Specialised Medicines Service Guideline ~ Modafinil for excessive sleepiness associated with narcolepsy with or without cataplexy

This guideline highlights significant prescribing issues. Not all prescribing information and potential adverse effects are listed. Please refer to SPC/data sheet for full prescribing data.

Specialist: Please complete letter at the end of this document and send together with the guideline to the GP.

GP: Please indicate whether you wish to share patient's care by completing letter at the end of this document and return to specialist.

GPs are invited to participate. If a GP is not confident to undertake these roles, then they are under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist

The doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Introduction and aims of treatment

Modafinil is an α1-adrenergic agonist which promotes wakefulness, although the precise mechanism(s) through which this occurs is unknown. Modafinil is licensed for use in adults for the treatment of excessive sleepiness associated with narcolepsy with or without cataplexy. Excessive sleepiness is defined as difficulty maintaining wakefulness and an increased likelihood of falling asleep in inappropriate situations.

MHRA Drug Safety Alert (August 2010): The European Medicines Agency has recommended that the use of modafinil should be restricted to treat only sleepiness associated with narcolepsy, and that it should no longer be used for the treatment of excessive sleepiness associated with obstructive sleep apnoea or chronic shift work sleep disorder.

This guideline refers to the use of modafinil, used in line with its licensed indication, for use in adults for the treatment of excessive sleepiness associated with narcolepsy with or without cataplexy. The use of modafinil for other indications is outside the scope of this guideline.

Specialist responsibilities

- For female patients of child-bearing age, exclude pregnancy prior to initiating treatment
- Undertake pre-treatment assessment, monitoring & follow up as described in "Monitoring" below
- Discuss with the patient (and/or carer) the benefits, side effects, frequency of dosing and monitoring requirements of modafinil treatment; provide relevant supporting information in writing.
- 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
- Discuss with the patient (and/or carer) the need to immediately consult their physician if there is a possibility of pregnancy
- Initiate treatment
- Send a letter to the GP, **within one week**, asking them whether they are willing to participate in the sharing of care for a particular patient. Include results of any relevant baseline tests

- Review and act on results of monitoring until GP agrees to share care and takes on responsibility for monitoring
- Advise the GP (in writing) of any dose changes required
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed, including the current dose to be prescribed
- Provide any other advice or information for the GP if required.

General practitioner responsibilities

- Ensure a timely reply is sent to specialist in response to request for sharing of care.

If GP has agreed to share care:

- Undertake ongoing monitoring and act on results/reported side effects as described in "Monitoring" section below
- Continue to prescribe modafinil in accordance with guidelines
- Report to and seek advice from a specialist on any aspect of patient care which is of concern to the GP and may affect treatment
- Report adverse events to specialist and to MHRA via the yellow card scheme
- Stop treatment/amend dose in the case of a severe adverse event or as per prescribing guideline.

Monitoring

Baseline assessment to be completed by the specialist service provider:

- Electrocardiogram – patients with abnormal findings should be further evaluated before modafinil treatment can be initiated
- Blood pressure.

Ongoing monitoring to be completed by the GP:

- Blood pressure, heart rate:
    - **For patients with existing hypertension/heart disease**, two weeks* from start of treatment, then after 1 month*, then as per all patients:
    - **All patients**, three monthly for 6 months, then six monthly
- Adverse effects including adverse behaviours or thoughts – at every contact.

*The specialist service provider must ensure the GP has accepted the sharing of care and has adequate notice to be able to undertake this early monitoring. Until this has been confirmed with the GP, specialist services retain responsibility for monitoring and prescribing.

Action to be taken by GP:

If patients develop arrhythmia or moderate to severe hypertension, discontinue modafinil and seek specialist advice. Modafinil should not be restarted until the condition has been adequately evaluated and treated.

Modafinil should be discontinued **and not re-started** at the first sign of rash; or if psychiatric disorders (including anxiety, suicide-related symptoms, psychotic or manic symptoms, bipolar disorders, and aggressive or hostile behaviour) develop.

Patient/carer responsibilities

- Ensure they understand the importance of monitoring treatment and attend specialist appointments and/ or GP appointments to ensure timely monitoring can be completed (in accordance with the prescribing guideline)
- Understand that treatment may be stopped if they do not attend for monitoring & treatment review
- Ensure they have a clear understanding of the treatment, expected benefits and potential side effects
- Take (or support administration of) medication as directed by the prescriber
- Report any adverse effects to the GP and/or specialist regarding their treatment, particularly any adverse behaviours or thoughts, such as suicidal ideation
- Sexually active women of child-bearing potential should use a reliable method of contraception during treatment and for two months after stopping (see “Pregnancy and lactation”, below)
- Advise the GP immediately if pregnancy is suspected
- Store their medicines safely and securely
  Patients with narcolepsy who hold a driving license must ensure the DVLA is aware of their diagnosis.

Supporting Information

Please refer to individual product SPCs for full prescribing data; these can be accessed at www.medicines.org.uk

Dosage and administration

Refer to the current BNF or individual product SPCs for Modafinil.

Usual dose:

- Adult over 18 years: initially 200 mg daily, either in 2 divided doses morning and at noon or as a single dose in the morning, dose adjusted according to response to 200–400 mg daily in 2 divided doses or as a single dose;
- Elderly: initiate at 100 mg daily

Patient specific guidance will be provided to the GP by the specialist.

Contraindications and precautions

Refer to individual product SPCs for Modafinil.

Modafinil is contraindicated in patients with uncontrolled moderate to severe hypertension and in patients with cardiac arrhythmias.

There is inadequate information to determine safety and efficacy of dosing in patients with renal impairment, specialist advice should be sought.

The dosage of modafinil should be reduced by half in patients with severe hepatic impairment.

Modafinil should be used with caution in patients with a history of:

- Psychosis, depression, or mania
- Abuse of alcohol, drugs, or illicit substances.

Such patients should be monitored closely and advised to report any suspected adverse behaviours or thoughts - patients should be assessed immediately and treatment stopped if appropriate.

Pregnancy and lactation

Refer to individual product SPCs for Modafinil.

There is limited data on the use of modafinil in pregnant women; studies in animals have shown reproductive toxicity. Modafinil is not recommended for use during pregnancy or in women of childbearing potential unless they are using effective contraception (See “Drug interactions”, below).

Modafinil should not be used during breast feeding.

Effects on ability to drive and use machines

Patients with abnormal levels of sleepiness who take modafinil should be advised that their level of wakefulness may not return to normal. Patients with excessive sleepiness, including those taking modafinil should be frequently reassessed for their degree of sleepiness and, if appropriate, advised to avoid driving or any other potentially dangerous activity

Undesirable effects such as blurred vision or dizziness might also affect ability to drive

Patients with narcolepsy who hold a driving license must ensure that the DVLA is aware of their diagnosis, for more information refer to https://www.gov.uk/narcolepsy-and-driving

Adverse effects

Refer to individual product SPCs for Modafinil.

The most commonly reported adverse drug reaction is headache; this is usually mild or moderate, dose-dependent and disappears within a few days.

Rash: Modafinil should be discontinued at the first sign of rash and not re-started.

Psychiatric disorders (including anxiety, suicide-related symptoms, psychotic or manic symptoms, bipolar disorders, and aggressive or hostile behaviour):

- For patients without underlying psychiatric disorders, if psychiatric disorders emerge, Modafinil should be discontinued and not re-started.
- For patients with underlying psychiatric disorders, modafinil should only be used when the benefits exceed the risks, and discontinuation of treatment with modafinil should be considered if there is a worsening of underlying psychiatric disorders. Seek specialist advice.

Abuse, misuse, and diversion

The possibility of dependence with long-term use cannot be entirely excluded; caution should be exercised in administering modafinil to patients with history of alcohol, drug or illicit substance abuse.

Drug interactions

This list is not exhaustive, for additional information and further interactions, consult the BNF and individual product SPCs for Modafinil.

- The effectiveness of steroidal contraceptives may be impaired 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.
- Warfarin levels may be increased by modafinil. Prothrombin times should be monitored regularly during the first 2 months of modafinil use and after changes in modafinil dosage.
- Phenytoin levels may be increased by modafinil. Monitor for signs of phenytoin toxicity.

The following drug interactions are classified in the online version of the BNF as **potentially serious;** concomitant administration of the drugs involved should be **avoided** (or only undertaken with caution and appropriate monitoring).

- **Bosutinib:** modafinil possibly reduces plasma concentration of bosutinib – manufacturer of bosutinib advises avoid concomitant use
- **Ciclosporin:** modafinil reduces plasma concentration of ciclosporin
- **Guanfacine:** modafinil possibly reduces plasma concentration of guanfacine – increase dose of guanfacine
- **Oestrogens:** modafinil accelerates metabolism of oestrogens (reduced contraceptive effect with combined oral contraceptives, contraceptive patches, and vaginal rings).

Support

Contact details
Specific contact and support details will be provided to the GP by the specialist when requesting the sharing of care. Consultants can also be contacted via the individual trusts' switchboards: Northern Devon Healthcare NHS Trust: 01271 322577 Plymouth Hospitals NHS Trust: 01752 202082 Royal Devon and Exeter NHS Foundation Trust: 01392 411611 Torbay and South Devon NHS Foundation Trust: 0300 456 8000 (local rate) or 01803 614567

Date ratified: January 2018

Shared Care Agreement Letter - Consultant Request

To:	**Dr:**
	Practice Address:
Patient Name:	
NHS Number:	
Date of birth:	
Address:	

Diagnosed condition:..……

I recommend treatment with the following drug: …….

At the following dosage: ……..……..

I request your agreement to continue the care of this patient according to the Specialised Medicines Service Guidelines for this drug. The patient has been initiated on treatment and stabilised in accordance with the appropriate Specialised Medicines Service Guidelines.

The results of any relevant baseline tests and any additional supportive information (target range, date of last blood test etc.) are included below:

Principles:

GPs are invited to participate, but **if the GP is not confident to undertake these roles then they are under no obligation to do so.** If so, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If asked to prescribe this drug the GP should reply to this request as soon as practical. Continuing the care assumes communication between the specialist, GP and patient; the intention should be explained to the patient and accepted by them.

Remember: the doctor who prescribes the medication has the clinical and legal responsibility for the drug and the consequences of its use.

Signed:			**Date:**
Consultant name:			
Telephone number:		**Fax number**	
Email address			

Please sign below and return promptly. Remember to keep a copy of this letter for the patient's records. If this letter is not returned sharing of the care for this patient will not commence.

GP Response

I agree / do not agree* to share the care of this patient in accordance with the Specialised Medicines Guideline.

Signed: …….. Date: …….

GP name: …… *Delete as appropriate.

Patient agreement

I understand and agree to my responsibilities as described above.

Signed: …….. Date: …….

Name: