THE SHEFFIELD AREA PRESCRIBING GROUP

Shared Care Protocol

for

Modafinil

Issue 2.1 April 2021

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Statement of Purpose

This shared care protocol (SCP) has been written to enable the continuation of care by primary care clinicians of **adult** patients initiated on modafinil for the licensed indication of narcolepsy at Sheffield Teaching Hospitals NHS Foundation Trust. The licensed indication for modafinil is restricted across Europe to narcolepsy only (MHRA 2014).

Unlicensed therapeutic indications that been approved by the STH Medicine Safety Committee are also detailed in this SCP and are clearly indicated in the table under "Indication". These indications are classified as red on the Sheffield Traffic Light Drug (TLD) List, as defined below:

'RED TLD: Prescribing and ongoing supply is normally undertaken by a consultant or other physician within a secondary care service. In some exceptional circumstances and following discussion between primary and secondary care, GPs may consider it to be in the patient's best interest for drugs in the Red section of the traffic light scheme to be prescribed in primary care.'

Users should be aware that this document is guidance on the management of a condition, not a commissioning arrangement.

Responsibilities of specialist clinician

- To discuss benefits and side effects of treatment with the patient/carer and obtained informed consent. Where the indication for modafinil is off-licence, in accordance with STH FT policy for the use of unlicensed and off-licence medicines, the prescriber will explain this to the patient with the potential benefits and risks of treatment
- To initiate modafinil in appropriate patients
- To check baseline BP (and document in patient held booklet) and ECG +/- 24 hour tape (if indicated – palpitations or cardiac risk factors)
- To ensure that arrangements are in place to undertake fortnightly BP monitoring and checks for side effects, including rash and hallucinations
    - This may be undertaken by a community pharmacist or by the patient themselves providing they have a BP meter which they have been trained to use and they know when to seek medical advice. BP results should be documented in the patient held booklet.
- To ensure that women of childbearing potential are aware of the possibility of congenital malformations when administered during pregnancy and of the interaction with oral hormonal contraception; to ensure they are receiving an appropriate contraceptive method.
- To prescribe modafinil until the dose is stabilised
- To contact patient's primary care prescriber to request prescribing under shared care and send a link to or copy of the shared care protocol
- To advise the primary care prescriber regarding continuation of treatment, including the length of treatment
- To discuss any concerns with the primary care prescriber regarding the patient's therapy
- To undertake annual monitoring of BP and ECG +/- 24 hour tape (where indicated)

Responsibilities of the primary care clinician

- To refer appropriate patients to secondary care for assessment
- To agree to prescribe for patients in line with the shared care agreement
- To ensure women of child bearing potential are receiving appropriate contraception
- To continue to prescribe for the patient as advised by the specialist
- To inform the specialist if the patient discontinues treatment for any reason
- To seek the advice of the specialist if any concerns with the patient's therapy, including waning of effect over time and problematic side effects

- To report any serious adverse reaction through the MHRA 'yellow card' reporting scheme and to the referring specialist
- To undertake blood pressure and heart rate monitoring as described in the monitoring protocol
- To conduct an annual medication review
- In the event that the primary care prescriber is not able to prescribe, or where the SCP is agreed but the specialist is still prescribing certain items e.g. hospital only product, the primary care prescriber will provide the specialist with full details of existing therapy promptly by a secure method on request
- For medication supplied from another provider prescribers are advised to follow recommendations for Recording Specialist Issued Drugs on Clinical Practice Systems

Responsibilities of Patients or Carers

- To be fully involved in, and in agreement with, the decision to move to shared care
- To attend hospital and primary care clinic appointments and to bring their patient held booklet; failure to attend will potentially result in the medication being stopped
- Present rapidly to the primary care prescriber or specialist should their clinical condition significantly worsen
- Report any suspected adverse effects to their specialist or primary care prescriber whilst taking modafinil
- To read the product information given to them
- To take modafinil as prescribed
- To take responsibility for appropriate contraceptive precautions, where applicable
- Inform the specialist, primary care prescriber or community pharmacist dispensing their prescriptions of any other medication being taken – including over-the-counter medication

Indication

	Indication	**Clinical Speciality**
1)	Hypersomnolence due to obstructive sleep apnoea despite CPAP (unlicensed indication)	Respiratory
2)	Fatigue or hypersomnolence associated with drug therapy prescribed for symptom management which is not responsive to methylphenidate or where methylphenidate is contra-indicated (unlicensed indication)	Palliative care
3)	Fatigue in multiple sclerosis (unlicensed indication)	Multiple sclerosis service
4)	a) Excessive sleepiness associated with narcolepsy with or without cataplexy (licensed indication) b) Idiopathic hypersomnolence (unlicensed indication) c) Excessive daytime sleepiness (EDS) secondary to neurological disorders other than narcolepsy with or without cataplexy (unlicensed indication)	Neurology sleep clinic

Selection of patients

Clinical Speciality	**Patient Selection Criteria**
1) Respiratory	Robust exclusion of other sleep disorders (respiratory, neurological, psychological) and optimisation of sleep hygiene issues. Exclusion of patients with contra-indications (severe hypertension and cardiac

	arrhythmias). Careful consideration will also be given to any precautions to use detailed in the SPC.
2) Palliative care	Patient under the care of palliative care and meet the criteria of symptom management which is not responsive to methylphenidate or where methylphenidate is contra-indicated. Exclusion of patients with contra-indications (severe hypertension and cardiac arrhythmias). Careful consideration will also be given to any precautions to use detailed in the SPC.
3) Multiple sclerosis	Patients under the care of the Multiple Sclerosis Service who have not responded to fatigue management and lifestyle advice with a clinical nurse specialist in MS or an Occupational Therapist or a trial of amantadine up to a maximum dose of 200mg morning and lunchtime. Exclusion of patients with contra-indications (severe hypertension and cardiac arrhythmias). Careful consideration will also be given to any precautions to use detailed in the SPC.
4) Neurology sleep clinic	Detailed clinical and polysomnographic evaluation will be undertaken for an accurate diagnosis. Exclusion of patients with contra-indications (severe hypertension and cardiac arrhythmias). Careful consideration will also be given to any precautions to use detailed in the SPC.

Dosage

Clinical Speciality	Dosing Regime
1) Respiratory	Initial dose: 50mg twice daily at 9am and 12pm. Increased to 100mg daily at 9am and 50mg daily at 12pm after 6 weeks. Increased to 100mg twice daily after a further 6 weeks. Incremental increases on a 6 week basis up to a maximum dose of 200mg twice daily or until side effects limit therapy.
2) Palliative care	Initial dose: 100mg each morning. Increased if necessary after one week to 200mg each morning. Maximum 400mg/24 hours.
3) Multiple sclerosis	Initial dose: 100mg each morning. Increased fortnightly, as necessary, by increments of 100mg to a maximum dose of 200mg twice daily The second dose should be taken no later than lunchtime.
4) Neurology sleep clinic (for all indications)	Initial dose: 100mg each morning. Increased fortnightly as necessary by increments of 100mg to a maximum dose of 400mg daily in one or two divided doses. The second dose should be taken no later than mid afternoon.

Contra-indications

Note: the current BNF and the SPC remain authoritative

- Hypersensitivity to the active substance or to any of the excipients
- Uncontrolled moderate to severe hypertension and in patients with cardiac arrhythmias
- Pregnancy. Post-marketing reports show that the use of modafinil in pregnancy is suspected to cause congenital malformations such as congenital heart defects, hypospadias, and orofacial clefts (MHRA Drug Safety Update). Modafinil should not be used during pregnancy; women of childbearing potential must use effective contraception (see drug interactions) during treatment and for at least 2 months after stopping modafinil. (For further advice see Guidance for primary care clinicians on 'Medicines with teratogenic potential: what is effective contraception and how often is pregnancy testing needed?').
  Refer women who become pregnant or who are planning conception to the specialist.
- Modafinil should not be used during breast feeding.

Side –effects

The details below are not a complete list and the current BNF and the SPC remain authoritative.

Common side effects include:

Headache, decreased appetite, nervousness, insomnia, anxiety, depression, abnormal thinking, confusion, dizziness, somnolence, paraesthesia, blurred vision, tachycardia, palpitation, vasodilatation, abdominal pain, nausea, dry mouth, diarrhoea, dyspepsia, constipation, asthenia, chest pain, abnormal liver function tests, dose related increases in alkaline phosphatase and gamma glutamyl transferase have been observed.

Patients and relatives /carers are to be made aware of the possibility of significant personality change.

Monitoring

Once stabilised, at least 3 monthly blood pressure and heart rate checks in primary care while on therapy.

Modafinil should be discontinued in patients who develop arrhythmia or moderate to severe hypertension (refer to NICE NG136 [August 2019], Hypertension in adults – diagnosis and management); and not restarted until the condition has been adequately evaluated and treated.

Serious rash requiring hospitalisation and discontinuation of treatment has been reported with the use of modafinil occurring within 1 to 5 weeks after treatment initiation. Modafinil should be discontinued at the first sign of rash and not re-started.

Although there have been a limited number of reports, multi-organ hypersensitivity reactions may result in hospitalization or be life-threatening. If suspected, modafinil should be discontinued.

If psychiatric symptoms develop in association with modafinil treatment, including psychotic, manic and suicide related symptoms, modafinil should be discontinued and not restarted.

Interactions

The details below are not a complete list and the current BNF and the SPC remain authoritative.

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.

Hormonal contraceptives: The effectiveness of oral hormonal contraceptives may be impaired due to induction of CYP3A4/5 by modafinil. The Faculty of Sexual and Reproductive Health (FSRH) guidance recommends depot medroxyprogesterone acetate, levonorgestrel-releasing intrauterine system, or the copper intrauterine device as suitable contraceptive methods alongside enzyme-inducing drugs. For emergency contraception a copper intrauterine device is recommended; if this is unsuitable a double dose (3mg) of levonorgestrel can be offered but its efficacy is unknown.

Adequate contraception will require continuation of these methods for at least 2 months after stopping modafinil, as per the SPC.

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.

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.

Financial implications

BNF December 2019 – Drug Tariff prices for non-proprietary products (**prescribe generically** - avoid brand name Provigil®, which is expensive):
30x100mg = £3.47
30x200mg = £6.92

Ordering information

Generic modafinil is available through regular pharmaceutical wholesale chains

Support, education and information

Respiratory
Dr Stephen Bianchi, Consultant in Respiratory and Sleep medicine, STHFT 01142714279/01142714646

Palliative Care
Contact the initiating Palliative Care Consultant
Phone numbers available via Sheffield Palliative Care Formulary which is available on STHFT website & on NHS Sheffield website

Neurology
MS service: Patients under the care of the Sheffield MS service have access to the MS Clinical Nurse Specialist Service. Primary care staff also have access to the MS Clinical Nurse Specialist Service and relevant Consultant Neurologists.

Sheffield sleep clinic: Dr Gary Dennis, Dr Siew Wong, Dr Channa Hewamadduma, Dr Andrew Gibson

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Full list of side-effects is given in the modafinil summary of product characteristics (SPC), available from www.emc.medicines.org.uk

Acknowledgement: Dr S Price, Consultant Neurologist, STHFT

Amendment Version 2:1:

- Pregnancy information updated;
- Wording amended in Indication table 4) to remove ambiguity.