

# Modafinil

## Traffic light classification - AMBER 2 Information sheet for Primary Care Prescribers

### Key Points

- Modafinil may be prescribed locally for narcolepsy and fatigue in MS (off-label) as per the APC formulary.
- Regular monitoring requirements include measurement of Heart Rate and Blood Pressure and assessment for any deterioration in Mental Health every 6 -months. No routine blood tests or ECG is required.
- Modafinil should not be used during pregnancy. Patients of childbearing potential must use reliable and effective contraception during treatment with, and for two months after stopping, modafinil.
- For contact details of named local Specialists who can offer support if you have a clinical query, see Page 5.

### Indications<sup>1</sup>

Modafinil is indicated in adults for the treatment of excessive sleepiness associated with narcolepsy with or without cataplexy (licensed indication).

It may also be used off-label for the treatment of fatigue in Multiple Sclerosis (MS).

### Therapeutic Summary

Modafinil is a wakefulness-promoting agent that acts on the CNS. It is an established first-line treatment for narcolepsy and, if effective and tolerated, treatment is envisaged to be lifelong.

For the treatment of fatigue in MS, treatment with modafinil may be considered as described in [NICE NG220: Multiple sclerosis in adults: management](#). Lifestyle measures are considered first line, but for some, these are insufficient and pharmacological treatments may be required.

### Medicines Initiation

For the treatment of narcolepsy, modafinil will be initiated by a Sleep Specialist and any decision to use it will be a joint decision made in the Neuro-respiratory Sleep Clinic at NUH.

For the treatment of fatigue in MS, modafinil will be initiated by a Specialist and prescribing responsibility should only be transferred to Primary Care once effectiveness and tolerability has been demonstrated and the person with MS is on a stable dose.

### Products available<sup>2</sup>

Modafinil is available generically as 100mg and 200mg tablets.

30 x 100mg tablets cost £1.90

30 x 200mg tablets cost £8.91

It is therefore more cost effective to prescribe 200mg doses as 2x100mg tablets.

## Dosages and route of administration<sup>1,3</sup>

### *Narcolepsy*

The recommended starting daily dose is between 100mg and 200 mg. It is recommended that patients over 65 years of age commence therapy at 100 mg daily. Doses of up to 400mg can be used in patients with insufficient response to the initial modafinil dose. The total daily dose may be taken in one to four divided doses.

### *Fatigue in MS*

Modafinil is usually used at a dose of 100mg daily, increasing to 100mg at morning and lunch after a week if necessary. In some patients upto 400mg/day may be needed.

## Duration of treatment

Narcolepsy is a lifelong condition and treatment should be continued for as long as it remains clinically effective and tolerated.

When used for fatigue in MS, treatment will be regularly reviewed by the specialist team to monitor effectiveness, safety and acceptability, adjust the dose, and decide whether to continue or stop the medicine. The frequency of review should take into account the medicine that they are taking, the need for dose adjustments and the person's preferences and circumstances.

## Monitoring Requirements and Responsibilities

Pre-treatment/baseline\* assessments will usually be performed by the specialist and will include: Medical history, measurements of heart rate and blood pressure (for cardiovascular status) and assessment for mental health illness. An ECG is recommended before starting modafinil to check for a normal QTc (<500ms). For those of childbearing potential, pre-conception counselling will be conducted. A pre-pregnancy plan should be made with the patient and shared with relevant health care professionals (see below).

\*Baseline investigations are usually performed by specialists, however there are some cases where primary care maybe requested to carry out these

### Ongoing monitoring

Ongoing monitoring <sup>1</sup>	Frequency <sup>1</sup>
Heart Rate and Blood Pressure	Baseline* then every 6 months. Also before and after each dose change**.  Refer to NICE guidelines for hypertension in adults <sup>4</sup>
Development or worsening of psychiatric disorders	Baseline* then every 6 months. Also before and after each dose change**.
Medication related side-effects	At each visit.
Risk of diversion, misuse / abuse	At each visit.
Reinforcement of pre-conception advice for those of childbearing potential (see below)	At each visit.
ECG	A regular ECG is not recommended unless there is a clinical indication (e.g. family history of cardiomyopathy or cardiac illness or hypertension or concomitant treatment with a medication that may pose an increased cardiac risk)
Routine blood tests	Not recommended unless there is a clinical indication.

\*Baseline investigations are usually performed by specialists, however there are some cases where primary care maybe requested to carry out these

\*\* After every change of dose: The specialist should determine the appropriate timing for this monitoring.

### Explicit criteria for review and discontinuation of the medicine

Sustained resting tachycardia (>120bpm)	Withhold/reduce dose and discuss with specialist team. Timely cardiology input.
Arrhythmia	Withhold/reduce dose and discuss with specialist team. Timely cardiology input.
Systolic blood pressure greater than the 95th percentile (or a clinically significant increase) measured on two occasions	Withhold/reduce dose and discuss with specialist team. Timely cardiology input.
Patient fails to attend for physical monitoring	Arrange a further appointment in a timely manner. If follow up appointments are not attended, do not provide further prescriptions and inform specialist team.
Insomnia	May respond to dose reduction or timing adjustment. Discuss with specialist team.
Reduced appetite, GI disturbance	May respond to dose reduction. Discuss with specialist team.
Development or worsening of psychiatric disorders (anxiety, depression, psychotic symptoms, mania, behavioural changes, suicide related behaviour)	Withhold and discuss with specialist team in a timely manner.
Suspected drug misuse and diversion	Discuss with specialist team.
Serious skin rash or hypersensitivity reaction	Withhold and discuss with specialist team. <b>Modafinil should be discontinued at the first sign of rash and not re-started</b> Although there have been a limited number of reports, multi-organ hypersensitivity reactions may result in hospitalization or be life-threatening. There are no factors that are known to predict the risk of occurrence or the severity of multi-organ hypersensitivity reactions associated with modafinil. Signs and symptoms of this disorder were diverse; however, patients typically, although not exclusively, presented with 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.  Because multi-organ hypersensitivity is variable in its expression, other organ system symptoms and signs, not noted here, may occur.
Pregnancy or patient wishes to conceive	If a patient falls pregnant modafinil must be <b>discontinued immediately</b> and urgent specialist advice should be sought.

	If a patient is planning a pregnancy, this should be discussed with the specialist team. Reinforce advice to not attempt to conceive before specialist review (see below).
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**IF YOU ARE IN ANY DOUBT ABOUT ANY POTENTIAL ADVERSE REACTION, PLEASE CONTACT THE SPECIALIST TEAM.**

### **Contraindications**<sup>1,3,5</sup>

1. Cardiac - uncontrolled moderate or severe hypertension, cardiac arrhythmias, history of clinically significant signs of CNS stimulant-induced mitral valve prolapse (including ischaemic ECG changes, chest pain and arrhythmias), cor pulmonale, left ventricular hypertrophy.
2. Endocrine - hyperthyroidism or thyrotoxicosis, phaeochromocytoma,
3. Psychiatric - anorexia, agitated states, psychosis, uncontrolled bipolar disorder, schizophrenia, suicidal tendencies, glaucoma, history of alcohol or drug abuse
4. Hypersensitivity to the active substance or to any of the excipients listed in the SPC.

### **Precautions**<sup>1,3,5</sup>

Caution should be exercised in giving modafinil to patients with a history of psychiatric disorders including psychosis, depression, mania, major anxiety, agitation, insomnia, co-morbid bipolar disorder or a history of alcohol, drug or illicit substance abuse

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

There is inadequate information to determine safety and efficacy of dosing in renal impairment.

### **Pregnancy and Breastfeeding**<sup>1,3,6,7</sup>

Modafinil should not be used during pregnancy. If a patient falls pregnant modafinil must be **discontinued immediately** and urgent specialist advice should be sought. Any patient that is planning a pregnancy should be referred back to the Specialist team.

Post-marketing reports show that the use of modafinil in pregnancy is associated with a higher rate of congenital malformations such as heart defects, hypospadias, and orofacial clefts. Hence, **patients of childbearing potential must use reliable and effective contraception** during treatment with, and for two months after stopping, modafinil.

**NB:** As modafinil may reduce the effectiveness of some hormonal contraceptives (the combined oral contraceptive pill, the progesterone-only pill and the contraceptive implant), additional methods of contraception are required, or else the woman should first switch to an alternative: the coil (Mirena, copper IUD), depot progestogen-only injectables, or sterilisation.

For further information regarding the risks of modafinil use during pregnancy see [MHRA alert](#).

Modafinil is excreted in breast milk and should not be used in those who are breastfeeding.

### **Driving**<sup>8</sup>

Patients must tell the DVLA of their narcolepsy or MS diagnosis. Please refer to government advice on [driving with medical conditions](#).

### **Clinically relevant medicine interactions and their management**<sup>1,3</sup>

- Anticonvulsants: Co-administration of potent inducers of CYP activity, such as carbamazepine and phenobarbital, could reduce levels of modafinil. Modafinil may decrease the clearance of

phenytoin - monitor for signs of phenytoin toxicity and consider monitoring plasma levels upon initiation or discontinuation of modafinil.

- 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. Adequate contraception will require continuation of these methods for two months after stopping modafinil. (See above for specifics).
- Antidepressants: modafinil may inhibit CYP2C19 mediated metabolism of tricyclic antidepressants and SSRIs, which may be the dominant metabolism pathway in some patients. Lower doses of antidepressants may be required in such patients.
- Anticoagulants: Modafinil may inhibit warfarin metabolism- monitor INR regularly during the first 2 months of modafinil use and after changes in modafinil dosage.
- Other medicinal products: Substances that are largely eliminated via CYP2C19 metabolism, such as diazepam, propranolol and omeprazole may have reduced clearance upon coadministration of modafinil and may thus require dosage reduction.
- Modafinil may induce CYP1A2, CYP2B6 and CYP3A4/5 activities. The largest effects may be on substrates of CYP3A4/5 that undergo significant pre-systemic elimination, particularly via CYP3A enzymes in the gastrointestinal tract. Examples include ciclosporin, HIV-protease inhibitors, buspirone, triazolam, midazolam and most of the calcium channel blockers and statins.

*For a full list of contraindications, precautions and drug interactions refer to the BNF/ product SPC.*

### Information Given to Patient

- The specialist will provide, where relevant, written information to people about diagnosis, assessment, support groups, self-help, psychological treatment, medicine treatment and possible side-effects.
- The patient must be warned to report any suspected adverse reactions to the GP for assessment and to report to their GP or specialist any heart palpitations, psychiatric symptoms or skin rash.
- Patients of childbearing potential should be fully informed of the potential risks to a foetus if modafinil is used during pregnancy and of the need to use effective contraception during treatment with, and for two months after stopping, modafinil. The patient must be warned to inform the GP or specialist of any planned pregnancy before stopping contraception.
- The patient should be warned not to stop medication suddenly, but discuss withdrawal with their specialist first.

### Resources for patients

Narcolepsy: [Narcolepsy - Treatment - NHS](#)

Fatigue in MS: [Modafinil \(Provigil\) | MS Trust](#)  
[Managing MS Fatigue - Help & Support | MS Society](#)  
[Online MS Fatigue Management Course | Multiple Sclerosis Society UK](#)

### ACCESS AND CONTACT POINTS

- **In working hours:**

**Narcolepsy:** Telephone: 0115 924 9924 extension 84777 (Dr Singhal's secretary)

Email: [sumeet.singhal@nuh.nhs.uk](mailto:sumeet.singhal@nuh.nhs.uk)

**MS:** Telephone: 0115 8493285 (MS nurses)

Email: [nuhnt.ms@nhs.net](mailto:nuhnt.ms@nhs.net)

#### **Pharmacy Medicines Information:**

Nottingham University Hospitals - Tel: 0115 970 9200 (patient line)

0115 924 9924 Extension 84185/81200 (**Healthcare professionals only**)

- **Out of Hours**

**Neurologist on-call contact via QMC Switchboard 0115 924 9924 (GPs only)**

## References

1. Modafinil 100mg tablets – Aurobindo Pharma - Milpharm Ltd. Summary of product characteristics [11/2022] available at <https://www.medicines.org.uk/emc/product/4319/smpc> [accessed 03/07/2023].
2. The Electronic Drug Tariff. Accessed via [dm+d browser \(nhsbsa.nhs.uk\)](https://dm+d.browser.nhs.uk) on 03/07/2023
3. BNF, accessed via [BNF \(British National Formulary\) | NICE](https://www.bnf.co.uk) on 03/07/2023
4. Hypertension in adults: diagnosis and management. NICE Clinical Guideline 136 (March 2022). Available: <https://www.nice.org.uk/guidance/ng136>
5. [MHRA: Drug Safety Update March 2011, vol 4 issue 8: A1. Modafinil \(Provigil\): now restricted to narcolepsy](#)
6. Direct Healthcare Professional Communication (DHPC) Modafinil: potential risk of congenital malformations during pregnancy, Jan 2020. Accessed at: <https://assets.publishing.service.gov.uk/media/5e43e03fe5274a6d34ddad60/Modafinil-Jan-2020.pdf>
7. [MHRA Drug Safety Update 2020. Modafinil \(Provigil\): increased risk of congenital malformations if used during pregnancy.](#)
8. DVLA. Narcolepsy and driving [accessed 03/07/2023]. Available from: <https://www.gov.uk/narcolepsy-and-driving>
9. DVLA Multiple Sclerosis and driving [accessed 16/01/2025]. Available from: [Multiple sclerosis and driving - GOV.UK](#)

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