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Royal Cornwall Hospitals NHS Trust

Riluzole for Amyotrophic Lateral Sclerosis Shared Care Guideline

V3.0

June 2019

1. Aim/Purpose of this Guideline

1.1. This guideline applies to medical, nursing and pharmacy staff in the safe and appropriate prescription and administration of Riluzole for amyotrophic lateral sclerosis.

1.2 This shared care guideline sets out details for the sharing of care of adults with Amyotrophic Lateral Sclerosis form of Motor Neurone Disease prescribed Riluzole. These guidelines provide additional limited information necessary to aid in the treatment these patients. As with all shared care guidelines they highlight relevant prescribing issues but should be used in conjunction with relevant NICE guidance, the BNF, ABPI summary of product characteristics and do not replace them.

1.3 This version supersedes any previous versions of this document.

1.4. Data Protection Act 2018 (General Data Protection Regulation – GDPR) Legislation

The Trust has a duty under the DPA18 to ensure that there is a valid legal basis to process personal and sensitive data. The legal basis for processing must be identified and documented before the processing begins. In many cases we may need consent; this must be explicit, informed and documented. We can't rely on Opt out, it must be Opt in.

DPA18 is applicable to all staff; this includes those working as contractors and providers of services.

For more information about your obligations under the DPA18 please see the 'information use framework policy', or contact the Information Governance Team rch-tr.infogov@nhs.net

2. The Guidance

2.1 Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, is a form of motor neurone disease. It is a progressive neurodegenerative disease causing degeneration of corticospinal neurones in the motor cortex (upper motor neurones) and brain stem and spinal cord motor neurones (lower motor neurones). Amyotrophic Lateral Sclerosis (ALS) is characterised by both upper and lower motor neurone signs and is the most common form of Motor Neurone Disease (MND), accounting for 65% to 85% of all cases.

In mainland Europe, the terms MND and ALS are often used interchangeably. ALS is the terminology used in the current product licence for Riluzole.

Commonly patients present with limb weakness, often beginning with foot drop, rapid muscle weakness becoming progressively worse and death is usually from respiratory failure as a result of diaphragmatic weakness which may be precipitated by aspiration pneumonia. Average life expectancy is between two to four years. Until the introduction of Riluzole treatment was supportive only.

Riluzole is a glutamate receptor antagonist. Glutamate acts as an excitatory amino-acid neurotransmitter, excess activity of which is thought to be neurotoxic and may be involved in the pathogenesis of MND.

Based on 2 multi centre double blind, placebo controlled trials there was a clear statistical benefit on survival at 12 to 18 months using Riluzole at 100mg daily. Patients enrolled in these studies already had advanced disease and had an increase in median tracheotomy free survival of 2 months compared to the placebo group. There was no significant improvement in functional measures used such as muscle strength.

The indication for the purpose of this guideline is to extend life or the time to mechanical ventilation for patients with ALS.

NICE recommendation states that ‘Riluzole therapy should be initiated by a neurological specialist with expertise in the management of MND’

2.2 Preparations and Dosage

50mg tablets taken 12 hourly. There is anecdotal information to indicate that the tablets may be crushed if necessary (see notes section).

2.3 Contraindications and Precautions

Contraindications are:

• Hepatic disease or baseline transaminases greater than 3 times the upper limit of normal or raised bilirubin.

• Renal impairment, (no formal studies have been carried out on patients in this group).

• Pregnancy and breastfeeding

2.3.1. Riluzole should be used with caution in history of abnormal hepatic function

2.3.2 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 medicinal product discontinuation and symptomatic treatment.

2.4 Monitoring

2.4.1. Regular hepatic function blood tests and Full Blood Count (baseline then every month for 3 months, then every 3 months for a further 9 months and annually thereafter) are recommended to monitor tolerability.

2.4.2. ALT levels should be measured more frequently in patients who develop elevated ALT levels >2x upper limit of normal e.g. weekly until level stabilises or falls.

2.4.3. If patient presents with febrile illness then monitoring white blood cell count for neutropenia is strongly recommended

STOP AND REFER TO THE NEUROLOGY TEAM IF:
• Liver function tests – ALT greater than 5 times the upper limit of normal.
• Blood disorders - WBC <3.5 x 10^9/l, Neutrophils <2 x 10^9/l

2.5 Side Effects

Very common > [1 in 10] > Common > [1 in 100] > Uncommon > [1 in 1000] > Rare > [1 in 10000] > Very rare

• **Very Common**
Asthenia, Nausea

• **Common**
Alterations in liver function tests, Headache, Abdominal pain, Pain, Vomiting, Dizziness, Tachycardia, Somnolence, Circumoral paraesthesia

• **Uncommon**
Neutropenia, Angioedema, Pancreatitis

2.6 Significant Drug Interactions

No clinical data are available but since Riluzole is extensively metabolised by the liver there is a possibility of interactions with a number of drugs.

Potential cytochrome P450 1A2 isoenzyme interactions of Riluzole	
Rate of Riluzole excretion decreased by:	Rate of Riluzole excretion increased by:
Caffeine Diclofenac Diazepam Clomipramine Imipramine Fluvoxamine Theophylline Amitriptyline Quinolones	Cigarette smoke Charcoal-grilled food Rifampicin Omeprazole

2.7 Notes

2.7.1. DRIVING: Dizziness or vertigo may affect performance of skilled tasks (e.g. driving)

2.7.2. Crushing tablets: Though not recommended in the drug licence there is supporting information for the practice of crushing or dispersing tablets to facilitate administration in those patients that cannot take the solid dose form. The drug has been administered in puree, yoghurt or a thick beverage via a nasogastric tube. Water is not a suitable diluent as the drug can sediment reducing the dose received and also cause oral anaesthesia. Administration by this route must follow nationally recognised guidelines on the covert administration of medicines.

2.7.3. Patients or their carers should be told how to recognise signs of neutropenia and advised to seek immediate medical attention if symptoms such as fever occur; white blood cell counts should be determined in febrile illness; neutropenia requires discontinuation of Riluzole.

2.8 Discontinuation

There are likely to be three main reasons for discontinuing Riluzole

1. Adverse drug reactions including those listed above.

2. Patient choice, usually because of lack of perceived benefit in the face of inexorable deterioration of the underlying illness.

3. Major clinical deterioration. It is likely that, depending on individual patient characteristics, there may come a point in the clinical course of the disease when continuation of Riluzole is no longer considered appropriate.

2.9 Patient information

For newly diagnosed patients, a booklet from the Motor Neurone Disease Association on practical management of the disease will be sent to the GP. A printable copy of the booklet can be found at:
http://www.mndassociation.org/downloads/Guide.pdf

2.10 References:

Summaries of Product Characteristics
NICE reviewed for new evidence January 2004 and deferred until January 2006 and again to an unspecified future date as no new evidence was available that would change the 2001 advice.

2.11. Areas of Responsibility for the Sharing of Care

2.11.1. These are suggested ways in which the responsibilities for the management of adult patients with who are prescribed **Riluzole** can be shared between the specialist and the general practitioners. The expectation is that these guidelines should provide sufficient information to enable GPs to be confident to take clinical and legal responsibility for prescribing these drugs. If a specialist asks the GP to prescribe this drug the GP should reply to this request as soon as practical. Sharing of care assumes communication between the

specialist, GP and patient. The intention to share care should be explained to the patient and be accepted by them.

2.11.2. In the NHS E guidelines on responsibility for prescribing (January 2018) between hospitals and GPs, it is advised that legal responsibility for prescribing lies with the doctor who signs the prescription.

2.11.3. Specialist:

2.11.3.1 Diagnosis of Amyotrophic Lateral Sclerosis after appropriate investigations.

2.11.3.2 Ensure that a baseline liver function test is recommended or carried out as a reference for subsequent monitoring. Any results from liver function test taking place in hospital should be copied to the GP.

2.11.3.3. Provide the patient or patient's parents/guardians/carers with suitable written and/or verbal information about the drug prior to starting medication e.g. patient information leaflet and the benefits, realistic outcomes and side effects of treatment (including how to recognize signs of neutropenia) and to confirm the main points of the discussion by letter to the patient. This may need to be repeated at a subsequent visit, as all the relevant information may not have been remembered.

2.11.3.4 Start drug treatment providing the first prescription and ensuring the patient's condition is stabilized (usually requires three month's treatment prescribed by the specialist).

2.11.3.5 Ensure monitoring of the patient with regard to side effects and liver function tests and FBC in the first 3 months of treatment.

2.11.3.6. Monitoring the progress of the disease.

2.11.3.7 Assessment of the continuing need for treatment including advice to GPs on when to stop treatment.

2.11.3.8. Ask the GP whether they are willing to participate in shared care using the shared care agreement letter.

2.11.3.9 Specify review dates at clinically relevant time intervals for both the GP and the consultant.

2.11.3.10 Prompt communication with GP of any changes in treatment, results of monitoring undertaken and assessment of adverse events.

2.11.3.11 Provide the GP with relevant contact information with clear arrangements for back-up advice and support should further assistance be required relating to this drug.

2.11.3. 12 Reporting adverse events to the MHRA.

2.11.4. General Practitioner:

2.11.4.1 If the GP disagrees to undertake shared care he/she will notify the consultant in writing without undue delay by completing the shared care agreement letter. Prescribing of Riluzole after communication with specialists regarding the need for treatment.

2.11.4.2 Undertake monitoring of side effects and liver function tests and FBC as outlined in the shared care guideline (as per 2.4).

2.11.4.3 Prompt referral to a specialist if there is a change in the patient's status, liver function or troublesome side effect.

2.11.4.4 Reporting to and seeking advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment.

2.11.4.5 Reporting adverse events to specialist and MHRA.

2.11.4.6 Stopping treatment in the case of a severe adverse event or as per shared care guideline

2.11.5. Patient / parent / guardian / carer:

- Sign the shared care agreement letter
- Report any adverse effects to their GP and/or specialist regarding their treatment.
- Ensure that they have a clear understanding of their treatment and relevant potential side effects.
- Ensure they attend for monitoring requirements as per shared care guideline.
- Awareness that treatment may be stopped under certain conditions.

2.11.7. BACK-UP ADVICE AND SUPPORT IS AVAILABLE FROM THE RELEVANT CLINICAL TEAM

3. Monitoring compliance and effectiveness

Element to be monitored	Compliance with prescribing and administration in accordance with this guideline (or other safe practice)
Lead	Head of Prescribing Support Unit
Tool	No specific tool
Frequency	As required according to clinical incident reports
Reporting arrangements	Via Cornwall Area Prescribing Committee / Medication Practice Committee
Acting on recommendations and Lead(s)	Relevant Clinical Staff
Change in practice and lessons to be shared	Lessons and changes in practice will be communicated through various channels to relevant staff

4. Equality and Diversity

4.1. This document complies with the Royal Cornwall Hospitals NHS Trust service Equality and Diversity statement which can be found in the 'Equality, Inclusion & Human Rights Policy' or the Equality and Diversity website.

4.2. Equality Impact Assessment

The Initial Equality Impact Assessment Screening Form is at Appendix 2.

Appendix 1. Governance Information

Document Title	Riluzole for Amyotrophic Lateral Sclerosis Shared Care Guideline V3.0		
Date Issued/Approved:	June 2019		
Date Valid From:	June 2019		
Date Valid To:	June 2022		
Directorate / Department responsible (author/owner):	Neurology Team / Pharmacy - Head of Prescribing Support Unit		
Contact details:	01872 253548		
Brief summary of contents	Some clinical issues and details of prescribing responsibilities for GP and specialists		
Suggested Keywords:	Riluzole		
Target Audience	RCHT	CFT	KCCG
	✓		✓
Executive Director responsible for Policy:	Medical Director		
Date revised:	May 2019		
This document replaces (exact title of previous version):	Shared care guideline for the treatment of Amyotrophic lateral sclerosis with Riluzole V2.0		
Approval route (names of committees)/consultation:	Cornwall Area Prescribing Committee		
Care Group Manager confirming approval processes	Robin Jones		
Name and Post Title of additional signatories	Not required		
Name and Signature of Divisional/Directorate Governance Lead confirming approval by specialty and divisional management meetings	{Original Copy Signed}		
	Name: Kevin Wright		
Signature of Executive Director giving approval	{Original Copy Signed}		

Publication Location (refer to Policy on Policies – Approvals and Ratification):	Internet & Intranet	✓	Intranet Only	
Document Library Folder/Sub Folder	Pharmacy			
Links to key external standards				
Related Documents:				
Training Need Identified?	No			

Version Control Table

Date	Version No	Summary of Changes	Changes Made by *(Name and Job Title)*
Mar'13	V1.0	Minor updating	M Wilcock, Head of Prescribing Support Unit
May'16	V2.0	Renewal	M Wilcock, Head of Prescribing Support Unit
May'19	V3.0	New format and slight text amendments to and inclusion of shared care agreement letter	M Wilcock, Head of Prescribing Support Unit

All or part of this document can be released under the Freedom of Information Act 2000

This document is to be retained for 10 years from the date of expiry.
This document is only valid on the day of printing

Controlled Document

This document has been created following the Royal Cornwall Hospitals NHS Trust Policy for the Development and Management of Knowledge, Procedural and Web Documents (The Policy on Policies). It should not be altered in any way without the express permission of the author or their Line Manager.

Appendix 2. Initial Equality Impact Assessment Form

<table>
<tr><td colspan="6">Riluzole for Amyotrophic lateral sclerosis Shared Care Guideline V3.0</td></tr>
<tr><td colspan="3">Directorate and service area: Pharmacy</td><td colspan="3">Is this a new or existing Policy?
Existing</td></tr>
<tr><td colspan="3">Name of individual completing assessment:
Dan Thomas, Pharmaceutical Services Contracting Team, NHS Kernow</td><td colspan="3">Telephone:
01726 627953</td></tr>
<tr><td>1. Policy Aim*

Who is the strategy / policy / proposal / service function aimed at?</td><td colspan="5">To provide information on prescribing of Riluzole to enable General Practitioners to take over prescribing responsibility from secondary care.</td></tr>
<tr><td>2. Policy Objectives*</td><td colspan="5">To promote a consistent level of shared care between primary and secondary care (in relation to RCHT catchment area)</td></tr>
<tr><td>3. Policy – intended Outcomes*</td><td colspan="5">Confident and competent prescribers, enabling medicines to be access in a primary care setting.</td></tr>
<tr><td>4. *How will you measure the outcome?</td><td colspan="5">Six monthly review</td></tr>
<tr><td>5. Who is intended to benefit from the policy?</td><td colspan="5">General practitioners, hospital specialists and community pharmacists – from understanding local guidance around use of these medicines. Patients/carers, from being able to access medicines from their GP.</td></tr>
<tr><td rowspan="3">6a Who did you consult with

b). Please identify the groups who have been consulted about this procedure.</td><td>Workforce</td><td>Patients</td><td>Local groups</td><td>External organisations</td><td>Other</td></tr>
<tr><td>X</td><td></td><td></td><td>X</td><td></td></tr>
<tr><td colspan="5">Please record specific names of groups
Cornwall Area Prescribing Committee</td></tr>
<tr><td>What was the outcome of the consultation?</td><td colspan="5">Agreed</td></tr>
</table>

7. The Impact
Please complete the following table. **If you are unsure/don't know if there is a negative impact you need to repeat the consultation step**.

Are there concerns that the policy **could** have differential impact on:				
Equality Strands:	Yes	No	Unsure	Rationale for Assessment / Existing Evidence
Age		**X**		
Sex (male, female, trans-gender / gender reassignment)		**X**		
Race / Ethnic communities /groups		**X**		
Disability - Learning disability, physical impairment, sensory impairment, mental health conditions and some long term health conditions.		**X**		
Religion / other beliefs		**X**		
Marriage and Civil partnership		**X**		
Pregnancy and maternity		**X**		
Sexual Orientation, Bisexual, Gay, heterosexual, Lesbian		**X**		

You will need to continue to a full Equality Impact Assessment if the following have been highlighted:

- You have ticked "Yes" in any column above and
- No consultation or evidence of there being consultation- this excludes any *policies* which have been identified as not requiring consultation**. or**
- Major this relates to service redesign or development

8. Please indicate if a full equality analysis is recommended.	**Yes**		**No**	**X**

9. If you are **not** recommending a Full Impact assessment please explain why.

Not indicated.

Date of completion and submission	Nov 2018	Members approving screening assessment	Policy Review Group (PRG) *'APPROVED' to be added here once reviewed at PRG.*

This EIA will not be uploaded to the Trust website without the approval of the Policy Review Group.

A summary of the results will be published on the Trust's web site.