NHS
Northern Lincolnshire
Area Prescribing Committee

HERPC
Hull & East Riding Prescribing Committee

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 <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

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.

3. 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.)

4. Duration of treatment

May be long term depending on patient response.

5. 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.

6. 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 or SPC (www.medicines.org.uk).

7. 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)

8. 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.

9. 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)

10. Responsibilities of clinicians involved

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 necessary Check baseline LFTs, blood pressure and heart rate Prescribe 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 treatment Provide adequate advice and support to GPs Inform GP of dose amendments if appropriate	Prescribe treatment once stabilised. Monitor patient for efficacy. Monitor for adverse effects. Refer to specialist where appropriate Check BP, heart rate and LFTs 6/12 when on stable dosing. See adverse effects section for advice on what to do if abnormalities identified.

Contact Details:

During office hours:

Neurology specialist pharmacist
Priscilla Kanyoka 01482 311679

Interface Pharmacist
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

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***