding:

Riluzole is contraindicated in breast-feeding women. Very limited published evidence indicates low levels in breast milk. The UK Drugs in Lactation Advisory Service recommends caution if used, and infants should be monitored for adverse effects associated with adult use.

Information for healthcare professionals: https://www.sps.nhs.uk/medicines/riluzole/

Paternal exposure:

Fertility studies in rats indicate slight impairment of reproductive performance and fertility at doses of 15 mg/kg/day (which is higher than the therapeutic dose), probably due to sedation and lethargy. The relevance of this to human fertility is not known. Breastfeeding:

13. Specialist contact information

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Speciality	Contact name	Contact Details
Neurology	**ESNEFT Ipswich Site**	
	Dr Clare Galton Kathryn Barber Dr Andrew Graham Dr Hadi Manji	Email Secretaries: neurologyipswich@esneft.nhs.uk Tel: 01473 704044 / 01473 704041
	ESNEFT Colchester Site	
	Neurology Team	Tel: 01206 742 552 Tel: 01206 742526 Tel: 01206 742526 Email Secretaries: ch.neurology@esneft.nhs.uk
	West Suffolk NHS Foundation Trust	
	Dr Smriti Agarwal Dr Charlotte Brierley Dr Francesca Crawley Dr Alexandre Costa Dr Kate Maresh Dr Edward Needham Dr Dunya Luke	Tel: 01284 712984 Tel: 01284 712984 Tel: 01284 712897 Tel: 01284 712846 Tel: 01284 712984 Tel: 01284 712897 Tel: 01284 712846 Email: NeurologySecretaries@wsh.nhs.uk

14. Additional information

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Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed. Ensure that the specialist is informed in writing of any changes to the patient's GP or their contact details.

15. References

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- MND association accessed via: https://www.mndassociation.org/about-mnd/what-is-mnd/basic-facts-about-mnd/ on 20/05/21
- MND Scotland accessed via https://www.mndscotland.org.uk/ 21/05/21
- eBNF. Riluzole. Accessed via https://bnf.nice.org.uk/drug/riluzole.html 21/05/21
- NICE TA20: Guidance on the use of Riluzole (Rilutek) for the treatment of Motor Neurone Disease. January 2001. Accessed via https://www.nice.org.uk/guidance/ta20 on 21/05/21
- NICE NG42: Motor neurone disease: assessment and management. Last updated July 2019. Accessed via https://www.nice.org.uk/guidance/ng42 on 02/09/21
- Riluzole 50 mg film coated tablets (Glentek®). Date of revision of the text 29/04/2020. Accessed via https://www.medicines.org.uk/emc/product/10060/smpc on 21/05/21
- Riluzole 50 mg film-coated tablets (Rilutek®) Date of revision of the text 01/01/2021. Accessed via https://www.medicines.org.uk/emc/product/1101/smpc on 21/05/21
- Riluzole 50 mg film-coated tablets (Ranbaxy UK Ltd). Date of revision of the text 15/02/2018. Accessed via https://www.medicines.org.uk/emc/product/5185/smpc on 21/05/21
- Riluzole 50mg Film-Coated Tablet (Accord-UK Ltd). Date of revision of the text 18/07/2019. Accessed via https://www.medicines.org.uk/emc/product/2831/smpc on 21/05/21
- Riluzole 5 mg/ml oral suspension (Teglutik®). Date of revision of the text 10/11/2019. Accessed via https://www.medicines.org.uk/emc/product/5060/smpc on 21/05/21
- Handbook of Drug Administration via Enteral Feeding Tubes. Riluzole. Last updated 15/02/18. Accessed via https://www.medicinescomplete.com/#/content/tubes/c330 on 20/05/21
- NEWT Guidelines. Riluzole. Last updated October 2020. Accessed via https://access.newtguidelines.com/R/Riluzole.html on 20/05/21
- Specialist Pharmacy Service. Riluzole Lactation Safety Information. Last updated 3 August 2020. Accessed via https://www.sps.nhs.uk/medicines/riluzole/ on 10/06/21
- NICE Clinical Knowledge Summaries. Neutropenic sepsis: management. Last revised March 2020. Accessed via https://cks.nice.org.uk/topics/neutropenic-sepsis/management/management/ on 11/06/21

16. Other relevant national guidance

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- Shared Care for Medicines Guidance – A Standard Approach (RMOC). Available from https://www.sps.nhs.uk/articles/rmoc-shared-care-guidance/

- NHSE guidance – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/
- General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care
- NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/

17. Local arrangements for referral

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Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.

To be agreed and completed locally

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 *IMOC* shared care protocol for *Riluzole* for the treatment of *MND,* 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*
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	

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 1 month 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 respond to this request for shared care, in writing, within 14 days of the request being made where possible.

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 SNEE**,** in conjunction with local acute trusts have classified *Riluzole* as a Shared Care drug, 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 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)**	

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