Title: Shared care guideline for Riluzole In Motor Neurone Disease	Salford Royal NHS NHS Foundation Trust University Teaching Trust safe • clean • personal
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Departments/Groups This Document Applies to: Neurology, Pharmacy, Primary Care	
Scope: Neurology and Primary Care	**Classification:** Shared Care Guidelines
Keywords: Riluzole, Neurology, Shared Care	**Replaces Issue No:** New
To be read in conjunction with the following documents: Current Summary of Product characteristics (http://www.medicines.org.uk) BNF	

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Document for Public Display: Y

Required NHSLA Evidence **N**

If this policy is required for NHSLA evidence, then this document must have been checked against the current standards for compliance. If this is not known by the author, confirmation should be sought from the Risk and Health and Safety Department.

Contents

Shared Care Protocol for Riluzole

1. Introduction

Motor Neurone Disease (MND or amyotrophic lateral sclerosis ALS) is a progressive and fatal neurodegenerative disorder with a poor prognosis. Patients experience a gradual loss of muscle function involved in swallowing and breathing. From onset of symptoms 5 year survival is 5 - 15% and median survival time is about 3 years. Riluzole is indicated to extend life or the time to mechanical ventilation in patients with MND.

2. Purpose and Scope

Shared care is an agreement between the GP and the consultant.

This shared care document has been developed to facilitate the safe and appropriate prescribing, supply and monitoring of riluzole in primary and secondary care. It is aimed at all healthcare professionals involved in prescribing, dispensing and monitoring riluzole.

This document must be agreed by SRFT and the patients CCG.

3. Policy statement

This shared care protocol must be adhered to by all medical, nursing, pharmacy and other staff who are involved in the care of patients who are suitable for shared care, as agreed by both the GP and hospital specialist caring for the patient.

4. Monitoring and review

This shared care protocol will be reviewed on a two yearly basis or in the intervening period if new research is published, or changes to the drug license that means an update is required before the two years have passed.

Drug Name & Formulation:	
1. Licensed Indications	Riluzole is indicated to extend life or the time to mechanical ventilation for patients with amyotrophic lateral sclerosis (ALS). Clinical trials have demonstrated that riluzole extends survival for patients with ALS. Survival was defined as patients who were alive, not intubated for mechanical ventilation and tracheotomy-free. There is no evidence that riluzole exerts a therapeutic effect on motor function, lung function, fasciculations, muscle strength and motor symptoms. Riluzole has not been shown to be effective in the late stages of ALS. Safety and efficacy of riluzole has only been studied in ALS. Therefore, should not be used in patients with any other form of motor neurone disease.
2. Therapeutic use & background	Riluzole is currently the only drug licensed for treating MND in the UK. The National Institute for Health and Care Excellence (NICE) has approved its use for MND, so it is available to people who have been diagnosed. In the trials in which Riluzole has shown some benefit, eligible patients were up to 75 years of age, were in a reasonable state of general health, had suffered from the disease for no greater than 5 years and had a forced vital lung capacity of not less than 60% predicted.
3a. Contraindications (please note this does not replace the SPC or BNF and should be read in conjunction with it).	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. Patients who are pregnant or breast-feeding.
3b With caution:	<u>Liver impairment</u>: Riluzole should be prescribed with care in patients with a history of abnormal liver function, or in patients with slightly elevated serum transaminases (ALT/SGPT; AST/SGOT up to 3 times the upper limit of the normal range (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 (see section 4.8). Because of the risk of hepatitis, serum transaminases, including ALT, should be measured before and during therapy with riluzole. ALT should be measured every month during the first 3 months of treatment, every 3 months during the remainder of the first year, and periodically thereafter. ALT levels should be measured more frequently in patients who develop elevated ALT levels.

	Riluzole should be discontinued if the ALT levels increase to 5 times the ULN. There is no experience with dose reduction or rechallenge in patients who have developed an increase of ALT to 5 times ULN. Readministration of riluzole to patients in this situation cannot be recommended. Neutropenia: Patients should be warned to report any febrile illness to their physicians. The report of a febrile illness should prompt physicians to check white blood cell counts and to discontinue riluzole in case of neutropenia. Interstitial lung disease Cases of interstitial lung disease have been reported in patients treated with riluzole, some of them were severe. If respiratory symptoms develop such as dry cough and/or dyspnea, chest radiography should be performed, and in case of findings suggestive of interstitial lung disease (e.g. bilateral diffuse lung opacities), riluzole should be discontinued immediately. In the majority of the reported cases, symptoms resolved after drug discontinuation and symptomatic treatment.
4. Prescribing in pregnancy and lactation	Use in pregnancy and breastfeeding is contraindicated. Clinical experience in pregnancy is lacking and it is not known whether riluzole is excreted in breast milk.

5. Dosage regimen for continuing care	**Route of administration:** Oral administration Although not strictly necessary, side effects such as nausea are less likely if riluzole is taken on an empty stomach (if possible, one hour before or two hours after a meal). It comes in tablet form and should be swallowed whole, but if there are problems swallowing, the tablets may be crushed and mixed with foods to aid swallowing. Riluzole should not be dissolved in water as it does not dissolve well. When crushed, the drug can produce a temporary numbing effect in the mouth. It may be easier to swallow if crushed and mixed with a soft food product such as a puree, yoghurt, ice cream or a thick beverage and eaten in the usual way. Once it is crushed riluzole should be taken immediately due to limited stability problems Please note: tablets should not be crushed in order to feed through a PEG tube as this may block the tubing. If swallowing riluzole becomes particularly problematic, please consult your health care team for advice.	
	Is titration required?	**No**
	Titration guidance: Not applicable	
	Adjunctive treatment regime: Not applicable	
	Conditions which might require dose reduction depending on clinical judgment: No dose reduction is required	
	Usual response time: Riluzole is not a cure, and will not reverse any damage to the motor neurones already present. After 18 months of treatment, it may increase survival by two to four months on average. Those taking riluzole will not be aware of any difference in the symptoms of their MND, but taking this drug may marginally slow down the progression of the disease.	
	Duration of treatment: Treatment will initially be for 12 months, with annual review. Treatment should cease when patients enter the terminal phase of the disease.	
	Treatment to be terminated by: Specialist Consultant or MND specialist nurse	

<table>
<tr><td>6.Drug Interactions

For a comprehensive list consult the BNF or Summary of Product Characteristics</td><td>The following drugs must <u>not</u> be prescribed without consultation with the specialist:
Not applicable</td></tr>
<tr><td></td><td>The following drugs may be prescribed with caution:
In vitro studies using human liver microsomal preparations suggest that CYP 1A2 is the principal isozyme involved in the initial oxidative metabolism of riluzole. Inhibitors of CYP 1A2 (e.g. caffeine, diclofenac, diazepam, nicergoline, clomipramine, imipramine, fluvoxamine, phenacetin, theophylline, amitriptyline and quinolones) could potentially decrease the rate of riluzole elimination, while inducers of CYP 1A2 (e.g. cigarette smoke, charcoal-broiled food, rifampicin and omeprazole) could increase the rate of riluzole elimination.

No drug interactions are listed for riluzole in the BNF.</td></tr>
<tr><td>7. Adverse drug reactions

For a comprehensive list (including rare and very rare adverse effects), or if significance of possible adverse event uncertain, consult Summary of Product Characteristics or BNF</td><td>Specialist to detail below the action to be taken upon occurrence of a particular adverse event as appropriate. Most serious toxicity is seen with long-term use and may therefore present first to GPs.

<table>
<tr><th>Adverse Event</th><th>Action to be taken</th><th>By whom</th></tr>
<tr><td>Interstitial lung disease</td><td>If respiratory symptoms develop such as dry cough and/or dyspnoea, the patient should be referred to the consultant neurologist and chest radiography should be performed. In findings suggestive of interstitial lung disease (e.g. bilateral diffuse lung opacities), riluzole should be discontinued immediately. In the majority of the reported cases, symptoms resolved after drug discontinuation and symptomatic treatment.</td><td>GP</td></tr>
<tr><td>Elevations in liver function tests</td><td>As per monitoring</td><td>GP</td></tr>
<tr><td>Neutropenia</td><td>As per monitoring</td><td>GP</td></tr>
<tr><td>Abdominal symptoms- nausea, diarrhoea, abdominal pain, vomiting</td><td>Symptomatic treatment</td><td>Patient/GP</td></tr>
<tr><td>Headache, dizziness, oral paraesthesia and</td><td>Symptomatic treatment</td><td>Patient/GP</td></tr>
</table>
</td></tr>
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	somnolence				
	Additional guidance / warnings: Patients should be made aware that they need to report any febrile illness.				
8.Baseline investigations	The Consultant will arrange for LFTs and FBC to be done at baseline. The Neurologist will review the patient every 3 months, advise the patient, carers and GP, enquire as to whether FBC and LFT testing are due and supervise other treatments that may be needed (physiotherapy, occupational therapy, speech therapy, dietary advice, gastrostomy, respiratory support).				
9. Ongoing monitoring requirements to be undertaken by GP	**Is monitoring required?**		**Yes or No (if yes complete following section)**		
	Monitoring	**Frequency**	**Results**	**Action**	**By whom**
	Serum trans-aminases	**Monthly for 3 months, 3-monthly for 12 months then annually thereafter.**	**Discuss with Consultant**	**Treatment should be stopped if the ALT rises to five times the upper limit of normal.**	**GP**
	Full Blood Counts	**Monthly during the first 3 months in view of the rare reported cases of neutro-penia**	**Discuss with Consultant**	**Discontinue riluzole in case of neutropenia.**	**GP**

10. Pharmaceutical aspects	This medicinal product does not require any special storage conditions.
11. Secondary care contact information	**If advice is required please contact:** A telephone helpline (0161 206 2920) SRFT MND Specialist Nurses or 08457 626262 (MND Connect) will be accessible to patients, carers, GPs and any other healthcare workers involved in the case to obtain rapid advice on any issues relating to the patient's care.
12. Criteria for shared care	Shared care is an agreement between the GP and the Consultant. This form is a request by the consultant to share the suggested care pathway of your patient. If you are unable to agree to the sharing of care and initiating the suggested medication, please make this known to the consultant within 14 days, ideally stating the nature of your concern.
13. Responsibilities of initiating specialist: Consultant	The Hospital Physician, preferably a Consultant Neurologist with expertise in managing MND patients, will: a) Confirm the diagnosis, if necessary by repeating the examination and tests such as neurophysiology. b) Ensure that the patient fulfils the criteria outlined in the Introduction section c) Check LFTs and FBCs before commencement of treatment d) Give the MND Association Riluzole information sheet to the patient and/or their carers stressing the importance of regular blood test monitoring, the need to report symptoms suggesting neutropenia e.g. fever, sore throat etc, bruising or unexpected bleeding e) Arrange follow up in the MND clinic at SRFT (typically three monthly) f) Provide the initial supply of riluzole – two weeks supply.
14. Responsibilities of the GP	Upon receipt of written confirmation of the diagnosis and the patient's eligibility for treatment, the General Practitioner will: • Monitor the FBC and LFTs at monthly intervals for the first 3 months, then every 3 months during the remainder of the first year and annually thereafter. If there are any abnormalities advice can be sought by ringing 0161 206 2920 or 0161 206 2393. Action as per section nine. • Monitor clinically for symptoms of liver dysfunction (jaundice, pain, bruising, bleeding) or bone marrow suppression (fever, sore throat, bruising bleeding) or respiratory symptoms (as in section seven.) • Prescribe Riluzole 50mg bd after the first two weeks have been provided by secondary care • Continue issuing prescriptions at 3-monthly intervals

15.Responsibilities of District Nurses	Not applicable
16. Responsibilities of the patient	• Attend out-patient and GP appointments • Collect prescriptions • Report any febrile illness, respiratory symtoms to the GP
17. Supporting documentation	Riluzole Summary of Product Characteristics, Sanofi-Aventis 7th July 2009 MND Association Info Sheet No 9. Riluzole version 2 Updated Aug 2013
18. Patient monitoring booklet	Not applicable
19. Shared care agreement form	Attached below

Appendix 1- *PLEASE ADAPT LETTERS AS APPROPRIATE TO DRUG*

Shared Care Agreement Letter

Shared care is an agreement between the GP and the hospital consultant. This form is a request by the consultant to share the suggested pathway of your patient. If you are unable to agree to the sharing of care and continued prescription of the suggested medication, please make this known to the Consultant within 14 days, stating the nature of your concern.

Please contact the consultant within 14 days if you have any concerns or implied consent applies.

(Insert patients name and identifier such as DOB) is being considered for treatment with (insert name of drug).
If this treatment should prove to be successful, the (insert name of drug) would need to be prescribed by yourself when your patient is discharged.
If you have any queries regarding this medication and its administration or if there is any reason why you do not wish this treatment to be undertaken, could you please contact myself, Dr ([insert Dr's Name) or Dr (insert Dr's name)'s secretary within the next fourteen days.
I will be happy to respond to any of your questions at any time.

Please find enclosed the Salford Royal NHS Foundation Trust Shared Care Protocol.

Kind regards

Yours sincerely,

(Insert Consultant's signature) (Insert signature of specialist nurse)

Dr (insert Dr's Name) (Insert name of specialist nurse)
Consultant (Insert Dr's role) (Print role of specilised nurse)

Appendix 2- *PLEASE ADAPT LETTERS AS APPROPRIATE TO DRUG*

Patient Information Letter

Dear (Insert patients name & hospital number),

As you are aware Dr (insert Dr's name) wants you to commence on treatment with (insert name of drug).

Your GP has agreed to prescribe this treatment and so your prescriptions will come from your GP surgery in the usual way.

If you have any queries please contact (insert contact name and details),

Kind regards

Yours sincerely

(Insert Consultant's signature)	(Insert signature of specialist nurse)
Dr (insert Dr's Name) Consultant (Insert Dr's role)	(Insert name of specialist nurse) (Print role of specilised nurse)

Appendix 2- PLEASE ADAPT LETTERS AS APPROPRIATE TO DRUG

Discharge Form for GP
Copy to be given to patient

Dear Dr [insert Doctors name here]

Patient name:[insert Patients name here]
Date of birth: [insert date of birth]
Diagnosis: [insert diagnosis here]

This patient is suitable for treatment with (insert name of drug) for the treatment of (insert name of indication)

This drug has been accepted for Shared Care.

Treatment was started on [insert date started] at a dose of [insert dose]

Further dosing instructions are listed below (include if appropriate, delete sentence if not).

The patient was discharged with [insert number of days of medication] supply of (insert name of drug)

[Insert any monitoring details]

Next review with this department: [insert date]

You will be sent a written summary within 14 days. The medical staff of the department are available at all times to give you advice.

The patient will not be discharged from out-patient follow-up while taking (insert name of drug).

Ongoing prescribing will depend on attendance at clinics as requested by the clinicians.

The Consultant or Specialist Nurse Prescriber is responsible for any dose adjustment.

Thank you.

Yours sincerely,

[insert Specialist signature]

[insert Specialist name and role]

Explanation of Terms Used
NOT APPLICABLE

References
No references used

Endorsed by:		
Name of Lead Clinician/Manager or Committee Chair	**Position of Endorser or Name of Endorsing Committee**	**Date**
Dr Hisham Hamdalla	Consultant Neurologist	March 2014
Dr John Ealing	Consultant Neurologist	March 2014
Dr John MacDonald	Chairman, Medicines Management Group	Jan 2014
Lindsay Harper	Director of Pharmacy	Jan 2014
Claire Vaughan	Head of Medicines Management NHS Salford Clinical Commissioning Group	Jan 2014

Record of Changes to Document - Issue number:				
Changes approved in this document by - Corporate Governance and Risk Management			Date: Jan 2014	
Section Number	Amendment (***shown in bold italics)***	Deletion	Addition	Reason
	The whole document has been re written and transferred to the new template			

Screening Equality Analysis Outcomes (Policies/Procedures)

The Trust is required to ensure that all our policies/procedures meet the requirements of its service users, that it is accessible to all relevant groups and **furthers the aims of the Equality Duty for all protected groups by age, religion/belief, race, disability, sex, sexual orientation, marital status/civil partnership, pregnancy/maternity, gender re-assignment. Due consideration may also be given to carers & socio/economic.**

Have you been trained to carryout this assessment? NO **If 'no' contact Equality Team 62598 for details.**	
Name of policy or document : Shared care guideline for Riluzole In Motor Neurone Disease **Key aims/objectives of policy/document (impact on both staff & service users):** To support the safe prescribing and monitoring of Riluzole in patients with Motor Neurone Disease. The guidelines are intended for use by the Neurology team at Salford Royal NHS Foundation Trust, and any GP who has responsibility for the care of such patients.	
1) a) Whom is this document or policy aimed at?	1a) The neurology team at SRFT and Primary Care Physicians
2) a) Is there any evidence to suggest that your 'end users' have different <u>needs</u> in relation to this policy or document; (e.g.health/employment inequality outcomes) (**NB If you do not have any evidence you should put in section 8 how you will start to review this data)**	2a) No
3) a) Does the document require any decision to be made which could result in some individuals receiving different treatment, care, outcomes to other groups/individuals?	3a) No
b) If yes, on what basis would this decision be made? **(It must be objectively justified)**	3b)
4) a) Have you included where you may need to make reasonable adjustments for disabled users or staff to ensure they receive the same outcomes to other groups ?	4a) Yes

5) a) Have you undertaken any consultation/involvement with service users or other groups in relation to this document?	5a) NHS Salford
b) If yes, what format did this take? face/face or questionnaire? (please provide details of this)	5b) face to face meeting (MMG)
c)Has any amendments been made as a result?	5c) No
6) a) Are you aware of any complaints from service users in relation to this policy?	6a) No
b) If yes, how was the issue resolved? Has this policy been amended as a result?	6b)

7) a) To summarise; is there any evidence to indicate that any groups listed below receive different outcomes in relation to this document?

	Yes		No	unsure
	Positive	Negative*		
Age			No	
Disability			No	
Sex			No	
Race			No	
Religion & Belief			No	
Sexual orientation			No	
Pregnancy & Maternity			No	
Marital status/civil partnership			No	
Gender Reassignment			No	
Carers *1			No	
Socio/economic2**			No	

1: That these two categories are not classed as protected groups under the Equality Act.

2: Care must be taken when giving due consideration to socio/economic group that we do not inadvertently discriminate against groups with protected

characteristics

Negative Impacts

*If any negative impacts have been identified you must either a) state below how you have eliminated these within the policy or b) conduct a full impact assessment:

8) How will the future outcomes of this policy be monitored?

By discussion of feedback at Exec MMG or MMG

9) **If any negative impact has been highlighted by this assessment, you will need to undertake a full equality impact assessment:**

Will this policy require a full impact assessment? No
(if yes please Contact Equality Officer on 206 7204, for further guidance)

High/Medium/Low Type/sign_E Wilson_____
date: 10th Jan 2014