Humber Area Prescribing Committee

SHARED CARE FRAMEWORK for Modafinil

HUMBER AREA PRESCRIBING COMMITTEE

DATE APPROVED BY APC: 6.4.2022

REVIEW DATE: APRIL 2025

PATIENT NAME	*NHS NUMBER*	*DATE OF BIRTH*
ADDRESS		
GP'S NAME		

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 Name: …… GMC No ……..

GP's Signature ……..... ……. Date:…….

If the General Practitioner is unable to accept prescribing responsibility for the above patient the consultant should be informed within two weeks of receipt of this framework and consultant's / nurse specialist's letter. In such cases the GP are requested to update the consultant, by letter, of any relevant changes in the patient's medication / medical condition.

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Specialist responsibilities

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
If patient of child bearing potential ensure signposted to appropriate service to arrange contraception and contraception is initiated prior to prescribing.
Prescribe and assess patient's response until dose stabilised.
Contact the GP to invite shared care for the patient and provide information on treatment.
Assess clinical response to treatment
Provide adequate advice and support to GPs
Inform GP of dose amendments if appropriate

Primary care responsibilities
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.

Patient responsibilities

General :

- To take this medicine as prescribed
- Ensure they have an adequate supply
- Report any possible side effects to their GP
- Attend appointments including those for routine blood tests and investigations.

Drug specific :

- Women of child bearing age must ensure adequate effective methods of contraception are maintained during treatment and for 2 months after treatment is stopped. See under interactions and pregnancy section for further information.
- Modafinil is not a replacement for good sleep hygiene.
- Side effects of most concern that need reporting include
    - Psychiatric symptoms such as suicidal ideation or anxiety
    - Skin reactions

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Shared Care Framework for *Modafinil in hypersomnolence with narcolepsy with or without cataplexy or excessive daytime sleepiness associated with Parkinson's disease*

1. Introduction:	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).	
3. Licensing Information	Modafinil is licensed in adults for the treatment of excessive sleepiness associated with narcolepsy with or without cataplexy. Use for excessive day time sleepiness with Parkinson's disease is an unlicensed indication. All other unlicensed indications remain red.	
4. Pharmaceutical Information	Route	Oral
	Formulation	Tablet (100mg and 200mg)
	Administration details	Should be swallowed whole
	Additional information	nil
5. Supporting evidence	*NICE NG 71 (Parkinson's disease in adults)*	
6. Initiation on ongoing dosage regimen	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.)	
7. Contraindications and Warnings:	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 (see sections 10 and 13 for further information).	

<table>
<tr><td></td><td colspan="2">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.</td></tr>
<tr><td>8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist</td><td colspan="2">ECG is required prior to initiation. 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

Clinical response and adverse effects will be monitored by specialist and general practitioner.</td></tr>
<tr><td rowspan="4">9. Ongoing monitoring requirements to be undertaken by primary care</td><td>Monitoring</td><td>Frequency</td></tr>
<tr><td>Blood pressure</td><td>As advised by specialist minimum of every 6 months</td></tr>
<tr><td>Heart rate</td><td>As advised by specialist minimum of every 6 months</td></tr>
<tr><td>LFTs</td><td>Every 6 months</td></tr>
<tr><td rowspan="6">10. Interactions</td><td colspan="2">The following drugs are known or suspected interactions and the GP may wish to discuss with the initiating specialist before commencing:</td></tr>
<tr><td>Interacting Drug</td><td>Advice</td></tr>
<tr><td>Anticonvulsants</td><td>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.</td></tr>
<tr><td>Antidepressants</td><td>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.</td></tr>
<tr><td>Anticoagulants (Warfarin)</td><td>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.</td></tr>
<tr><td>Ciclosporin</td><td>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.</td></tr>
<tr><td>Contraceptives</td><td>Women should be advised that modafinil interacts with combined hormonal contraceptives (oral, patch and ring), progestogen only oral</td></tr>
</table>

		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 full list see SPC at www.medicines.org.uk/emc and BNF	
11. Adverse effects and management For complete list always check with BNF www.bnf.org.uk or SPC (www.medicines.org.uk).	Adverse effects	Action for GP
	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 long-term 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.
12. Advice to patients and carers The specialist will counsel the patient with regard to the benefits and risks of treatment and will	**The patient should be advised to report any of the following signs or symptoms to their GP without delay:** The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant	

provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.	information and advice, including patient information leaflets on individual medicines. The patient should be advised to report any of the following signs or symptoms to their GP without delay: • Psychiatric symptoms such as suicidal ideation or anxiety • Skin reaction Women of child-bearing potential should be advised as below regarding contraceptive use.
13. Preconception, Pregnancy, paternal exposure and breast feeding It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both the GP and the specialist.	**Preconception** Sexually active women of child-bearing potential should be established on a contraceptive programme before taking modafinil. Since the effectiveness of steroidal contraceptives may be reduced when used with modafinil, alternative or concomitant methods of contraception are recommended, and for two months after discontinuation of modafinil. 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/ Further information is available in *MHRA Drug Safety Update Modafinil (Provigil): increased risk of congenital malformations if used during pregnancy* If patients decline recommended contraception and chooses alternative method (e.g. barrier or abstinence) they can be initiated on therapy as long as aware of risks and documented decision, this should be reviewed at each review or change in circumstances. **Pregnancy:** **Modafinil is a known teratogen and should not be used during pregnancy.** If patient becomes pregnant while taking refer to specialist urgently. **Breastfeeding:** Modafinil should not be used during breast feeding. **Paternal Exposure:** There is no information on paternal exposure

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14. Specialist contact information	Name: *Consultant neurologist as per clinic letter* Role and specialty: *As per clinic letter* Daytime telephone number: *01482 875 875 HUTH switchboard or as per clinic letter* Alternative contact: *Priscilla Kanyoka – Advanced Clinical Pharmacist – Neurology (Priscilla.Kanyoka1@nhs.net) Or Jane Morgan – Interface Pharmacist (jane.morgan14@nhs.net) 01482 461519* Out of hours contact details: *contact on call neurology registrar/consultant via switchboard*
15. Local arrangements for referral .	For urgent enquiries contact on call neurologist via switchboard. Advice and guidance can be sought via A&G portal for non-urgent enquiries.
16. To be read in conjunction with the following documents	https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf

Document control	**This information is not inclusive of all prescribing information and potential adverse effects. Please refer to the SPC (data sheet) or BNF for further prescribing information.**		
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V1	Jane Morgan	Principal Pharmacist – Interface	New document (adapted from HERPC and NLAPC SCF).