

SHARED CARE GUIDELINE

Drug: Riluzole

<p>Introduction</p>	<p>Indication: To extend life or the time to mechanical ventilation for adult patients with amyotrophic lateral sclerosis (ALS) ^{1,2}, variant of Motor Neurone Disease (MND). Safety and efficacy of riluzole has only been studied in ALS. Therefore, riluzole should not be used in patients with any other forms of MND. Riluzole should only be initiated by a neurological specialist with expertise in the management of MND (as per NICE TA 20, 2001) ³ It is expected that most patients will be managed by secondary care however this guideline is for those patients who need to be managed in community.</p> <p>Background: ALS is the most common variant of MND accounting for 65% to 85% of all cases. It is a progressive, fatal neurodegenerative disorder with a median survival of 37 to 49 months. It is characterised by progressive degeneration of motor neurones resulting in both upper and lower motor neurone signs. Death usually results from ventilatory failure, resulting from progressive weakness and wasting of respiratory and bulbar muscles within approximately 3 years of symptom onset. Although the pathogenesis of ALS is not completely elucidated, 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. In vitro, riluzole inhibits the release of glutamate, an excitatory neurotransmitter and thus protects cells from glutamate-mediated neurotoxic damage. Riluzole is the only drug currently licensed for the treatment of ALS however symptomatic management, supportive, and palliative care are also available for patients with ALS.</p>
<p>Dose & Administration ^{1,2}</p>	<p>Available as 50mg tablets or 5mg/ml suspension. The recommended dose is 50mg twice a day, 12 hours apart, on an empty stomach (1hour before or 2 hours after food). The rate and extent of absorption is reduced when riluzole is administered with high-fat meals.</p> <p>The liquid formulation should be reserved for use in patients identified by specialist nurses who have bulbar symptoms and risk of dysphagia or bulbar symptoms and poor compliance secondary to dysphagia</p> <p>The suspension must be gently shaken for at least 30 seconds by rotating the bottle by 180° until it has an appearance of even consistency. A syringe-adaptor is supplied with the suspension for measurement (follow product information sheet for further instructions on use and wash the syringe with tap water after use). NB: after 1st opening the liquid should be used within 15 days.</p> <p><u>Patients should be aware that they will not experience any subjective benefit from taking the medication and may experience unwanted side effects.</u></p>
<p>Secondary Care Responsibilities</p>	<ol style="list-style-type: none"> 1. Confirm the diagnosis of ALS variant of MND 2. Assess the need for and appropriateness of riluzole 3. Discuss the benefits and side effects of treatment with the patient. 4. Perform pre-treatment screening (full blood count and serum transaminases) 5. Prescribe and monitor riluzole for 12 months to establish efficacy and safety (see MONITORING below) 6. Write to the patient's GP and ask if they are willing to take part in shared care. GPs should take on prescribing if they feel competent to do so. If shared care is agreed, share patient treatment plan. 7. Review the patient every three months to monitor the patient's response to therapy. 8. Request copies of test results for the patient's GP by completing the "copy to" section on the pathology form. 9. Advise patients or their carers how to recognise signs of neutropenia and advise them to seek immediate medical attention if symptoms such as fever occur 10. Ensure that clear backup arrangements exist for GPs to obtain advice.

	11. Promptly inform the GP of any changes in treatment or treatment plan following hospital admission / out-patient consultation / ad hoc patient consultation
Primary Care Responsibilities	<ol style="list-style-type: none"> 1. Provide the patient with prescriptions for riluzole 50mg tablets or 5mg/ml suspension after the initial minimum 12 months treatment 2. Monitor the patient's overall health and well being and report signs of disease progression to the consultant or the specialist nurse 3. Arrange ongoing monitoring at the recommended frequencies (see MONITORING below) 4. Request copies of test results for the patient's consultant by completing the "copy to" section on the pathology form. 5. Report any adverse events to the consultant or specialist nurse and stop treatment on their advice or immediately if an urgent need arises 6. Report any serious suspected adverse events to the MHRA 7. Advise patients and their carers on how to recognise signs of neutropenia and to seek immediate medical attention if symptoms such as fever occur 8. Report any febrile illness to the specialist team and check the white blood cell count 9. Symptomatic management of minor adverse effects
Monitoring	<p>At introduction of the drug FBC (including differential WBC), U&E and LFT (incl ALT) monthly for the first three months of treatment then three monthly up to one year – more frequently if patient develops raised ALT levels</p> <p>After the initial minimum 12 months prescribed by secondary care:</p> <ul style="list-style-type: none"> • FBC (including differential WBC) and LFTs repeated annually <p>Discontinue riluzole and seek advice if:</p> <ul style="list-style-type: none"> • ALT levels increase to five times the upper limit of normal range (≥ 225 IU/l) • There is evidence of neutropenia • There is evidence of interstitial lung disease
Adverse Effects	<p>The most common side effects are: -</p> <ul style="list-style-type: none"> • Gastrointestinal upsets including nausea, diarrhoea, vomiting, abdominal pain • Tiredness and fatigue (asthenia) • Headache, dizziness, somnolence (patients should be warned about not driving or operating machinery if affected) • Tachycardia • Elevation of ALT levels <p>It is estimated that approximately 10% of patients are likely to experience side effects of such intensity that they consider discontinuing the drug.</p> <p>Anaphylactoid reaction, angio-oedema, neutropenia and pancreatitis have been reported rarely</p> <p>If respiratory symptoms develop e.g. 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.</p> <p>Any reports of febrile illness should result in discontinuation of riluzole and differential FBC to assess for neutropenia</p> <p>Patients should be warned about the potential for dizziness or vertigo, and advised not to drive or operate machinery if these symptoms occur</p> <p>Always consult the latest version of the Summary of Product Characteristics (SPC) at www.medicines.org.uk for full details</p>
Common Drug Interactions	<p>There have been no clinical studies to evaluate the interactions of riluzole with other medicinal products.</p> <p>However, as Riluzole is metabolised by the liver, there is a possibility that it may interact with:</p> <ul style="list-style-type: none"> • CYP1A2 inhibitors that may potentially decrease the rate of riluzole eliminations e.g. diclofenac, diazepam, clomipramine, imipramine, theophylline, amitriptyline and quinolones • CYP1A2 Inducers that could increase the rate of riluzole elimination e.g. cigarette smoke, charcoal broiled food, rifampicin and omeprazole.
Contraindications	<ul style="list-style-type: none"> • Previous history of liver disease or if their baseline ALT/AST levels are greater than three times the upper limit of normal • Impaired renal function (no relevant data.90% dose excreted in urine) • Previous allergic reaction to Riluzole • Neutropenia • Signs of dementia and/or major psychiatric disorders • May be pregnant or are breastfeeding

- Unlikely to comply with the requirements of treatment i.e. blood tests

This guidance does not replace the SPC, which should be read in conjunction with this guidance.

References

1. Riluzole 50 mg film-coated tablets SPC <https://www.medicines.org.uk/emc/product/5185/smpc>
2. TEGLOTIK 5 mg/ml oral suspension <https://www.medicines.org.uk/emc/product/5060/smpc>
3. Guidance on the use of Riluzole (Rilutek) for the treatment of Motor Neurone Disease NICE TS 20 <https://www.nice.org.uk/guidance/ta20/chapter/About-this-guidance>

Version Control

Version Number	Amendments	Author	Date
Version 1.0	1 st Version approved		December 2015
Version 1.1.	Liquid formulation incorporated	SMcK Midlands & Lancashire CSU	March 2016
Version 1.2	Updated in line with SPC. Content reviewed by Prof. Chhetri.	SA	June 2019

RELEVANT CONTACT LIST

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