Prescribing Framework for Riluzole for treatment of motor neurone disease

Patients Name:…… Unit Number: ……

Patient's Address:……(Use addressograph sticker)

GP's Name:……..

Communication

We agree to treat this patient within this Prescribing Framework

Specialist Prescriber's Name…… Prof Reg. No. ……

Specialist Prescriber's Signature…… Date:……..

Where prescriber is <u>not</u> a consultant:

Consultant's Name: …… GMC No ……..

Consultant's Signature ……... ……. Date:……..

GP's Signature:…… Date:……..

GP's Name (if different from listed above)……..

The front page of this form should be completed by the specialist and the form sent to the patient's general practitioner.
The patient's GP should sign and send back to specialist, to confirm agreement to enter into shared care arrangement. If the General Practitioner is **<u>unwilling</u>** to accept prescribing responsibility for the above patient the specialist should be informed within two weeks of receipt of this framework and specialist's letter.

Full copy of framework can also be found at: http://www.hey.nhs.uk/amber.htm

1. Background

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”.

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. Dose

The license dosage of riluzole is 100mg per day (50mg twice per day).

Preparations available:
Riluzole tablets 50mg
Riluzole Suspension 5mg/ml
Generic tablets should be prescribed in preference

Patients with dysphagia (swallowing difficulties)
Please contact the MND specialists should the patient become dysphagic and subsequently unable to swallow tablets.

Oral administration:

- 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

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.

4. Duration of treatment

May be long term, as advised by specialist.

5. Contraindications and cautions

Riluzole is contraindicated in the presence of hepatic and/or renal impairment and during pregnancy and breast-feeding.

6. Adverse effects

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

- **Neutropenia** –isolated reports, see monitoring (below)
- **Anaemia**
- **Dizziness and Vertigo –** patients should be advised if affected not to drive or operating machinery

7. Interactions

No interactions are known, but as riluzole is metabolised by the liver the potential for interactions should be considered.

8. Monitoring

The main caution for use of riluzole is history of abnormal hepatic function. The specialist will be responsible for monitoring the progress of the disease and the safe use of riluzole. The needs of people with MND demand flexibility and this monitoring role can be taken up by the general practitioner or by other physicians involved in providing shared care.
If results are abnormal contact the specialist for advice on treatment.

LFTs	Baseline before starting treatment. Monthly for 3 months, then 3 monthly for 9 months then annually thereafter The specialist will monitor baseline LFTS. GP to monitor monthly for first 3 months then every 3 months for further 9 months then

	annually thereafter (unless abnormal blood results then increase frequency) Riluzole should be discontinued if the ALT levels increase to 5 times the ULN. Readministration of riluzole to patients in this situation cannot be recommended.
FBC	Baseline before starting treatment. Monthly for 3 months, then 3 monthly for 9 months then annually thereafter The specialist will monitor baseline FBC. GP to monitor monthly for first 3 months then every 3 months for further 9 months then annually thereafter (unless abnormal blood results then increase frequency) Patients should be made aware they need to report any febrile illness. Discontinue riluzole and contact specialist team in case of neutropenia: WCC <3.5 Neutrophils <2.0
U+Es	Baseline before starting treatment by specialist

9. Information to patient

Patients should be advised to report any febrile illness to their GP. The report of febrile illness should prompt doctors to check white cell counts and check for neutropenia.

9. 10. Responsibilities of clinicians involved

Stage of Treatment	Hospital Specialist	General Practitioner
Initiation	Patients will have been diagnosed using the agreed criteria. Patients will receive the first 1months of treatment before referral to their G.P for prescribing. Monitor baseline LFTs, FBCand U&Es The G.P. will receive a letter indicating details of the patient's clinical history.	
Maintenance	Provide advice and guidance as needed relating to queries.	Patients will be monitored for their overall health. Blood monitoring as per monitoring above. Patients will be monitored for adverse drug reactions. Patients will receive their follow-up prescription needs.

During office hours:

Motor Neurone Disease Specialist Nurses
Vanessa Baker (01482) 816781
Neurology specialist pharmacist
Jane Morgan Via switchboard (01482 875875)
Consultant neurologist
As per clinic letter Via switchboard

Out of hours: contact on call registrar for neurology via switchboard

APPROVAL PROCESS

Written by:	Jane Morgan, Medicines Information Pharmacist, HEY Reviewed by Jane Morgan, MI Pharmacist HEY May 17, Reviewed by Jane Morgan, Interface Pharmacist HUTH March 2020
Consultation process:	Dr A Ming, Consultant Neurologist, HEY, Dr Nandakumar, Consultant Neurologist, HUTH.
Approved by:	MMIG
Ratified by:	HERPC
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