



Surrey (East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG & Surrey Heath) North East Hampshire & Farnham CCG, Crawley CCG and Horsham & Mid-Sussex CCG

SHARED CARE PRESCRIBING GUIDELINE

Modafinil (Provigil®) for the treatment of adults with excessive sleepiness with narcolepsy

Prescribing Clinical Network classification: Amber

(Note: Modafinil is considered Red for all unlicensed indications)

N.B. The eligibility criteria included here apply to new patients commencing treatment under this guideline & not to existing patients whose treatment was initiated under the previous version. However, monitoring and discontinuation criteria apply to all patients.

NOTES to the GP

Amber drugs: Prescribing to be initiated by a hospital specialist (or if appropriate by a GP with specialist interest) but with the potential to transfer to primary care. The expectation is that these guidelines should provide sufficient information to enable GPs to be confident to take clinical and legal responsibility for prescribing these drugs.

The questions below will help you confirm this:

- Is the patient's condition predictable?
- Do you have the relevant knowledge, skills and access to equipment to allow you to monitor treatment as indicated in this shared care prescribing guideline?
- Have you been provided with relevant clinical details including monitoring data?

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility. Sign and return a copy of page 4 to the requesting consultant at the Acute Trust. Until the requesting consultant at the Acute Trust has received a signed copy of page 4 indicating that shared care has been agreed all care (including prescribing) remains with the consultant at the Acute Trust.

If the answer is NO to any of these questions, you should not accept prescribing responsibility. You should write to the consultant outlining your reasons for NOT prescribing. If you do not have the confidence to prescribe, we suggest you discuss this with your local Trust/specialist service, who will be willing to provide training and support. If you still lack the confidence to accept clinical responsibility, you still have the right to decline. Your PCT pharmacist will assist you in making decisions about shared care.

Prescribing unlicensed medicines or medicines outside the recommendations of their marketing authorisation alters (and probably increases) the prescriber's professional responsibility and potential liability. The prescriber should be able to justify and feel competent in using such medicines.

The patient's best interests are always paramount

The GP has the right to refuse to agree to shared care, in such an event the total clinical responsibility will remain with the consultant

Reason for Update: New		Prepared by: Linda Honey
Valid from: November 2014	Review date: November 2017	Approved by: PCN Nov 2014
Version: 0.1	Supersedes version: N/A	Approved by: N/A

Information

This information sheet does not replace the SPC, which should be read in conjunction with this guidance. Prescribers should also refer to the appropriate paragraph in the current edition of the BNF.

Link to the relevant SPC website: <https://www.medicines.org.uk/emc/search>

The Prescribing Clinical Network have endorsed the use of modafinil as **amber** on the traffic light system when used within its licensed indication 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. For all other indications modafinil is considered as **red** on the traffic light system.

Modafinil should be used only in patients who have had a complete evaluation of their excessive sleepiness, and in whom a diagnosis of narcolepsy, has been made in accordance with ICSD diagnostic criteria. Such an evaluation usually consists, in addition to the patient's history, sleep measurements testing (for example an Epworth Sleepiness Scale score¹ of 11 or more) in a laboratory setting and exclusion of other possible causes of the observed hypersomnia. The precise mechanism(s) through which modafinil promotes wakefulness is unknown.

In November 2010 the EMA's CHMP concluded that the benefits of modafinil continued to outweigh the risks only in the treatment of narcolepsy. The CHMP also concluded that modafinil should **no** longer be used to treat:

- Obstructive sleep apnoea; (including in patients with excessive sleepiness despite correctly using a Continuous Positive Airway Pressure machine)
- Shift work sleep disorder
- Idiopathic hypersomnia

1. Dose

The recommended starting daily dose is 200 mg. The total daily dose may be taken as a single dose in the morning or as two doses, one in the morning and one at 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.

Initiation and dose adjustment will be the responsibility of the Specialist Centre. Treatment should be continued only when it is considered to be having a worthwhile effect in terms of maintaining wakefulness.

2. Contraindications

Modafinil is contraindicated in those with:

- Hypersensitivity to the active substance or to any of the excipients
- Uncontrolled moderate to severe hypertension
- Cardiac arrhythmias

3. Special warnings and precautions for use

- 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, alternative / concomitant methods of contraception are recommended (and for 2 months after discontinuation). **For women not wishing to use either a barrier method or a non-medicated IUD, alternatives are; increasing the dose of oestrogen in a combined pill, injections of some progestogens or a medicated IUD such as Mirena²**
- 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 be regularly monitored in patients receiving modafinil. 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

¹ http://www.britishsnoring.co.uk/sleep_apnoea/epworth_sleepiness_scale.php

² <http://www.narcolepsy.org.uk/NewsEvents/Modafinilcontraceptives.aspx>

- It is recommended that modafinil tablets not be used in patients with a history of left ventricular hypertrophy or cor pulmonale. Modafinil should not be used in patients with mitral valve prolapse who have experienced the mitral valve prolapse syndrome when previously receiving CNS stimulants
- Patients should be advised that modafinil is not a replacement for sleep and good sleep hygiene should be maintained. Steps to ensure good sleep hygiene may include a review of caffeine intake
- **Serious skin reactions:** Stevens Johnson Syndrome, erythema multiforme, and toxic epidermal necrolysis have been reported with modafinil.³ These conditions usually occurred in the first 5 weeks of treatment, although there have been isolated cases after more than 3 months' treatment. In clinical trials, the risk of rash resulting in discontinuation of modafinil treatment was higher in children than adults (0.8% vs no cases). Modafinil is not authorised for use in children.
- **Psychiatric symptoms:** suicidal ideation, hallucinations, delusion, aggression, psychosis and mania have been reported in association with modafinil. These reactions have occurred mainly, but not exclusively, in patients with a history of psychosis, depression or mania.

Advice for healthcare professionals:

- Modafinil should be discontinued at the first sign of rash and not restarted
- Modafinil should be discontinued in patients who experience any psychiatric symptoms and not restarted
- Modafinil should be used with caution in patients with a history of psychosis, depression or mania
- Modafinil should be used in caution in patients with a history of alcohol, drug or illicit substance abuse
- An ECG is recommended before modafinil is initiated. Blood pressure and heart rate should be regularly monitored in patients receiving modafinil

4. Interactions

- **Ciclosporin:** modafinil reduces plasma concentration of ciclosporin
- **Oestrogens:** modafinil accelerates metabolism of oestrogens (reduced contraceptive effect)
- **Phenytoin:** modafinil possibly increases plasma concentration of phenytoin

5. Adverse drug reactions (all serious adverse events should be reported using the yellow card system)

- **Headache:** very common affecting approx. 21% of patients. Usually mild or moderate, dose dependent and disappears within a few days. Discuss with specialist if persists
- **Tachycardia / palpitations:** common >1/100 to <1/10. Discontinue in patients who develop arrhythmia and do not restart until the condition has been adequately evaluated and treated
- **Gastrointestinal:** common >1/100 to <1/10. Include abdominal pain, nausea, dry mouth, diarrhoea, dyspepsia, constipation and decreased appetite. Discuss with specialist if severe or persistent.
- **Serious skin reactions:** including erythema multiforme, Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis and drug rash with Eosinophilia and Systemic Symptoms (DRESS). Discontinue at the first sign of rash and do not restart.
- **Psychiatric symptoms:** including psychosis, mania, delusions or hallucinations and suicidal ideation. Discontinue in patients who experience any psychiatric symptoms and do not restart.
- **Various:** common >1/100 to <1/10. Include:
 - Abnormal LFTs (dose related increases in ALP & GGT)
 - Dizziness, somnolence, paraesthesia, blurred vision
 - Vasodilation, chest pain
 - Asthenia
 - Nervousness, insomnia, anxiety, depression, abnormal thinking, confusion
 Discuss with specialist if substantial or persistent.

³ The FDA reported that it had received 6 cases of severe cutaneous adverse effects associated with modafinil from its initial marketing in Dec 98 to Jan 07; of these, 5 required hospitalisation.

RESPONSIBILITIES and ROLES

Specialist responsibilities	
1	Diagnosis of narcolepsy in accordance with ICSD diagnostic criteria
2	Evaluation of excessive sleepiness which usually consists, in addition to the patient's history, sleep measurements testing (for example an Epworth Sleepiness Scale score of 11 or more) in a laboratory setting and exclusion of other possible causes of hypersomnia
3	To discuss the aims, benefits and side effects of treatment with the patient aswell as their role (particularly skin reactions and psychiatric symptoms)
4	Explain to the patient their treatment plan including the dosing schedule
5	Baseline monitoring undertaken: <ul style="list-style-type: none"> • Physical examination • FBC, U&Es, creatinine, eGFR, LFTs & TFTs • ECG – pts with abnormal findings should receive further specialist evaluation and treatment before modafinil treatment is considered
6	To initiate therapy by prescribing for a minimum of 3 months and make any dosage adjustments
7	Monitor and evaluate response to treatment, including adverse drug reactions, with the patient and to continue / discontinue treatment in line with agreed treatment plan
8	Discuss the possibility of shared care with the patient and ensure they understand the plan for their subsequent treatment
9	Supply GP with summary of patient review (including anticipated length of treatment) and a copy of the shared care guideline recommending that a shared care arrangement is initiated.
10	To re-evaluate the long-term use for the individual patient on a 6-monthly basis (yearly once stable). This will include assessment of any development of <i>de novo</i> or exacerbation of pre-existing psychiatric disorders – particularly the appearance or worsening of suicide-related behaviour.
11	To undertake LFTs at 2, 6 and 12 months after initiation and yearly thereafter. The dose of modafinil should be reduced by half in patients with severe hepatic impairment.
12	Advise GP if treatment is to discontinue at any point (eg for reasons of efficacy or tolerability)
13	Inform GP if patient does not attend planned follow-up
General Practitioner responsibilities	
1	To return the shared care agreement form to the requesting consultant
2	Once the patient is on stable dose, to issue ongoing prescriptions for modafinil as per dosage schedule recommended by the specialist
3	Ongoing physical health monitoring and management (BP and heart rate should be monitored every 6 months - 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)
4	Monitoring response and report any adverse drug reactions (ADRs) to the MHRA and the consultant
5	Seek advice from consultant if there is a significant change in the patient's condition, or if there are any concerns with the patient's therapy
6	Reduce/stop treatment in line with secondary care clinician's advice
Patient's / Carer's role	
1	Ask the specialist or GP for information, if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with modafinil
3	Tell the specialist or GP of any other medication being taken, including over-the-counter products.
4	Read the patient information leaflet included with your medication and report any side effects or concerns you have to the specialist or GP

BACK-UP ADVICE AND SUPPORT

Contact details	Specialist	Telephone No.	Email address: (NHS NET)
Specialist:			
Hospital Pharmacy:			
Out of hours contact:			

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Agreement for transfer of prescribing to GP

Patient details / addressograph:

Name.....
 Address.....
,
,
,
 DOB.....
 Hospital No.....

Drug name and dose:

The following tests, investigations have been carried out:

List any relevant tests:

Date initiated:.....

At the last patient review the drug appeared to be effectively controlling symptoms/ providing benefit:
 Yes / No

The patients has now been stabilised on a dose of:

I will arrange to review this patient regularly. Date of next clinic appointment:.....

Consultant: Address: Contact Number
GP: Address: Contact Number
Main Carer: Contact Number:
Key worker if appropriate: Contact Number:

Agreement to shared care, to be signed by GP and Consultant. Consultant Signature: Date:
GP Signature: Date:
If shared care is agreed and GP has signed above please return a copy of this page to the requesting consultant or alternatively fax to: Acute Trust please insert appropriate Fax Number: