# Agenda Item: 7a(II)

**Report to: Primary Care Commissioning Committee**

**Date of meeting: 12/10/2021**

**Date paper distributed: 05/10/2021**

**Subject: Neurology Shared Care Frameworks**

**Presented by: Rachel Barrowcliff/ James Ledger**

**Previously distributed to: Northern Lincolnshire Area Prescribing Committee**

**STATUS OF THE REPORT *(auto check relevant box****)*

**Decision required** [x]

**For Discussion to give Assurance** [ ]  *(Only if requested by Committee member prior to meeting)*

**For Information** [ ]

**Report Exempt from Public Disclosure**  [x]  No [ ]  Yes

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| --- | --- |
| **PURPOSE OF REPORT:** | To set out two new shared care prescribing frameworks for the management of neurological conditions.  |
| **Recommendations:** | The committee is recommended to approve the frameworks for addition to the Enhanced Service for shared care  |
| **Clinical Engagement**  | CCG Prescribing Lead, Northern Lincolnshire APC |
| **Patient/Public Engagement** |  |
| **Committee Process and Assurance:** | Northern Lincolnshire Area Prescribing Committee (NLAPC) |

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| **Link to CCG’s Priorities** | * Sustainable services
* Empowering people
 | [x] [ ]  | * Supporting communities
* Fit for purpose organisation
 | [ ] [x]  |
| **Are there any specific and/or overt risks relating to one or more of the following areas?** | * Legal
* Finance
* Quality
* Equality analysis (and Due Regard Duty)
 | [ ] [x] [ ] [ ]  | * Data protection
* Performance
* Other
 | [ ] [ ] [ ]  |

**Provide a summary of the identified risk**

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| The provision of shared care requires a shift of resources from secondary to primary care.  |

**Executive Summary**

This paper sets out two new shared care prescribing frameworks for management of neurological conditions;

# Prescribing Framework for Modafinil for Daytime Hypersomnolence and excessive daytime sleepiness in Parkinsons disease

# Prescribing Framework for Riluzole for treatment of motor neurone disease

These shared care agreements have been approved by the Northern Lincolnshire Area Prescribing Committee and the Hull and East Riding Prescribing Committee.

Following approval by the committee, the provision will be commissioned from Primary Care in line with the developing Joint Shared Care Framework for Northern Lincolnshire.

# Prescribing Framework for Modafinil for Daytime Hypersomnolence and excessive daytime sleepiness in Parkinsons

### Patients Name:………………………… Unit Number: ………………

Patients Address:………………………(Use addressograph sticker)

G.P’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 not 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 **unwilling** 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>

## **Background**

Modafinil is a non-amphetamine central nervous system stimulant which improves the level and duration of wakefulness and daytime alertness. It is licensed for treatment of daytime hypersomnolence associated with narcolepsy with or without sleep apnoea.

These guidelines aim to provide clinicians in primary care with relevant information when prescribing modafinil.

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**

Idiopathic daytime hypersomnolence with narcolepsy with or without cataplexy.

Excessive daytime sleepiness associated with Parkinson’s disease (PD) where a detailed sleep history has excluded reversible pharmacological and physical causes (NICE NG71 July 2017). Unlicensed indication for a licensed drug.

Other unlicensed indications remain RED.

1. **Dose**

Initially 100mg daily increased to 400mg daily, as advised by specialist.

Can be taken as single daily dose or more commonly taken in 2 divided doses, in the morning and at noon.

(Dose should be halved in patients with severe renal or hepatic impairment.)

1. **Duration of treatment**

May be long term depending on patient response.

## **Contraindications and cautions**

Modafinil is contraindicated in patients with uncontrolled moderate to severe hypertension, or arrhythmia, history of left ventricular hypertrophy, cor pulmonale, or of clinically significant signs of CNS stimulant-induced mitral valve prolapse (including ischaemic ECG changes, chest pain and arrhythmias).

Also contraindicated during pregnancy and lactation.

Use with caution in patients with history of psychosis, anxiety, depression, mania, bipolar disorder, alcohol or drug abuse. Discontinue treatment if psychiatric symptoms develop, possibility of dependence or if rash develops.

1. **Adverse effects**

**Cardiovascular:** Tachycardia, hypertension, palpitations. An ECG is recommended in all patients before modafinil treatment is initiated. Blood pressure and heart rate should be regularly monitored (see “Disease and drug monitoring” below). **Modafinil should be discontinued in patients who develop arrhythmia or moderate to severe hypertension and not restarted until the condition has been adequately evaluated and treated.**  For hypertension refer to NICE NG136 [August 2019], Hypertension in adults – diagnosis and management. Up to 2% of patients can suffer from palpitations or tachycardia (pulse rate >100 BPM).

**Gastrointestinal**: GI disturbances e.g. reduced appetite, nausea, gastric discomfort – minimise by taking dose with food. Diarrhoea, constipation and dry mouth.

**Hepatic**: Dose related increase in alkaline phosphatase and gamma GT. Deranged LFTs have been reported (incidence 1-10%). Monitor LFTs if there are signs of hepatotoxicity. Dose related increases in alkaline phosphatase and gamma glutamyl transferase have been observed. If levels >3 times the upper limit of normal occurs, the specialist should be contacted via Advice and Guidance. **If levels >5 times the upper limit of normal the specialist urgently and discontinue treatment.**

**Skin reactions:** Serious rashes (including Stevens - Johnson syndrome,

Toxic Epidermal Necrolysis and Drug Rash with Eosinophilia and Systemic Symptoms) have been reported early on in treatment (1-5 weeks) but occasionally after prolonged treatment. **Modafinil should be discontinued and not restarted in cases of skin or hypersensitivity reaction.**

**Psychiatric symptoms such as psychosis, suicide related behaviour** –mainly but not exclusively in those with a history of psychosis, depression, mania. Patients should be monitored for the appearance of psychiatric symptoms. **Should these emerge whilst on therapy, modafinil should be discontinued and not restarted.** Modafinil is also associated with the onset or worsening of anxiety.

**Aggressive or hostile behaviour:** The onset or worsening of aggressive or hostile behaviour can be caused by treatment with modafinil. If symptoms occur, discontinuation of modafinil may be required.

**Hypersensitivity reactions** – Multi-organ hypersensitivity reactions have been reported. Typically, although not exclusively, this presents as fever and rash associated with other organ system involvement. Other associated manifestations included myocarditis, hepatitis, liver function test abnormalities, haematological abnormalities (e.g., eosinophilia, leukopenia, thrombocytopenia), pruritus, and asthenia. **If multi-organ hypersensitivity is suspected, modafinil should be discontinued.**

**Dependence and abuse potential** - the possibility of dependence with longterm use cannot be entirely excluded.

**Other reactions** – vasodilation, dizziness, somnolence, paraesthesia, blurred vision. Headache can occur in up to 21% of patients and can be managed with simple analgesia and resolves within a few days.

For complete list always check with BNF [www.bnf.org.uk](http://www.bng.org.uk) or SPC ([www.medicines.org.uk](http://www.medicines.org.uk)).

1. **Interactions**

The effectiveness of combined and progestogen only contraceptives may be reduced when used with modafinil. Alternative or concomitant methods of contraception are recommended, and for two months after discontinuation of modafinil.

**Anticonvulsants** - Care should be observed when used in combination with anticonvulsant drugs. Modafinil levels may be reduced by carbamazepine and phenobarbitone and phenytoin levels may be increased by modafinil. Measurement of phenytoin plasma levels may be appropriate on initiation or discontinuation of treatment with modafinil.

**Antidepressants** - Serotonin syndrome has been reported when MAOIs have been used concurrently with modafinil and should be used together with caution. Metabolism of some TCADs (amitriptyline, clomipramine, imipramine and SSRIs (citalopram) may be inhibited by modafinil and lower doses of these antidepressants may be required.

**Anticoagulants (Warfarin)** - modafinil may increase the anticoagulant effect of warfarin. The INR should be monitored regularly during the first 2 months of modafinil use and after changes in modafinil dosage.

**Ciclosporin** – modafinil may reduce plasma concentrations of ciclosporin. Advice may need to be sought from the specialist as to the significance of this interaction and ciclosporin levels rechecked as necessary.

**Contraceptives** - women should be advised that modafinil interacts with combine hormonal contraceptives (oral, patch and ring), progestogen only oral contraceptives and the progestogen only implant, including when used for emergency contraception.

Additional precautions or an alternative method should be continued for 2 months after stopping modafinil treatment (as per the manufacturer (but note the Faculty of Family Planning state 4 weeks)

Appropriate alternative methods of contraception include the copper IUD, progestogen only injection and levonorgestrel releasing IUD.

For the most up to date advice refer to the advice on the Faculty of Family Planning website.

<https://www.fsrh.org/standards-and-guidance/documents/ceu-clinical-guidance-drug-interactions-with-hormonal/>

For complete list always check with BNF or Data Sheet (available electronically at [www.medicines.org.uk](http://www.medicines.org.uk/) )

1. **Monitoring**

ECG is required prior to initiation.

Blood pressure and heart rate should be monitored regularly as advised by specialist (at least every 6 months).

Clinical response and adverse effects will be monitored by specialist and general practitioner.

1. **Information to patient**

Patient should be advised of risks and benefits of treatment. (where relevant, patients should be warned that side effects may impair ability to drive, operate machinery)

1. **Responsibilities of clinicians involved**

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| --- | --- | --- |
| **Stage of Treatment** | **Hospital Specialist** | **General Practitioner** |
| Initiation | Select patients appropriate for treatment.Inform patient of risks and benefits of treatment and supply arrangements.Arrange for baseline ECG and interpret ECG. Patients with abnormal findings should receive further specialist evaluation and treatment before modafinil treatment is considered, e.g. by referral to a cardiologist where necessaryCheck baseline LFTs, blood pressure and heart ratePrescribe and assess patient’s response until dose stabilised.Contact the GP to invite shared care for the patient and provide information on treatment. |  |
| Maintenance  | Assess clinical response to treatmentProvide adequate advice and support to GPsInform GP of dose amendments if appropriate | Prescribe treatment once stabilised.Monitor patient for efficacy.Monitor for adverse effects.Refer to specialist where appropriateCheck BP, heart rate and LFTs 6/12 when on stable dosing. See adverse effects section for advice on what to do if  |

**Contact Details:**

During office hours:

 Neurology specialist pharmacist

Priscilla Kanyoka 01482 311679

Jane Morgan 01482 461519

 Consultant neurologist

 As per clinic letter Via switchboard

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

**APPROVAL PROCESS for Shared Care Framework**

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| --- | --- |
| **Written by:** | **Marie Miller, Interface Pharmacist****Reviewed Jane Morgan, Neurology Specialist Pharmacist, Dec 2013 and Nov 2017 and Nov 2020** |
| **Consultation process:** | **Dr A Ming, Consultant Neurologist** |
| **Approved by:** | **Medicines Management Interface Group (June 2010)** |
| **Ratified by:** | ***HERPC Jan 2014, Jan 2021*** |
| **Review date:** | ***Jan 2024***  |

# 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 not 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 **unwilling** 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.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

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

**6.Interactions**

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

## **7. 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 thereafterThe 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 thereafterThe 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 |

**8. 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.

1. **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 or Priscilla Kanyoka 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 |
| **Review date:** | November 2023 |