Healthier Together
Improving health and care in Bristol, North Somerset and South Gloucestershire

BNSSG Shared Care Guidance
Please complete all sections

Section 1: Heading

Drug	Modafinil
Amber *three months*	
Indication	Excessive sleepiness associated with narcolepsy with or without cataplexy. Idiopathic hypersomnia.

Section 2: Treatment Schedule

Usual dose and frequency of administration *(Please indicate if this is licensed or unlicensed and any relevant dosing information)*	The recommended starting daily dose is 200mg. The total daily dose may be taken as a single dose in the morning or as two doses, one in the morning and at one noon, according to physician assessment of the patient and the patient's response. Doses of up to 400mg in one or two divided doses can be used in patients with insufficient response to the initial 200mg modafinil dose. In view of the potential for lower clearance and increased systemic exposure, it is recommended that patients over 65 years of age commence therapy at 100mg daily.
Route and formulation	100mg and 200mg tablets to be taken orally.
Duration of treatment	Treatment may be long term.

Section 3: Monitoring

Please give details of any tests that are required before or during treatment, including frequency, responsibilities (please state whether they will be undertaken in primary or secondary care), cause for adjustment and when it is required to refer back to the specialist.

Baseline tests - where appropriate
To be taken in secondary care: Urea and electrolytes, avoid in chronic renal impairment (eGFR <20mL/min) LFTs, the dosage of modafinil should be reduced by half in patients with severe hepatic impairment. An ECG is recommended in all patients before modafinil treatment is initiated. Patients with abnormal findings should receive further specialist evaluation and treatment before modafinil treatment is considered. Blood pressure and heart rate should also be checked.
Subsequent tests - where appropriate *(Please indicate who takes responsibility for taking bloods and interpreting results)*
To be taken in primary care:

1. Annual review for efficacy, tolerance, BP and heart rate. In those patients who develop moderate to severe hypertension use should be discontinued and not restarted until the condition has been adequately evaluated and treated. Similarly, those whose heart rate is monitored and arrhythmia detected should be assessed before treatment continues. If annual review shows lack of efficacy please refer back to the clinical team for treatment review.

2. Periodic testing of renal and hepatic function with doses adjusted accordingly in those with renal or hepatic impairment.

   References suggest modafinil can be used at normal doses until eGFR is less than 10ml/min. In these cases starting doses would be reduced by 50% and increased according to response.

   The summary of product characteristics states that where patients have severe hepatic impairment doses should be reduced by half. Severe hepatic impairment is difficult to clearly quantify but those with decompensated liver disease or AST/ALT over 3 times normal limits should be referred for consultant review.

Test	Frequency	Who by	Action/management

Section 4: Side Effects

Please list only the most pertinent side effects and management. Please provide guidance on when the GP should refer back to the specialist. For everything else, please see BNF or SPC.

Side effects and management	The most commonly reported adverse drug reaction is headache, affecting approximately 21% of patients. This is usually mild or moderate, dose-dependent and disappears within a few days. Serious rash requiring hospitalisation and discontinuation of treatment has been reported with the use of modafinil and rare cases of serious or life-threatening rash, including Stevens - Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN), and Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) have been reported in adults and children in worldwide post-marketing experience. **Modafinil should be discontinued at the first sign of rash and not restarted.** If new or worsening of existing psychiatric symptoms develop in association with modafinil treatment, modafinil should be discontinued and not restarted. Patients should be monitored at each dose adjustment and regularly throughout treatment. Modafinil is associated with the onset or worsening of anxiety. Patients with major anxiety should only receive treatment with modafinil in a specialist unit. Modafinil is associated with the onset or worsening of psychotic symptoms or manic symptoms (including hallucinations, delusions, agitation or mania) and with the onset or worsening of aggressive or hostile behaviour. Other commonly reported adverse effects include GI upset, decreased appetite, nervousness, insomnia, anxiety, depression, abnormal thinking,

	confusion, irritability, dizziness, somnolence, blurred vision, tachycardia and vasodilation.
Referral back to specialist	Any sign of rash or hypersensitivity reaction (discontinue modafinil) Headache that is severe, persistent or otherwise not tolerated. Development, or exacerbation, of psychiatric disorders, at the onset or worsening of aggressive or hostile behaviour and in the case of suicidal ideation. Abnormal liver function tests; the dosage of modafinil should be reduced by half in patients with severe hepatic impairment.

Section 5: Other Issues

(e.g. Drug Interactions, Contra-indications, Cautions, Special Recommendations)

Please list only the most pertinent action for GP to take (For full list please see BNF or SPC)

Issues	**Significant Drug Interactions** 1. **Anticonvulsants:** Co-administration of potent inducers of CYP activity, such as carbamazepine and phenobarbital, could reduce the plasma levels of modafinil. Due to a possible inhibition of CYP2C19 by modafinil and suppression of CYP2C9 the clearance of phenytoin may be decreased when modafinil is administered concomitantly. Patients should be monitored for signs of phenytoin toxicity, and repeated measurements of phenytoin plasma levels may be appropriate upon initiation or discontinuation of treatment with modafinil. 2. **Steroidal contraceptives:** The effectiveness of steroidal contraceptives may be impaired due to induction of CYP3A4/5 by modafinil. Alternative or concomitant methods of contraception are recommended for patients treated with modafinil. Adequate contraception will require continuation of these methods for two months after stopping modafinil. 3. Sexually active women of child-bearing potential should be established on a contraceptive programme before taking modafinil. Since the effectiveness of oral contraceptives may be reduced with modafinil, manufacturers recommends alternative/concomitant methods of contraception are recommended (and for 2 months after discontinuation). For women not wishing to use either a barrier method or non-medicated IUD, alternatives that could be considered include; increasing the dose of oestrogen in a combined pill, injections of some progestogens or a medicated IUD however risks and benefits of each option should be considered. Please see FSRH guidance for further information on contraception with enzyme inducing drugs. https://www.fsrh.org/documents/ceu-clinical-guidance-drug-interactions-with-hormonal/ 4. **Antidepressants:** A number of tricyclic antidepressants and selective serotonin reuptake inhibitors are largely metabolised by CYP2D6. In patients deficient in CYP2D6 (approximately 10% of a Caucasian population) a normally ancillary metabolic pathway involving CYP2C19 becomes more important. As modafinil may inhibit CYP2C19, lower doses of antidepressants may be required in such patients. 5. **Anticoagulants:** Due to possible suppression of CYP2C9 by modafinil the clearance of warfarin may be decreased when

	modafinil is administered concomitantly. Prothrombin times should be monitored regularly during the first 2 months of modafinil use and after changes in modafinil dosage. **Contraindications** 1. Hypersensitivity to the active substance or to any of the excipients. 2. Uncontrolled moderate to severe hypertension and in patients with cardiac arrhythmias. **Cautions** Prescribers should be aware of the theoretical potential for diversion- In the USA, modafinil is increasingly being diverted for nonmedical use by healthy individuals in the expectation that it will improve cognitive performance. Other specific to drug Responsibilities for Secondary Care 1. Clinical assessment of the need for treatment should be performed on a periodic basis. 2. Dose titration as appropriate. Responsibility for Primary Care 1. Clinical assessment of the need for treatment should be performed on a periodic basis.
Reminder to ask patient about specific problems	Enquire about the occurrence of rash, hypersensitivity reactions, mental health issues or behavioural changes.

Section 6: Advice to the patient

Advice for prescribing clinician to inform patient

1. Modafinil is not recommended for use during pregnancy or in women of childbearing potential unless they are using effective contraception. As modafinil may reduce the effectiveness of oral contraception, alternative additional methods of contraception are required.
2. To inform a clinician immediately if they develop any rash or other hypersensitivity reactions.
3. To inform a clinician if they experience any mental health issues or behavioural changes.

Section 7: Generic principles of shared care for SECONDARY CARE

Please do not amend.

Core responsibilities

1. Initiating treatment and prescribing for the length of time specified in **section 1.**
2. Undertaking the clinical assessment and monitoring for the length of time specified in **section 1** and thereafter undertaking any ongoing monitoring as detailed in **section 3.**
3. Communicate details of the above in 1 and 2 to GP within the first month of treatment. This information should be transferred in a timely manner.
4. Refer patients to GP and provide information of further action where appropriate e.g. if blood test is due.
5. To provide advice to primary care when appropriate.
6. Review concurrent medications for potential interaction prior to initiation of drug specified in **section 1.**
7. Stopping treatment where appropriate or providing advice on when to stop.
8. Reporting adverse events to the MHRA.
9. Reminder to ask patients about particular problems see **section 5.**

Section 8: Generic principles of shared care for PRIMARY CARE

Please do not amend.

Core responsibilities

1. Responsible for taking over prescribing after the length of time specified in **section 1.**
2. Responsible for any clinical assessment and monitoring if detailed in **section 3** after the length of time specified in **section 1.**
3. Review of any new concurrent medications for potential interactions.
4. Reporting adverse events to the MHRA.
5. Refer for advice to specialist where appropriate.
6. Reminder to ask patients about particular problems see **section 5.**

Section 9: Contact Details

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Section 10: Document Details

Date prepared	May 2024
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Section 11: Collaboration

All shared care protocols should be BNSSG wide where possible. Specialists in any one discipline are encouraged to collaborate across the health community in preparing shared care guidance. Please give details

1. Click here to enter details

Section 12: References

Please list references

1. Summary of Product Characteristics, Modafinil 100mg. Available from: https://www.medicines.org.uk/emc/product/4319/smpc Last update 20 Feb 2024
2. BNF87, March - September 2024
3. The Renal Drug Database, Modafinil. Available from: https://www.renaldrugdatabase.com/s/article/MODAFINIL

4. Stockleys Drug Interactions – Online (https://www.medicinescomplete.com/#/interactions/stockley)
5. Faculty of Sexual and Reproductive Health, CEU clinical guidance: Drug Interactions with Hormonal Contraception 2022 https://www.fsrh.org/documents/ceu-clinical-guidance-drug-interactions-with-hormonal/