Shared Care Guideline

Riluzole – For the treatment of adult patients with the amyotrophic lateral sclerosis form of motor neurone disease

Executive Summary

- Riluzole is used to extend life or the time to mechanical ventilation for patients with amyotrophic lateral sclerosis (ALS).
- NICE technology appraisal (TA20) issued Jan 2001 recommends that riluzole should be made available for patients with the amyotrophic lateral sclerosis (ALS) form of MND.
- Progressive Bulbar Palsy (PBP) is considered a form of ALS; these patients are eligible for riluzole.
- Riluzole is not licensed for other forms of MND.
- Therapy should be initiated by a neurological specialist with expertise in MND management.
- Recommended daily dose in adults and the elderly is 50 mg twice daily (every 12 hours).
- Riluzole tablets may be crushed (if necessary) immediately prior to administration. A pharmacist will be able to give further advice if necessary.
- GP's should prescribe the drug as outlined in this document and following any other information from the neurology specialist.
- The hospital specialist is responsible for checking full blood counts (FBC's) and liver function tests (LFT's) on commencing treatment.
- The GP is responsible for monitoring FBC's and LFT's as outlined in this document or as otherwise advised by the hospital specialist.
- The GP is responsible for checking that any newly prescribed medication does not interact with riluzole as per this guideline and the SPC.
- Further information regarding riluzole can be found on the manufacturers summary of product characteristics: Rilutek® and Teglutik® or as generic via www.medicines.org.uk
- The responsibilities of the hospital specialist, GP and patient for this Shared Care Guideline can be found within this document on page 5.

Sharing of care depends on communication between the specialist, GP and the patient or their parent/carer. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. The doctor/healthcare professional who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

1. Scope

Prescribing and monitoring by General Practitioners.

2. Aim

To provide advice on safe prescribing and monitoring of riluzole for the treatment of adult patients with the amyotrophic lateral sclerosis form of motor neurone disease.

3. Introduction

- Riluzole is used to extend life or the time to mechanical ventilation for patients with amyotrophic lateral sclerosis (ALS).
- NICE guidance, number 20, issued in January 2001 recommends that riluzole should be made available for the treatment of individuals with the amyotrophic lateral sclerosis (ALS) form of Motor Neurone Disease (MND).
- Riluzole is not licensed for other forms of MND.
- Progressive Bulbar Palsy (PBP) is considered by NICE to be a form of ALS, and is also eligible for treatment with riluzole.
- Riluzole therapy should be initiated by a neurological specialist with expertise in the management of MND. Routine supervision of therapy should be managed as indicated in this shared care guideline.
- Unless there are adverse effects, Riluzole is usually continued life-long, including when a person requires ventilation in the latter stages of the disease. Treatment with Riluzole can be stopped at the request of the person living with MND at any stage.

4. Abbreviations

ALS	Amyotrophic Lateral Sclerosis
MND	Motor Neurone Disease
PBP	Progressive Bulbar Palsy
ULN	Upper Limited of Normal
ALT	Alanine transaminase
FBC	Full Blood Count
LFT	Liver Function Test

5. Dose and Administration

Riluzole is available as 50mg film coated tablets (Rilutek®) and riluzole oral suspension 5mg/mL (Teglutik®) or generic liquid.

Adult dosage

- Recommended daily dose in adults and the elderly is 50 mg twice daily (every 12 hours).
- There is no significant benefit in increasing the dose further.

Special populations

- Children & Adolescents: not recommended due to a lack of safety and efficacy data.
- Impaired renal function: insufficient data to recommend dosage adjustment. Discuss with specialist.
- Abnormal liver function: contra-indicated if transaminases ≥3 x ULN or known liver disease. Use with caution with slightly elevated transaminases with more frequent monitoring.

Where swallowing is impaired

- Riluzole tablets may be crushed (if necessary) immediately prior to administration. A pharmacist will be able to give further advice if necessary.
- If nasogastric (NG) fed, stop the feed, administer the crushed tablet or liquid (mix with 15-30mL of water) administer and flush the tube and re-start the feed.
- Administration of the liquid via the NG or percutaneous endoscopic gastrostomy (PEG) is safe, ensure the tube is flushed with 10mL of water after administration to ensure full dose has been pushed through the line.

6. Adverse Effects

Very common (≥ 1 in 10)

- Asthenia
- Nausea

Common (≥ 1 in 100 and < 1 in 10)

- Headache
- Abdominal pain
- Pain
- Vomiting
- Diarrhoea
- Dizziness
- Tachycardia
- Somnolence
- Oral paraesthesia Oral paraesthesia

Uncommon (≥ 1 in 1000 and < 1 in 100)

- Pancreatitis
- Anaemia

Rare (≥ 1 in 10000 and < 1 in 1000)

- Neutropenia (rare)
- Hepatitis (very rare)
- Interstitial lung disease

7. Cautions

- History of abnormal liver function or slightly elevated serum transaminases up to 3 x ULN.
- Ability to drive may be affected, due to dizziness/vertigo.
- Febrile illness/neutropenia.

8. Contraindications

- Hepatic disease or where baseline transaminase are > 3 x ULN.
- Patients with baseline elevations of **several** liver-related biochemical parameters (especially bilirubin)
- interstitial lung disease
- patients who are pregnant
- breastfeeding
- Where there is known hypersensitivity to riluzole or any of the tablet excipients.

9. Interactions

No clinical studies have been done to evaluate the interactions of riluzole. Potential interactions may occur with:

Enzyme Inhibitors – may decrease the rate of riluzole elimination.

- Caffeine
- Diclofenac
- Diazepam
- Theophylline
- **Tricyclic antidepressants**
  - Amitriptyline, imipramine, clomipramine etc…
- **Macrolides**
  - Erythromycin, clarithromycin etc…
- **Quinolones**
  - Ciprofloxacin, ofloxacin, norfloxacin etc…
- Fluvoxamine
- Nicergoline
- Phenacetin

Enzyme Inducers – may increase rate of riluzole elimination.

- Rifampicin
- Omeprazole
- Chronic smoking/ cigarette use

Further information about dose and administration, adverse effects, cautions, contraindications and interactions can be found in the Summary of Product Characteristics Rilutek® *and* Teglutik® *or* www.medicines.org.uk

10. Monitoring Standards & Actions to take in the event of abnormal test results/symptoms

Pre initiation of therapy (baseline):

Parameter	Responsibility for monitoring
Full blood count (particularly WBC counts) and serum transaminases including ALT.	Hospital specialist

During therapy:

GPs are responsible for the monitoring below and should take action as indicated. They should contact the hospital specialist to discuss any concerns.

Full Blood Count (with differential) – to be checked monthly for first 3 months then 6 monthly unless clinical indication/concern.

Liver Function Tests – to be checked monthly for 3 months then 3 monthly for remainder of first year. 6 monthly thereafter unless clinical indication/concern ion/concern.

Test	Action in response to abnormal result
WBC < 3.60 x 10^9/L (or below lower limit of local reference range)	Seek guidance from neurologist if WBC count falls below normal range and no clinical evidence of sepsis following initiation of riluzole. **If clinical evidence of febrile illness/neutropenia, patient should seek immediate medical attention and riluzole stopped.**
PLT count < 160 x 10^9/L (or below lower limit of local reference range)	Seek appropriate guidance using professional clinical judgment from neurologist or other specialist (e.g. haematologist) if PLT count falls below normal range following initiation of riluzole.
Lymphocyte count < 1.10 x 10^9/L (or below lower limit of local reference range)	Seek appropriate guidance from neurologist if Lymphocyte count falls below normal range and no clinical evidence of sepsis following initiation or riluzole.
Neutrophil count < 1.50 x 10^9/L (or below lower limit of local reference range)	If evidence of neutropenia (i.e. Neutrophil count falls below normal range following the initiation of riluzole), riluzole should be discontinued and the hospital specialist contacted.
ALT > 40 U/L (or above upper limit of local reference range)	Riluzole should be discontinued if, during treatment, ALT levels increase to five times the upper limit of the appropriate normal range (ULN). Where this occurs, re-administration of riluzole is not recommended and the hospital specialist should be contacted.

11. Shared Care Responsibilities

a. Hospital specialist:

The decision to start riluzole will be made by the appropriate hospital department. A copy of the shared care guidelines will be sent to the GP. If the GP has any queries about the prescribing or monitoring of riluzole, they should contact the relevant hospital specialist as soon as possible.

- Send a letter to the GP requesting shared care for the patient.
- Routine clinic follow-up on a regular basis.
- Inform the GP after each clinic attendance if there is any change to treatment or monitoring.
- Evaluation of any reported adverse effects by GP or patient.
- Inform GP of patients who do not attend clinic appointments and advice regarding arrangements for further follow up.
- To provide any advice to the patient/carer when requested.
- Ensure that backup advice is available at all times.

b. General Practitioner:

- Agreement to shared care guideline by the GP.
- Report any adverse events to the hospital specialist, where appropriate.
- Request advice from the hospital specialist when necessary.
- Prescribe the drug treatment as described.
- Monitor blood results (FBC, creatinine and electrolytes and LFTs) in line with recommendations from hospital specialist.
- Be available to assess the patient taking riluzole when clinically required and liaise with hospital specialist appropriately as part of shared care.

c. Patient or parent/carer:

- Report to the hospital specialist or GP as appropriateif they do not have a clear understanding of their treatment - GP to contact Hospital Specialist for support and guidance as appropriate.
- Patients must not exceed the recommended dose.
- Patients must attend their scheduled clinic and blood test appointments (where relevant).
- Must inform other clinical staff that they are receiving treatment.
- Report any adverse effects to the hospital specialist or GP.
- Check that where possible the specialists have provided a patient-held record or information sheet for monitoring and/ or to alert other clinical staff to the treatment they are receiving.
- Share any concerns they have in relation to treatment with riluzole.
- Participate in the monitoring of therapy and the assessment of outcomes, to assist health professionals to provide effective, safe, appropriate treatment.
- To seek appropriate attention if any concerns
- To report any episode of suspected infection

12. Contact numbers for advice and support

Cambridge University Hospitals NHS Foundation Trust

Specialist	Post	Telephone
Dr Rhys Roberts	Consultant Neurologist	01223 274261
Neurology SpR	Registrar	01223 245151 via switchboard
Victoria Edwards / Louise Boardman	MND Care Co-ordinators	01223 216631
Medicines Information Department	Medicines Information Pharmacist/Technician	01223 217502

North West Anglia NHS Foundation Trust

Specialist	Post	Telephone
Dr Dirk Baumer	Consultant Neurologist	01733 673549

13. Monitoring compliance with and the effectiveness of this document

Neurology will continue to monitor feedback from GPs with regard to the guideline and the use of the drug on a regular basis (normally yearly) and make changes as appropriate.

14. Equality and Diversity Statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service Equality and Diversity statement.

15. Disclaimer

It is **your** responsibility to check against the electronic library that this printed out copy is the most recent issue of this document.

16. Document Management

Ratification Process	Details
Authored by:	Cambridge University Hospitals NHS Foundation Trust
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The information contained in this guideline is issued on the understanding that it is accurate based on the resources at the time of issue. For further information please refer to the most recent Summary of Product Characteristics Rilutek® and Teglutik® or www.medicines.org.uk

Shared Care Guideline Title - Template Letter

{GP ADDRESS}

Dear Dr,

{PATIENT DETAILS}

Your patient was seen on ***{Insert date}*** with a diagnosis of ***{Insert diagnosis}***. He/she has the amyotrophic lateral sclerosis form of motor neurone disease. I have therefore initiated riluzole and am writing to ask you to participate in the shared care for this patient.

This medication and indication has been accepted as suitable for shared care by the Cambridgeshire and Peterborough Integrated Care System. I agree to the secondary care responsibilities set out in the shared care agreement for this medication. I am therefore requesting your agreement to share the care of this patient.

Medication name:	**Riluzole**
Current dose:	50mg twice daily
Date medication started:	{Insert date}
Date after which GP to start prescribing:	{Insert date}[1]

{Insert if applicable - Last bloods were taken on {Insert date} and these show {Insert blood test details} within the normal range. The latest results are attached below.}

{Insert if applicable - The dose has been titrated and is stable.}

I confirm I have explained to the patient: the risks and benefits of treatment, the baseline tests conducted and the need for monitoring, how monitoring will be arranged, and the roles of the consultant/nurse specialist, GP and the patient in shared care.

I confirm the patient has understood and is satisfied with this shared care arrangement.

Yours sincerely

{Consultant name}

[1]This should be the date when the last prescription was issued. It is expected that patients will request a repeat prescription sometime after this date.