BEDFORDSHIRE AND LUTON JOINT PRESCRIBING COMMITTEE SHARED CARE GUIDELINE FOR THE USE OF RILUZOLE IN THE TREATMENT OF MOTOR NEURONE DISEASE

PATIENT'S NAME: PATIENT'S ADDRESS: HOSPITAL NAME AND NUMBER / PATIENT IDENTIFIER: CONSULTANT'S NAME: NAME OF GP:

SHARED CARE RESPONSIBILITIES (Summarised)

PRESCRIBING ARRANGEMENTS

- The Consultant Neurologist will provide an initial prescription for 3 months therapy and complete a high cost drug proforma either via Blueteq or in paper format.
- The General Practitioner will then take over prescribing responsibility by agreement.

MONITORING

- The Consultant Neurologist will undertake pre-treatment baseline monitoring of Full blood Count (FBC) and Liver Function Tests (LFTs).
- The Consultant Neurologist will undertake monitoring of White blood cell count (WBC) and LFTs at monthly intervals for the first three months of treatment.
- Subsequent monitoring of LFTs at 3 monthly intervals during the remainder of the first year and periodically thereafter (unless patient develops elevated ALT levels, when ALT levels should be measured more frequently) will be undertaken by the General Practitioner or Consultant Neurologist (please delete as appropriate by agreement).
- WBC to be checked in the event of febrile illness.
- The Neurologist will review the patient regularly at intervals that reflect the needs of the patient, carer and General Practitioner.

COMMUNICATION

- The GP will be contacted to discuss shared care arrangements **before** treatment is commenced to ensure that he/she is willing to jointly manage the patient's therapy after a 3 month trial of treatment.
- The Consultant Neurologist will formally ask the GP to take over prescribing responsibility, when the patient's therapy is stabilised (not normally before an initial 3 months of treatment) and will **send the GP a copy of the shared care guidelines.**

- Wherever blood tests are undertaken (in secondary care or via the GP), the results will be clearly and promptly communicated by the health care professional (GP or Consultant Neurologist) to the other party and the patient/carer (if appropriate).
- The Consultant Neurologist and GP should clearly explain the dosage regimen to the patient and carer.
- The patient/carer should be warned to report any febrile illness to their doctor.
- Any changes to drug therapy should be clearly and promptly communicated by the health care professional making the change (GP or Consultant Neurologist) to the other party and the patient/carer.

MOTOR NEURONE DISEASE

Background
Motor neurone disease (MND) is characterised by progressive degeneration of the motor neurones of the brain, brain stem or spinal cord. Depending on the site of the lesions, characteristic signs may include spasticity, muscle stiffness, brisk or diminished reflexes, muscle wasting and fasciculation, both flaccid and/or spastic weakness.

The term 'Motor Neurone Disease' is used to describe variants of the disease – namely progressive muscular atrophy (PMA) and amyotrophic lateral sclerosis (ALS) which includes Progressive Bulbar Palsy (PBP). ALS, which is characterised by both upper and lower motor signs, is the most common form of MND, accounting for 65% to 85% of all cases. Adult onset MND usually starts insidiously 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.[i]

Diagnosis
There is no diagnostic test for MND. The diagnosis requires the demonstration of clinical signs affecting both the brain and spinal cord. Diagnosis is often delayed and can take more than 16 months from the onset of initial symptoms, which are commonly non-specific and include general fatigue.[i]

General Treatment and Management
Pharmacological interventions are aimed at providing symptomatic relief for people with MND. Surgical interventions may be necessary and include percutaneous gastrostomy to enable feeding and tracheostomy with or without ventilatory support to aid breathing as respiratory muscle weakness increases. A wide range of multidisciplinary health and social services are required for people with MND, particularly in the late stages of the disease. These need to be tailored to suit individual needs.[i]

Likely Outcome
Prognosis is poor – 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.

RILUZOLE (TABLETS or SUGAR-FREE ORAL SUSPENSION®

Consult eBNF (https://bnf.nice.org.uk) or Summary of Product Characteristics (SpC) (www.medicines.co.uk) for full prescribing details.

a) Criteria for patient selection[ii,i]

- Riluzole may be used in patients in whom the diagnosis of the ALS form of MND is considered definite by a Consultant Neurologist (with expertise in the management of MND), after appropriate investigations. (i.e. in line with the NICE Guidance)
- It is probably best used early rather than late in the course of the disease.

b) Indication[i,iii,iv]
Riluzole is indicated to extend life or the time to mechanical ventilation for patients with the amyotrophic lateral sclerosis (ALS) form of MND.

NB. Safety and efficacy of riluzole has only been studied in ALS, therefore riluzole should not be use in any other form of MND.

c) Dosage and administration [iii,v]

Recommended dose in adults or elderly is 50mg every 12 hours.
The oral suspension is considerably more expensive than the generic riluzole tablet and therefore the suspension should be restricted to use in patients with swallowing difficulties. Initiation of the suspension is a secondary care/specialist service decision, following (and based on) a SALT assessment of the patient.

d) Contra-indications [iii,v]

- Previous allergic reaction to riluzole or any component of the tablet or suspension.
- Patients who have liver disease or who have baseline transaminases greater than 3 times the upper limit of normal.
- Pregnancy
- Breastfeeding mothers
- Neutropenia
- Acute Porphyria

e) Cautions/Precautions [iii,v]

- Not recommended for use in children.
- Not recommended for use in patients with impaired renal function.
- Use with care in patients with a history of abnormal liver function, or in patients with slightly elevated transaminases, bilirubin and/or gamma-glutamyl transferase. Baseline elevations of several liver function tests should preclude the use of riluzole.
- Neutropenia: Patients should be warned to report any febrile illness to their doctor. If neutropenia is confirmed, patients should be advised to stop taking riluzole immediately.
- Interstitial lung disease: if respiratory symptoms (e.g. dry cough +/- dyspnoea) develop, perform chest x-ray; discontinue if interstitial lung disease is diagnosed.

f) Side-effects [iii, iv v]

Nausea, vomiting, diarrhoea, abdominal pain, pain, abnormal LFTs; tachycardia; asthenia, headache, dizziness, drowsiness, oral paraesthesia; *less commonly* interstitial lung disease, pancreatitis, anaphylactoid reaction angioedema and anaemia*; rarely* neutropenia; *very rarely* hepatitis.

g) Drug Interactions [ii,iii]

There have been no clinical studies to evaluate the interactions of riluzole with other drugs. *In vitro* studies suggest that following drugs may affect the elimination of riluzole:

- Increased elimination – e.g. cigarette smoking, rifampicin and omeprazole.
- Reduced elimination – e.g. caffeine, diclofenac, diazepam, clomipramine, imipramine, fluvoxamine, theophylline, amitriptyline and all quinolone antibiotics.

h) Monitoring [ii,iii,iv]

- The Consultant Neurologist will carry out baseline monitoring requirements, which include a full biochemical screen and full blood count prior to the commencement of treatment.

- The Consultant Neurologist will check WBC and LFTs monthly for the first three months.
- LFTs to be checked at 3 monthly intervals during the remainder of the first year and periodically thereafter (unless patient develops elevated ALT levels, when ALT levels should be measured more frequently). The ongoing monitoring of LFTs will be arranged by agreement, either via the General Practitioner or Consultant Neurologist.
- WBC to be checked in the event of a febrile illness.
- Wherever blood tests are undertaken (in secondary care or via the GP), the results will be clearly and promptly communicated by the health care professional (GP or Consultant Neurologist) to the other party and the patient/carer (if appropriate).
- If respiratory symptoms develop (e.g. dry cough and/or dyspnoea) a chest x-ray should be performed.
- The Neurologist will review the patient regularly at intervals that reflect the needs of the patient, carer and General Practitioner.

i) Indications for discontinuation of Riluzole [iii,iv]

- Elevation of liver enzymes to 5 times more than the upper limit of normal.
- Neutropenia (usually within the first 2 months of treatment).
- Diagnosis of interstitial lung disease
- Intolerable side-effects.
- Patient decision in consultation with GP/Specialist.

j) Patient/Carers Advice[v]

Driving and Skilled Tasks
Dizziness or vertigo may affect performance of skilled tasks (e.g. driving)

Blood Disorders
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.

k) Cost (Chemist and Druggist and Drug Tariff, October 2017)

Product	Annual Cost
Rilutek® Tablets	£4,164
Riluzole Tablets (generic)	£183.43
Riluzole Oral Sugar-free Suspension (Teglutik®) (NB: Only for use in patients with swallowing difficulties- SALT assessment required)	£1,200

l) Prescribing Arrangements

- The Consultant Neurologist will provide an initial prescription for 3 months therapy and complete a high cost drug proforma either via Blueteq or in paper format.
- The General Practitioner will then take over prescribing responsibility, by agreement.

- Any changes to drug therapy should be clearly and promptly communicated by the health care professional making the change (GP or Consultant Neurologist) to the other party and the patient/carer.
- **Riluzole should be prescribed generically.**

CONTACT NAMES

Note to Specialist Team – please feel free to add in any additional contact names and numbers e.g. clinic nurse, bleep number of other doctors in your team.

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These guidelines were produced by Bedfordshire Joint Prescribing Committee in consultation with local specialists – Updated December 2017.

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[i] Guidance on the Use of Riluzole (Rilutek) for the Treatment of Motor Neurone Disease, Technology Appraisal Guidance – No. 20, January 2001, National Institute for Clinical Excellence.
[ii] Advice received from Dr Gale, Consultant Neurologist, Luton & Dunstable Hospital.
[iii] Summary of Product Characteristics for Rilutek® (Riluzole tablets) (http://www.medicines.org.uk/emc/medicine/1672), 18/12/13, accessed 23/10/17.
[iv] Summary of Product Characteristics for Teglutik® (Riluzole oral suspension), 23/3/2016 http://www.medicines.org.uk/emc/medicine/31219 accessed 23/10/17
[v] eBNF (https://bnf.nice.org.uk/), accessed 23/10/17.