

Shared Care Guideline Riluzole Treatment of Motor Neurone Disease

Dear GP

The information in the shared care guideline has been developed in consultation with Primary Care and it has been agreed that it is suitable for shared care.

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

Contents

1. Introduction Target audience	2
2. Shared Care criteria	2
3. Shared care responsibilities.....	3
3.1. Consultant and /or Specialist Nurse	3
3.2. General Practitioner	3
3.3. Patient responsibility.....	4
3.4. Clinical Commissioning Group	4
4. Indications	4
5. Dose and Administration	4
6. Adverse effects	4
7. Cautions	5
8. Clinical Monitoring.....	6
9. Contraindications.....	6
10. Drug Interactions	6
11. References	7
12. Contact Details.....	7
Appendix 1: Riluzole transfer form: from [Trust] to GP practice	9

1. Introduction Target audience

This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing this drug.

Motor neurone disease (MND) is characterised by progressive degeneration of the motor neurones of the brain, brain stem or spinal cord. Depending on the site of the lesions, characteristic signs may include spasticity, muscle stiffness, brisk or diminished reflexes, muscle wasting and fasciculation, and both flaccid and/or spastic weakness.

It is hypothesised that excessive stimulation of glutamate receptors on neurones may cause or play an important role in the destruction of motor neurones in MND. Glutamate is a neurotransmitter that tends to excite motor neurone cells. In vitro, riluzole inhibits the release of glutamate which decreases firing of motor neurones induced by glutamate receptor agonists protecting cells from glutamate-mediated damage. Riluzole is indicated to extend life or the time to mechanical ventilation for patients with amyotrophic lateral sclerosis (ALS).

Other pharmacological interventions are aimed at providing symptomatic relief for people with MND. Surgical interventions may be necessary and include percutaneous gastrostomy to enable feeding and tracheostomy with or without ventilatory support to aid breathing. A wide range of multidisciplinary health and social services are required for people with MND, particularly in the late stages of the disease. These need to be tailored to suit individual needs.

[NICE technology appraisal 20](#) recommends riluzole for the treatment of patients with the ALS form of MND. Prescribing within NCL is in line with NICE TA20 in that it is initiated by a neurological specialist with expertise in the management of MND..

Indication

To extend life or time to mechanical ventilation for patients with amyotrophic lateral sclerosis (ALS).

The licensed dose of riluzole is 50mg twice daily (no titration is required). Once a patient has been stabilised on treatment (3 months), a shared care arrangement with you will be requested.

It will clarify responsibilities between the specialist and general practitioner (GP) for managing the prescribing of riluzole such as:

- Who will prescribe;
- Who will monitor;
- Any tests required (e.g. blood tests), the exact names/nature of the tests, why they are needed, the frequency of testing, the location in which these will be carried out and action to be taken for any abnormal results;
- Which clinician will be responsible for receipt and review of the results;
- Who will communicate any necessary changes in dose to the patient and the GP;

2. Shared Care criteria

Patients who are stabilised on riluzole (after 3 months) and have been monitored appropriately (as per section 8 – clinical monitoring) at baseline and after initiation of treatment with no problems identified during this period.

3. Shared care responsibilities

3.1. Consultant and /or Specialist Nurse

Send a letter to the GP along with shared care criteria and transfer form requesting shared care for this patient.

- 1) Before initiating treatment, perform baseline liver function tests and ensure riluzole is compatible with the patients current medication at baseline Liver function tests will be measured for at least 3 months in secondary care, before transfer to primary care for ongoing monitoring.
- 2) Discuss the benefits and side effects of treatment with the patient Provide the patient with a patient information leaflet, explain it and ensure that the patient understands the reason for the treatment, and dosing regimen
- 3) Ensure the patient understands that he/she must report the warning symptoms as listed under “adverse effects” (e.g neutropenia and signs/symptoms to look out for).
- 4) Initiate treatment and prescribe until the GP formally agrees to share care (until patient is stabilised). Patients will be seen in clinic prior to consideration of shared care
- 5) Discuss the shared care arrangement with the patient
- 6) Provide results of baseline tests and recommend frequency of monitoring to patient and GP. The consultant must also explain what the recommended tests are, why they are needed and the location in which these tests will be carried out
- 7) Send a letter to the GP after each clinic attendance ensuring current dose, weight, most recent blood results and frequency of monitoring are stated
- 8) Inform GP of blood test results, actions to take in case of abnormal results, and advise the GP on when to adjust the dose, stop treatment, or consult with specialist
- 9) Periodically review the patient’s condition and communicate promptly with the GP when treatment is changed.
- 10) Evaluate adverse effects reported by GP or patient
- 11) Report adverse events to the MHRA (via yellow card scheme) and GP
- 12) Inform GP of patients who do not attend clinic appointments
- 13) Ensure that clear backup arrangements exist for GPs to obtain advice and support (see contact details section)

3.2. General Practitioner

Complete transfer form and send back to *hospital* confirming acceptance/ rejection of shared care for patient. If GP unable to agree to shared care, inform the Hospital team stating reasons within **14 days** of receipt of request. If no response is received within 14 days, the Consultant will assume the GP has accepted shared care.

- 1) Monitor patient’s overall health and well-being
- 2) Prescribe the drug treatment as described (but not to alter the dose unless advised to do so by the specialist). The term “as directed” **SHOULD NOT** be used
- 3) Ensure that the patient understands the dosing
- 4) Ensure the patient understands that he/she must report the warning symptoms as listed under “adverse effects”
- 5) Ensure compatibility with concomitant medication
- 6) Monitor results at recommended frequencies as described under “clinical monitoring” and inform the Consultant if abnormal (as per Section 8 – clinical monitoring).
- 7) Adjust the dose as advised by the specialist (where applicable) and counsel patient on any dose changes

- 8) Report any adverse events and non-compliance to the hospital specialist and the MHRA (via YellowCard), where appropriate
- 9) Stop treatment on advice of specialist or immediately if urgent need arises
- 10) Help in monitoring the progression of disease and inform the hospital team of any changes to medication
- 11) All requests for repeat prescriptions should be reviewed individually prior to issuing

3.3. Patient responsibility

- 1) Attend all hospital and GP appointments
- 2) Take medicines as agreed
- 3) Report to the specialist or GP if he/she does not have a clear understanding of the treatment
- 4) Inform specialist or GP of any other medication being taken, including over-the-counter products
- 5) Report any adverse effects or warning symptoms to GP or specialist
- 6) Inform hospital and GP of any changes in address or telephone numbers

3.4. Clinical Commissioning Group

- 1) To provide feedback to Trusts from the standard letter, via the shared care forum.
- 2) To support GPs to make the decision whether or not to accept clinical responsibility for prescribing.
- 3) To support Trusts in the resolving issues that may arise as a result of shared care.

4. Indications

Riluzole is for the treatment of adults with amyotrophic lateral sclerosis (ALS) form of motor neurone disease

5. Dose and Administration

The licensed dose is 50 mg twice a day

The oral suspension is licensed for administration via an enteral feeding tube.

The film-coated tablets have been crushed and dispersed in water (off-label use) for enteral tube administration however there have been reports of crushed riluzole tablets blocking enteral feeding tubes, therefore if used the tube should be flushed well after use.

Renal impairment: Riluzole is not recommended for use in patients with renal impairment

Hepatic impairment: There is no information available on dose adjustment in patients with hepatic impairment. Caution is advised when prescribing in patients with slightly elevated liver function tests (see "Section 7 – cautions" for more information)

Preparations available

Riluzole 50mg film-coated tablets

Riluzole 5mg/1ml oral suspension

Riluzole (Emylif) 50mg orodispersible tablets

6. Adverse effects

Adverse effect	Frequency	Suggested management by GP
Nausea, abnormal liver function tests, asthenia	Very common (≥1/10)	ALT increases seen in first 3 months are usually transient and return to normal with continued treatment. If ongoing, discuss with specialist; Discontinue treatment

		and refer back if ALT increases are 5 times the upper limit of normal or higher (as per Section 8 – clinical monitoring)
Headache, dizziness, oral paraesthesia, somnolence, tachycardia, diarrhoea, abdominal pain, vomiting	Common (≥1/100 to <1/10)	As per routine management. If ongoing, discuss with specialist
Interstitial lung disease	Uncommon (≥1/1000 to <1/100)	If respiratory symptoms develop such as dry cough and/or dyspnoea, chest radiography should be performed (see section 7 – Cautions for more information)
Anaemia, anaphylactoid reaction, angioedema, pancreatitis	Uncommon (≥1/1000 to <1/100)	As per routine management. If ongoing, discuss with specialist
Febrile illness and/or severe neutropenia	Not known	Early symptoms of severe neutropenia can present as febrile illness. The report of febrile illness should prompt a blood test for FBC to check for neutropenia or decreased white cell count. Severe neutropenia is usually treated in secondary care. Refer to the hospital and discuss with specialist if necessary.
Hepatitis	Not known	As per liver function monitoring (Section 8 – “Clinical Monitoring”)

7. Cautions

Hepatic impairment

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 LFTs (especially elevated bilirubin) should preclude the use of riluzole.

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 annually 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. Re-administration 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 dyspnoea, 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.

Renal impairment

Studies at repeated doses have not been conducted in patients with impaired renal function. If renal function deteriorates during treatment with riluzole, the GP should seek specialist advice.

For a full list of cautions, refer to the Summary of Product Characteristics.

8. Clinical Monitoring

Test	Frequency	Action if out of range
Liver function tests	Monthly for the first three months, 3 monthly for remainder of the 12 months then annually thereafter	If ALT is elevated 3-5 times the upper limit of normal, exclude other causes and recheck LFTs 1 month later; if LFTs remain elevated, discuss with the initiating specialist. If ALT is elevated 5 times the upper limit of normal or higher, stop treatment and refer back to the initiating specialist.
Renal function tests	At least annually unless otherwise indicated	Inform specialist and seek further advice if renal function is impaired (i.e CrCl <60ml/min).

9. 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
- Patients who are pregnant or breast-feeding
- The suspension formulation contains liquid sorbitol (E420) therefore patients with rare hereditary problems of fructose intolerance should not take this.

For a full list of contraindications, refer to the Summary of Product Characteristics.

10. Drug Interactions

There have been no clinical studies to evaluate the interactions of riluzole with other medicinal products. 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.

For a full list of drug interactions, refer to the Summary of Product Characteristics.

11. References

1. Rilutek 50 mg film-coated tablets-Summary of Product Characteristics. Sanofi. accessed via <https://www.medicines.org.uk/emc> on 15/04/2022. Date of last revision of text 01/01/2021;
2. Teglutik 5 mg/ml oral suspension- Summary of Product Characteristics. Martindale Pharma. accessed via <https://www.medicines.org.uk/emc> on 15/04/2022. Date of last revision of text 10/11/2019;
3. BNF. Last updated 04/04/2022. Accessed via <https://bnf.nice.org.uk> on 14/04/2022;
4. NICE Technology appraisal guidance no 20. Guidance on the use of riluzole for the treatment of motor neurone disease. 2001. <https://www.nice.org.uk/guidance/ta20>

12. Contact Details

Hospital: National hospital for Neurosurgery and Neurology (UCLH)

Hospital switchboard:	02034567890
Consultant: Dr Robin Howard Dr Katie Sidle Dr Pietra Fratta Dr Andrea Malaspina Dr Rickie Patani Dr Ross Nortley	Consultants' secretary: 0203 448 3899
Consultant nurse: Jan Clarke and Emma Townsley	Via switchboard
Specialist or Dept Pharmacist: Pharmacy department at NHNN	0203 4483160
Further information and support: MND support number	0203 448 3517

Document control

Date	Version	Amendments
November 2023	Version 2	Share Care produced by UCLH and NCL ICB Barnet borough Medicines Management Team Agreed by NCL Shared Care Group: 14 th November 2023

Appendix 1: Riluzole transfer form: from [Trust] to GP practice

Section A: to be completed by secondary care *Send to practice*

This document is to request the shared care pathway of your patient and comprises an agreement between the GP and named consultant. The patient will continue to be seen by the named consultant as regular follow up.

Fix address label here (ensure NHS no.on)		Clinic stamp or give details below	
Department	<input type="text"/>		
Clinic phone	<input type="text"/>		
Consultant	<input type="text"/>	Email	<input type="text"/>
Indication for prescription	<input type="text"/>		
Drug prescribed	<input type="text"/>		
Date	Drug started <input type="text"/>	Current dose	<input type="text"/>
Relevant conditions	<input type="text"/>		
Monitoring variations	<input type="text"/>		
Date next blood test	<input type="text"/>	Next disease review due in	<input type="text"/> months' time.

Section B: [Accept Shared Care] to be completed by practice *Send back FAO referring consultant above*

The above patient has been accepted into our monitoring service.

Practice date for next blood test

Practice stamp

Signed /
Designation

Date

Section B: [Reject Shared Care] to be completed by practice *Send back FAO referring consultant above*

The above patient has not been accepted into our monitoring service.

Reason

Practice stamp

Signed /
Designation

Date

Section C: Shared Care Agreement (Trust specific information)

This section (and reference to it: Consultant Shared Care Responsibilities point 3) can be removed if all Trusts and CCGs have the same contractual arrangements.

Contact details	
Clinic / service	
Address	
Email	
Telephone	

Contractual details

CCG 1	
No. weeks Trust to prescribe	
Treatment reviews to be conducted by trust (frequency)	

CCG 2	
No. weeks Trust to prescribe	
Treatment reviews to be conducted by trust (frequency)	

CCG 3	
No. weeks Trust to prescribe	
Treatment reviews to be conducted by trust (frequency)	