NORFOLK AND WAVENEY STP THERAPEUTICS ADVISORY GROUP (TAG)

SHARED CARE AGREEMENT FRAMEWORK

Shared care guidelines - Riluzole for patients with amyotrophic lateral sclerosis (ALS)

Monitoring Level 0 - Prescribe the drug and perform a basic level of monitoring, e.g., a standard annual review

Drug Infromation	
Riluzole, available as tablet, oral suspension and orodispersible film Please see Netformulary for further guidance	
Indications for shared care	
Licensed indication: to extend life or the time to mechanical ventilation for patients with amyotrophic lateral sclerosis (ALS).	
Specialist Prescribing and Monitoring Responsibilities	**GP / Community Team - Primary Care Prescribing and Monitoring Responsibilities**
• Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol 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 to enable the patient to reach an informed decision. Obtain and document patient consent. Provide an appropriate patient information leaflet. • Assess for contraindications, cautions and interactions • Conduct required baseline investigations and monitoring • Initiate treatment. 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 • 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 and communicate the results to primary care. • Reassume prescribing responsibilities if a woman becomes or wishes to become pregnant. • Provide advice to primary care on management of adverse effects • Advise primary care if treatment to be discontinued	• Accept shared care request and prescribe ongoing treatment as detailed in the specialist request, taking into any account potential drug interactions. • Supporting specialists in monitoring hepatic function and blood count monitoring by providing phlebotomy services as described under **Specialist monitoring** below • Manage adverse effects 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 Information

- 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. Keep contact details up to date. Be aware that medicines may be stopped if they do not attend.
- 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. Inform the specialist or GP immediately if they become pregnant or wish to become pregnant.

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.

Patients are routinely seen following diagnosis by one of the Neurology Specialist Nurses who provide further explanations about the drug, including symptoms to recognise and report such as fever (which may indicate the need to check the white cell count), dizziness and somnolence, particularly in relation to driving.

The Neurology Specialist Nurses supervise the clinical care of the patient and refer to other members of the multidisciplinary health care team, including physiotherapists, speech and language therapists, dieticians, occupational therapists, gastroenterology and respiratory medicine according to the needs of the patient. NeurologySpecialistNurses@nnuh.nhs.uk

Specialist Contact Details

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GENERAL PRINCIPLES FOR SHARED CARE PRESCRIBING

- Shared Care is only appropriate if it provides the optimum solution for the patient.
- GPs are **invited** to participate. If GPs are not confident to undertake these roles, they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.
- **If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable if they are unwilling to do so.**
- Prescribing responsibility will only be transferred when it is agreed by the consultant and the patient's GP and when the patient's condition is stable or predictable.
- Safe prescribing must be accompanied by effective monitoring.
- **The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.**

Background to Treatment

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.

Licensed use and agreed local off-label use

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

Following diagnosis of MND by an appropriate neurological specialist, treatment should be initiated by the specialist, if it is deemed to be clinically appropriate. Following an initial period of 3 months, continued prescription of riluzole may then be undertaken by the general practitioner in a shared-care arrangement with the specialist

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

Criteria for Patient Selection

Clinical diagnosis of motor neurone disease (limb-onset and bulbar-onset forms) made by neurologist with appropriate investigations including neurophysiology.

Form and strength of preparation

See link to BNF/SPC for available preparations

- Tablets
- Oral suspension
- Orodispersible film

Side Effects and Management

Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme.

Visit www.mhra.gov.uk/yellowcard

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.

Drug Interactions

- Link to BNF
- Link to SPC

Cautions and 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).

Initiation of therapy

- Initiation of therapy should be by a neurological specialist with expertise in the diagnosis and management of MND. In most situations this would be a neurologist.

- Transfer of 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.

Initial dose and method of administration and supply

Usual dose - 50mg twice daily.

Conditions requiring dose adjustment - None

Route of administration – Oral

Available formulations – tablets, oral suspension, orodispersible tablet

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.

Patients should be warned about the potential for dizziness or vertigo and advised not to drive or operate machinery if these symptoms occur.

Maintenance Dose and Administration

The initial maintenance dose must be prescribed by the initiating specialist

Duration of therapy / How the treatment will be reviewed and if appropriate, stopped

In the latter stages of the disease patients may wish to review the continued use of riluzole and they should be provided with the opportunity to discontinue treatment, if after discussion with the responsible clinician, they consider it appropriate.

Specialist monitoring responsibilities

Monitoring 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 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:
Baseline blood tests (liver function and full blood count) before initiation of treatment with riluzole.

On-going monitoring:
Regular blood testing is recommended to monitor hepatic function and blood count – every month for 3 months, then every 3 months for a further 9 months and annually thereafter. More frequent monitoring is advised if the hepatic function is found to be abnormal.

Riluzole should be discontinued in the presence of neutropenia or if the ALT level increases to more than 5 times the upper limit of normal.

Revised arrangements related to monitoring responsibility (May 2013):
Because patients taking riluzole are often debilitated, it has been agreed that blood forms will be issued by the Hospital Trust and that the results will go back to the specialists for monitoring. This applies to the first 3 months of tests and also all tests thereafter. The phlebotomy service should be provided within Primary Care, as may the prescribing of the medication, but the monitoring and issue of the blood test forms should remain within secondary care.

The specialist will continue to be responsible for monitoring the clinical progression of the disease.

GP / Community Team or other Primary Care monitoring responsibilities

Supporting specialists in monitoring hepatic function and blood count monitoring by providing phlebotomy services as described under **Specialist monitoring** above.

Consultant / Specialist prescribing responsibilities

- Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol 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 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 and interactions
- Conduct required baseline investigations and monitoring
- Initiate treatment. 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
- 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 and communicate the results to primary care.
- 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.

GP prescribing responsibilities

- Accept shared care request and prescribe ongoing treatment as detailed in the specialists request, taking into any account potential drug interactions.

- Manage adverse effects 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.

Indications for referral back to Specialist

None expected other than clinical signs of adverse reactions assessed as being attributed to treatment with riluzole

Pregnancy, paternal exposure and breast feeding

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

Further information and supporting documents

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

Resources used by RMOC in development of SCA:

- 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

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Document history:

Version	Date	Author / Editor	Status	Comment
1.	July 2007	Dr Jeffrey Cochius, Consultant Neurologist, NNUH / Fiona Marshall TAG Lead Pharmacist	Superseded	Due for review July 2009
2.	Nov 2009	Dr Jeffrey Cochius, Consultant Neurologist, NNUH / Fiona Marshall TAG Lead Pharmacist	Superseded	No changes from July 2007. Supported by the TAG.
3.	May 2013	Dr Jeffrey Cochius, Consultant Neurologist,	Superseded	Changes to November 2009 version discussed in TAG

		NNUH / Fiona Marshall TAG Lead Pharmacist		meetings from November 2012 to May 2013. On-going monitoring responsibility regarding hepatic function and haematology returned to neurology specialists. Phlebotomy services to be provided by primary care. Agreement confirmed by NNUH Neurology Specialist Nurses at May 2013 TAG meeting. Supported by the N&W Drugs & Therapeutics Commissioning Group May 2013
4.0	June 2015	Dr Jeffrey Cochius, Consultant Neurologist, NNUH / Fiona Marshall TAG Lead Pharmacist, NEL CSU (Anglia)	Draft	Due for review May 2015. Modified in line with current TAG SCA template. Sent via NNUH Pharmacy for author review and any recommendations for update. Discussed at the July 2015. NNUH reported that most prescribing of riluzole is undertaken by NNUH Neurology Nurse Specialists therefore continued need for the SCA is questionable. Check with NNUH nurse specialists.
4.1	Aug 2015	As per 4.0	Draft	ePACT data indicates continued prescribing of riluzole across all N&W CCGs – therefore SCA still required. No direct feedback on the content of the SCA received from the NNUH neurologists. Revised draft e-mailed to recently acquired nurse specialist contacts.
4.2	Sep 2015	Dr Jeffrey Cochius, Consultant Neurologist and Clinical Director of Neurology, and Neurology Nurse Specialists (NNUH) - Praseeda Aju, Esther Cockram, Rachael Rendell and Felicity Roberts.	Final	Feedback from the Consultant Neurologist and Neurology Specialist Nurses (NNUH) did not indicate any issues with the content of the shared care agreement. Neurology nurse specialists explained that raising monitoring forms occurs in a number of ways, depending on the patients' circumstances. Monitoring

				responsibility remains with the specialists. The TAG agreed to continue use of the share care agreement to facilitate prescribing responsibility for riluzole to pass from specialists to GPs after an initial 3 month period.
5.0	Dec 2017	As for 4.2 plus Dr Dick and Dr Rafiq	Draft for consultation	Need for review highlighted by Helen Copsey, NNUH MND CRN Coordinator. Oral suspension added to available formulations. Reviewed by FM and updated in line with current BNF (side effects, cautions and interactions) – hyperlinks added. Sent to NNUH for consideration.
5.1	Dec 2017	As per 5.0 minus Praseeda Aju and Bronnie Roper, plus Debbie Davey & Helen Copsey	Draft	Neurology Nurse Specialists updated. MND Care and Research Network Coordinator contact details added
5.	Jan 2018	As for 5.1	Final	Supported by the TAG and the N&W D&TCG
6.0	Aug 2021	Jen Carroll, TAG Lead Technician	FINAL	Discussed at August 2021 TAG meeting. Review dates extended for a year from meeting due to covid pressures
7.0	Feb 2023	Jen Carroll, TAG Lead Technician	Draft	Existing local SCA merged with RMOC SCA guidance
7.1	April 2023	Jen Carroll, TAG Lead Technician	Final	Updated to reflect existing local monitoring. Supported by the TAG, D+TC and Planned Care Meds Management Group
7.2	July 2023	Jen Carroll, TAG Lead Technician	Final	Updated to include new orodispersible formulation that will be available from mid-July