Humber Area Prescribing Committee

SHARED CARE FRAMEWORK for Riluzole

HUMBER AREA PRESCRIBING COMMITTEE

DATE APPROVED BY APC: 10/06/24

REVIEW DATE: JUNE 2027

PATIENT NAME	*NHS NUMBER*	*DATE OF BIRTH*
ADDRESS		
GP'S NAME		

We agree to treat this patient within this Prescribing Framework

Specialist Prescriber's Name…… Date:……

Specialist Prescriber's Signature……

Professional register name and registration number ……..

Consultant's name (if working under direction of Consultant) ……

Speciality/Department:……..

Primary care prescriber's name: …… Date:……

Primary care prescriber's Signature ……..... ……

Professional register name and registration number:……

If the Primary Care Prescriber is unable to accept prescribing responsibility for the above patient the Specialist Prescriber should be informed within two weeks of receipt of this framework and Specialist Prescriber letter. In such cases the Primary care Prescriber are requested to update the Specialist Prescriber, by letter, of any relevant changes in the patient's medication / medical condition.

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Shared Care Framework for *Riluzole for Amylotrophic Lateral Sclerosis*

Specialist responsibilities

- Diagnose the patient according to national criteria; ensure that this diagnosis is communicated to primary care.
- Discuss the benefits and risks of the treatment with the patient and provide the appropriate counselling, to enable the patient to reach an informed decision. Provide a patient information leaflet.
- Assess for contraindications, cautions and interactions.
- Conduct required baseline investigations and initial monitoring as detailed in section 8
- Initiate and optimise treatment as outlined in section 6.
- Prescribe the maintenance treatment for at least 12 weeks and until optimised.
- Once treatment is optimised, complete the shared care documentation and send to patient's GP detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required.
- Prescribe sufficient medication to enable transfer to primary care.
- Conduct the required annual reviews and monitoring detailed in specialist section 8
- Review treatment 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.

Primary care responsibilities

- Respond to the request from the specialist for shared care in writing within 14 days.
- If shared care is accepted, prescribe ongoing treatment as detailed in the specialist's request and as per section 6, taking into any account potential drug interactions in section 10.
- Adjust the dose of riluzole prescribed as advised by the specialist.
- Conduct the required monitoring as outlined in section 9.
- Assess for possible interactions with riluzole when starting new medicines (see section 9)
- Manage any adverse effects as detailed in section 11 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 arrange for chest x-ray if the patient experiences symptoms such as dyspnoea or dry cough
- Stop riluzole and make an urgent referral to the specialist if ALT rises to more than 5 times the Upper limit of normal (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 responsibilities

- Take riluzole as prescribed, and avoid abrupt withdrawal unless advised by GP or specialist.
- Attend regularly for monitoring and review appointments with primary care and specialist.
- Report adverse effects to their GP. Seek immediate medical attention if they develop any symptoms as detailed in section 11, particularly if signs of febrile illness
- Report the use of any over the counter medications to their GP 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.
- Women of child-bearing potential should inform the specialist or GP immediately if they become pregnant or wish to become pregnant.

1. Introduction:	The term 'Motor Neurone Disease' is used to describe variants of the disease - namely progressive muscular atrophy (PMA) and amyotrophic lateral sclerosis (ALS). ALS, which is characterised by both upper and lower motor neurone signs, is the most common form of MND, accounting for 65% to 85% of all cases. Adult-onset MND usually starts with symptoms and signs including stumbling, foot drop, weakened grip, slurred speech, cramp, muscle wasting, twitching and tiredness. Other symptoms of MND include muscle stiffness, paralysis, in-coordination and impaired speech, swallowing and breathing. Most individuals die from ventilatory failure, resulting from progressive weakness and wasting of limb, respiratory and bulbar muscles within approximately 3 years of the onset of symptoms. The incidence of ALS ranges from 1.8 to 2.2 per 100,000 population and prevalence ranges from 4.0 to 4.7 per 100,000 population in UK. Therefore, at any one time about 2000 individuals per year in England and Wales are affected by ALS. Four randomised controlled trials (including a number of UK centres) in patients who fall within the diagnostic category of ALS have compared riluzole with placebo (a total of 1477 individuals). All trials used tracheotomy-free survival as a primary outcome. All four of the trials identified and reported riluzole to be associated with a relative reduction in hazard ratio for tracheotomy-free survival at 18 months of 17% (i.e. hazard ratio of 0.88, 95% CI: 0.75-1.02). The National Institute for Health and Clinical Excellence (NICE) produced guidance on the use of riluzole in January 2001 (TAG No. 20) which recommended use in patients with the ALS form of MND. The guidelines should be read in conjunction with the general guidance on prescribing matters given in EL (91) 127 “Responsibility for prescribing between hospitals and GPs”.

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2. Indication:	Riluzole is recommended for the treatment of individuals with the amyotrophic lateral sclerosis (ALS) form of Motor Neurone Disease (MND). Riluzole is currently the only drug licensed for treating ALS in the UK	
3. Licensing Information	Riluzole tablets are licensed to be swallowed whole. Crushing tablets is an unlicensed use of a licensed medicine. Riluzole liquid (Teglutik) is licensed for oral administration as well as via feeding tubes. Riluzole orodispersible films are licensed for oral use only.	
4. Pharmaceutical Information	Route	Oral including administration via feeding tubes
	Formulation	Generic riluzole 50mg tablets – these are the preferred formulation Teglutik® riluzole 5mg/ml suspension 50mg orodispersible film
	Administration details	**Oral administration:** • Tablets should be swallowed whole • Riluzole suspension (Teglutik™) is licensed orally for patients with ALS. Please discuss with the MND team before switching to the liquid formulation. • If needed, the riluzole tablets may be crushed and mixed with soft food such as yoghurt or puree. They should be administered within fifteen minutes. The crushed tablets may have a local anaesthetic effect in the mouth. It should also be noted that absorption may be affected by fatty food. This is an unlicensed use of a licensed medication • Orodispersible film should only be handled with clean dry hands, and should not be folded. Orodispersible film should not be taken with liquids, or chewed. Patients should not talk while the film dissolves and food should be taken with caution after administration due to local anaesthetic effect. Wash hands after administration. For administration via feeding tubes: • The manufacturers of riluzole oral suspension (Teglutik™) advise that it can be administered through an enteral feeding tube. This is a licensed use of a licensed medicine • The manufacturer of Rilutek® brand has anecdotal reports that the tablets can be crushed and mixed with water. The 'resulting suspension' should be administered within 15 minutes for enteral administration. This is an unlicensed use of a licensed medication

		• Administration of riluzole through enteral tubes will have to be a clinical decision on an individual basis. There have been reports of crushed riluzole tablet suspension blocking enteral feeding tubes, so ensure the tube is flushed with at least 30mls sterile water after administration
	Additional information	**Patients with dysphagia (swallowing difficulties)** Please contact the MND specialists should the patient become dysphagic and subsequently unable to swallow tablets.
5. Supporting evidence	TA20 Guidance on the use of Riluzole (Rilutek) for the treatment of Motor Neurone Disease NG 42 - Motor neurone disease: assessment and management	
6. Initiation and ongoing dosage regimen	Transfer of monitoring and prescribing to primary care is normally after at least 12 weeks, and when the patient's dose has been optimised 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. **Usual dose:** 50mg twice daily The initial maintenance dose must be prescribed by the initiating specialist. **Conditions requiring dose adjustment:** None	
7. Contraindications and Warnings:	Please see SPC for comprehensive information. **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, or with 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. • Renal Impairment (due to lack of data).
8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist	Monitoring at baseline and during initiation 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 and monitoring be transferred to the GP. **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:** LFTs, including alanine aminotransferase (ALT), should be measured every month during the first 3 months of treatment, every 3 months during the remainder of the first year, or until transferred to primary care. FBC and WCC every month during the first 3 months of treatment and every 3 months during the remainder of the first year until transferred to primary care. **Ongoing monitoring:** Routine review to assess effectiveness and ongoing appropriateness of treatment every 6 months, or as clinically indicated. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.
	Monitoring | Frequency

9. Ongoing monitoring requirements to be undertaken by primary care	LFTs, FBC & WCC	Every month during the first 3 months of treatment, then every 3 months for the remainder of the first year. NB: where monthly or quarterly monitoring is performed in secondary care prior to transfer, there is no need to repeat individual tests. Annually after the first year.
10. Interactions	The following drugs are known or suspected interactions and the GP may wish to discuss with the initiating specialist before commencing:	
	Interacting Drug	Advice
	Riluzole is metabolised by cytochrome P450 isoform 1A2 (CYP1A2), and has the potential to interact with drugs which inhibit or induce CYP1A2. The clinical relevance of these interactions has not been established, and some of these medicines are frequently used with riluzole without incident. Discuss with specialist team if there are any concerns. CYP1A2 inhibitors include caffeine, diclofenac, diazepam, clomipramine, imipramine, fluvoxamine, phenacetin, theophylline, amitriptyline, quinolones (e.g. ciprofloxacin), mexiletine, nicergoline, rucaparib, vemurafenib, combined hormonal contraceptives CYP1A2 inducers include cigarette smoke, charcoal-grilled food, rifampicin, omeprazole	
	Other interacting agents: nil know *If immunosuppressant include vaccines info here* **For full list see SPC at www.medicines.org.uk/emc and BNF**	
11. Adverse effects and management	Adverse effects	Action for GP
	Altered LFTs: Elevated up to 5 times ULN	Continue riluzole and discuss with specialist. Increase monitoring frequency if ALT is elevated
	ALT greater than 5 time ULN	Stop riluzole and inform specialist. Riluzole should not be restarted
	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 (Neutrophil<2.0)	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 (WCC <3.5)	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.
	The most commonly reported adverse reactions were: • **GI disturbance** – nausea, diarrhoea, abdominal pain and vomiting. • **Abnormal liver function tests** - increased alanine aminotransferase usually appears within 3 months after the start of therapy with riluzole; they are usually transient and levels return to below twice the ULN after 2 to 6 months while treatment was continued. These increases could be associated with jaundice. • **Headache, oral paraesthesia, somnolence, tachycardia and asthenia** Other adverse effects include • **Anaemia** **Dizziness and Vertigo –** patients should be advised if affected not to drive or operating machinery	
12. Advice to patients and carers The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.	**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. <u>Patient information</u> • MND association riluzole information leaflet https://www.mndassociation.org/app/uploads/2015/07/5A-Riluzole.pdf	

	• NHS.uk. Low white blood cell count https://www.nhs.uk/conditions/low-white-blood-cell-count/
13. Preconception, 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 GP and the specialist.	**Preconception** If a patient on riluzole is planning a pregnancy the specialist service should be informed. **Pregnancy:** Riluzole in contraindicated in pregnancy due to lack of data on pregnancy **Breastfeeding:** Riluzole is contraindicated in breast-feeding women. Very limited published evidence indicates low levels in breast milk. **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.
14. Specialist contact information	Name: *Dr Nandakumar or other consultant neurologist as specified in clinic letter* Role and specialty: *Consultant Neurologist* Daytime telephone number: *via HUTH switchboard (01482 875875) or details as per clinic letter* Email address: *as per clinic letter.* Alternative contact: Motor Neurone Disease Specialist Nurse (Hull and East Riding CCG patients only) – Vanessa Baker (01482) 816781 Neurology Specialist Pharmacist: Priscilla Kanyoka priscilla.kanyoka1@nhs.net Interface Pharmacist: Jane Morgan 01482 461519 or jane.morgan14@nhs.net Out of hours contact details: *contact oncall registrar or consultant for neurology via switchboard (01482 875875)*
15. Local arrangements for referral Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.	For urgent enquiries contact on call neurologist via switchboard. Advice and guidance can be sought via A&G portal for non-urgent enquiries.
16. To be read in conjunction with the following documents	• Shared Care for Medicines Guidance – A Standard Approach (RMOC). Available from https://www.sps.nhs.uk/articles/rmoc-shared-care-guidance/ • NHSE guidance – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/

	• General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/good-practice-in-prescribing-and-managing-medicines-and-devices/shared-care • NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/.
17. **References**	1. MND Association accessed via: https://www.mndassociation.org/about-mnd/what-is-mnd/basic-facts-about-mnd/ on 12/10/23. 2. MND Scotland accessed via https://www.mndscotland.org.uk/ 12/10/23. 3. British National Formulary. Riluzole. Accessed via https://bnf.nice.org.uk/drug/riluzole.html on 12/10/23. 4. 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 12/10/23. 5. NICE NG42: Motor neurone disease: assessment and management. Last updated July 2019. Accessed via https://www.nice.org.uk/guidance/ng42 on 12/10/23. 6. Rilutek 50 mg film-coated tablets. Sanofi. Date of revision of the text 12/04/23. Accessed via https://www.medicines.org.uk/emc/product/1101/smpc on 12/10/23. 7. Riluzole 50 mg film coated tablets. Glenmark Pharmaceuticals. Date of revision of the text 11/01/23. Accessed via https://www.medicines.org.uk/emc/product/10060/smpc on 12/10/23. 8. 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. 9. Teglutik 5 mg/ml oral suspension. Martindale Pharma. Date of revision of the text 10/11/2019. Accessed via https://www.medicines.org.uk/emc/product/5060/smpc on 12/10/23. 10. Emylif 50 mg orodispersible film. Zambon UK. Date of revision of the text April 2023. Accessed via https://www.medicines.org.uk/emc/product/14754/smpc on 12/10/23. 11. Handbook of Drug Administration via Enteral Feeding Tubes. Riluzole. Last updated 10/10/23. Accessed via https://www.medicinescomplete.com/#/content/tubes/c330 on 12/10/23.

12. NEWT Guidelines. Riluzole. Last updated October 2020. Accessed via https://access.newtguidelines.com/R/Riluzole.html on 12/10/23.
13. Specialist Pharmacy Service. Riluzole Lactation Safety Information. Last updated 3 August 2020. Accessed via https://www.sps.nhs.uk/medicines/riluzole/ on 12/10/23.
14. NICE Clinical Knowledge Summaries. Neutropenic sepsis: management. Last revised March 2020. Accessed via https://cks.nice.org.uk/topics/neutropenic-sepsis/management/management/ on 12/10/23.

Document and version control	**This information is not inclusive of all prescribing information and potential adverse effects. Please refer to the SPC (data sheet) or BNF for further prescribing information.**		
	Date approved by Guidelines and SCF Group:		15/05/2024
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Version number	Author	Job title	Revision description:
1	Jane Morgan	Principal Pharmacist HUTH	New document – current document approved by both APCs transferred to new template and merged with additional information from RMOC draft document
2	Jane Morgan	Principal Pharmacist	Updated with RDTC document – addition of orodispersible films