North Central London
Joint Formulary Committee

Shared Care Guideline
Riluzole
Treatment of Motor Neurone Disease

Dear GP

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of riluzole for patients with the amyotrophic lateral sclerosis form of motor neurone disease (MND) can be shared between the specialist (Consultant neurologist), the patient and you as the patient's general practitioner (GP).

The information in this shared care guideline has been developed in consultation with Primary Care in North Central London (NCL) and it has been agreed that it is suitable for shared care.

Sharing of care assumes effective communication between the specialist (neurologist), GP and patient. The intention to share care should be fully 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.

Introduction

This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing riluzole to patients with amyotrophic lateral sclerosis (ALS).

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 and it is on the UCLH formulary for the above indication. Link to guidance: https://www.nice.org.uk/guidance/ta20.

The licensed dose of riluzole is 50mg twice daily (no titration is required). Once a patient has been stabilised on treatment, a shared care arrangement with you will be requested. The shared care guideline will clarify responsibilities between the specialist and general practitioner (GP) for managing the prescribing of riluzole and will cover the following areas:

1. Who will prescribe.
2. Who will monitor.
3. How often blood tests will be conducted and in which location.
4. Which clinician will be responsible for receipt and review of the results.

Shared Care eligibility criteria

Patients with the AML form of MND who are stabilised on riluzole and who have been monitored appropriately at baseline and after initiation of treatment with no problems identified during this period.

Shared care responsibilities

The Consultant Neurologist and/or Specialist Nurse will:

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

1. Before initiating treatment carry out baseline liver function tests (LFTs).
2. Initiate and optimise (stabilise) treatment with riluzole for at least two months and continue to prescribe until the GP agrees to provide share care through the responsibilities listed below (under "General Practitioner"). Patients will be seen in clinic prior to consideration of shared care.
3. Complete Blueteq form.
4. Discuss the benefits and side effects of riluzole treatment with the patient. Provide the patient with a patient information leaflet (PIL), explain it and ensure that the patient understands the reason for the treatment and dosage regimen.
5. Discuss the shared care arrangement with the patient.
6. Clinically supervise patient by routine clinic follow-ups every 4-6 months and monitor response to treatment. Provide a copy of the current patient care plan for the GP following each clinic visit.
7. Provide results of baseline tests (LFTs) to the GP and recommend the LFT monitoring for the GP. Once shared care has been accepted, LFTs should be monitored as per the SPC for riluzole i.e. every month during the first 3 months of treatment, every 3 months during the remainder of the first year then annually thereafter. Please increase monitoring frequency if patient develops abnormal LFTs.
8. Inform GP, by letter, of clinic visits and action taken for management of patient and tests performed in secondary care.
9. Advise GP following patient review on duration or discontinuation of treatment where necessary
10. Inform GP if any blood tests are taken, actions to take in case of abnormal results, and advise the GP on when to adjust the dose, stop treatment, or consult with specialist. In the event of a recommendation to stop treatment this will be communicated by either a phone call, letter to the GP or by e-mail (if available).
11. Evaluate adverse effects reported by GP or patient.
12. Report adverse events to the MHRA via http://yellowcard.mhra.gov.uk.
13. Ensure that backup advice is available for patient and GP at all time by way of phone and e-mail which will be monitored to ensure responses to queries will be answered within 5 working days.

14. Inform GP of patients who do not attend hospital clinic appointments.

General Practitioner

Complete transfer form and send back to hospital confirming acceptance/ rejection of shared care for patient. If GP is unable to agree to shared care, inform the Hospital team stating reasons within ***14 days*** of receipt of request. If no response is received with 14 days, the Consultant/Specialist Nurse 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. Once shared care has been accepted, LFTS should be monitored as per the SPC for riluzole i.e. every month during the first 3 months of treatment, every 3 months during the remainder of the first year then annually thereafter. Please increase monitoring frequency if patient develops abnormal LFTs.
7. Refer promptly to specialist if the patient develops signs of liver dysfunction.
8. Report all adverse events and non-compliance to the hospital specialist.
9. Stop treatment on advice of specialist or immediately if urgent need arises.
10. Report adverse events to the specialist and MHRA.
11. Help in monitoring the progression of disease and inform the hospital team of any changes to medication (in the context of the disease).
12. All requests for repeat prescriptions should be reviewed individually prior to issuing.

Patient responsibility

1. Attend all hospital and GP appointments.
2. Take riluzole 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.
7. Share any concerns in relation to treatment with riluzole with Consultant neurologist.
8. Have regular monitoring blood tests undertaken according to an agreed programme.
9. Report any changes in disease symptoms to the Consultant Neurologist, motor neurone disease nurse specialist or GP.

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 resolving issues that may arise as a result of shared care.

Indications

Riluzole is indicated to extend life or the time to mechanical ventilation for patients with amyotrophic lateral sclerosis (ALS). This is a licensed indication.

Dose and Administration

The licensed dose is 50mg twice daily.

Riluzole is not recommended for patients with any level of impaired renal function. (See below for hepatic impairment)

Preparations available
Riluzole 50 mg film-coated tablets
Riluzole 5mg/1ml oral suspension

Neither preparation is licensed for administration via enteral feeding tubes however the liquid has been used in practice. The film-coated tablets have been crushed and dispersed in water 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.

Adverse Effects

Very common (≥1/10): Nausea, abnormal liver function tests, asthenia.

Other reported adverse effects are headache, abdominal pain, vomiting, dizziness, tachycardia, somnolence and circumoral paraesthesia.

For a full list of adverse effects, refer to the Summary of Product Characteristics for riluzole.

Serious suspected reactions (even if well recognised or causal link uncertain) should be reported to the Commission on Human Medicines (CHM) via http://yellowcard.mhra.gov.uk.

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 which 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.

Riluzole may cause dizziness and somnolence, if affected patients should not drive or operate machinery.

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

Clinical Monitoring

Possible adverse events should be reported to the GP and consultant neurologist and additional monitoring as required.

LFTs should be monitored monthly for the first 3 months, 3 monthly for 12 months then annually thereafter. Refer promptly to the specialist if the patient develops signs of liver dysfunction.

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.

Acute porphyrias.

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

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.

References

1. Rilutek 50 mg film-coated tablets-Summary of Product Characteristics.Sanofi. accessed via https://www.medicines.org.uk/emc. Date of last revision of text 25/03/2013
2.Teglutik 5 mg/ml oral suspension- Summary of Product Characteristics. Martindale Pharma. accessed via https://www.medicines.org.uk/emc. Date of last revision of text 25/03/2016
3.BNF September 2017. https://www.bnf.org/products/bnf-online/.
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.

Contact Details

UCLH – National Hospital for Neurology and Neurosurgery
Hospital switchboard: 020 3456 7890

Consultants:
Dr Robin Howard
Dr Richard Orrell
Dr Katie Sidle
Dr Pietra Fratta
Dr Sharma

Email: uclh.referrals.mnd.care@nhs.net

Consultants' secretary: Telephone: 0203 448 3517

Motor neurone disease nurse specialist: Jan Clark. Via switchboard.

Pharmacy Department at NHNN: Telephone 020 3448 3160

Document Control		
Date	**Version**	**Action**
October 2018	V1	Share Care produced by UCLH Agreed by NCL Medicines Optimisation Network: 02/10/2018 Ratified by NCL Joint Formulary Committee: 15/10/2018 **Review date: October 2021**

xxx 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 ar 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			
Clinic phone (remove)		Fax	
Consultant		Email	
Indication for prescription			
Drug prescribed			
Date	Drug started		Current dose
Relevant conditions			
Monitoring variations			
Date next blood test		Next disease review due in	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 *Add fax no. below*
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 *Add fax no. below*
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)	