DRUG:

Introduction:

Modafinil for narcolepsy (adults)

Indication: Narcolepsy

A review by the EMA found that modafinil is strongly linked to a risk of serious skin, psychiatric reactions and cardiovascular adverse effects. This led to its restricted license only for narcolepsy.


Licensing Information: Treatment of excessive sleepiness associated with narcolepsy with or without cataplexy, in adults.

Formulations: 100mg and 200mg tablets

Dosage & administration:

- The recommended starting daily dose is 200 mg taken as a single dose in the morning or 100mg twice daily, morning and at noon. In the elderly (age ≥65) a starting dose of 100mg in the morning is advised.
- The total daily dose may be increased by 100mg every 2-4 weeks if there has been an inadequate response and if tolerated. An inadequate response would be where a patient continues to experience rapid onset of involuntary sleep during the day. A good response would be one where sleep is mainly restricted to night time.
- Locally the usual maximum total daily dose that is used is 300mg although the licensed maximum is 400mg daily in one or two divided doses.
- In patients with severe hepatic impairment, and severe renal impairment (CrCl <10mL/min), the dose should be halved.
- Modafinil is not recommended in women of child-bearing age unless they are using adequate effective contraception.
- Patients with major anxiety should only receive treatment with modafinil in a specialist setting.

Contraindications & Warnings:

Contraindicated in:

- Pregnancy and lactation.
- Uncontrolled hypertension or cardiac arrhythmias.
- Hypersensitivity to modafinil or any excipients in the product.
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.
- Patients with a history of left ventricular hypertrophy or cor pulmonale and in patients with mitral valve prolapse who have experienced mitral valve prolapse syndrome from previous CNS stimulants.
Caution is required:
- In patients with a history of psychiatric disorders including psychosis, depression, mania, major anxiety, agitation, insomnia or substance abuse. If psychiatric symptoms develop whilst receiving treatment with modafinil, modafinil should be discontinued and not restarted.
- In patients with a history of alcohol, drug or illicit substance abuse as the possibility of dependence cannot be excluded.
- The effectiveness of steroidal contraceptives may be reduced when used with modafinil (see “Interactions”, below).

**Interactions:**

Modafinil is a hepatic enzyme inducer and has the potential to increase hepatic metabolism of a number of drugs.

**Steroidal contraceptives** - The effectiveness of steroidal contraceptives may be impaired by modafinil and this may impair effectiveness. Effective, alternative and/or concomitant methods of contraception are recommended and should be continued for two months after stopping modafinil.

**Anticonvulsants** - Care should be observed when used in combination with anti-convulsant drugs. Modafinil levels may be reduced by carbamazepine and phenobarbital and phenytoin levels may be increased by modafinil. Measurement of phenytoin plasma levels may be appropriate on initiation or discontinuation of treatment with modafinil.

**Antidepressants** - Serotonin syndrome has been reported when MAOIs have been used concurrently with modafinil and should be used together with caution. Metabolism of some TCADs (amitriptyline, clomipramine, imipramine, fluoxetine) and SSRI (citalopram) may be inhibited by modafinil and lower doses of these antidepressants may be required.

**Warfarin** - modafinil may increase the anticoagulant effect of warfarin. The INR should be monitored regularly during the first 2 months of modafinil use and after changes in modafinil dosage.

**Ciclosporin** – modafinil may reduce plasma concentrations of ciclosporin. Advice may need to be sought from the specialist as to the significance of this interaction and ciclosporin levels rechecked as necessary.

For full list see SPC at [www.medicines.org.uk/EMC](http://www.medicines.org.uk/EMC)

**Adverse Effects:**

**Cardiovascular:** Tachycardia, hypertension, palpitations. An ECG is recommended in all patients before modafinil treatment is initiated. Blood pressure and heart rate should be regularly monitored (see “Disease and drug monitoring” below). 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.

**Gastrointestinal:** GI disturbances e.g. reduced appetite, nausea, gastric discomfort – minimise by taking dose with food. Diarrhoea, constipation and dry mouth.
Hepatic: Dose related increase in alkaline phosphatase and gamma GT

Skin reactions - Serious rashes (including Stevens - Johnson syndrome, Toxic Epidermal Necrolysis, and Drug Rash with Eosinophilia and Systemic Symptoms) have been reported early on in treatment (1-5 weeks) but occasionally after prolonged treatment. **Modafinil should be discontinued and not restarted in cases of skin or hypersensitivity reaction.**

Psychiatric symptoms such as psychosis, suicide related behaviour – mainly but not exclusively in those with a history of psychosis, depression, mania. Patients should be monitored for the appearance of psychiatric symptoms. **Should these emerge whilst on therapy, modafinil should be discontinued and not restarted.**

Hypersensitivity reactions - Multi organ hypersensitivity reactions have been reported. Typically, although not exclusively, this presents as 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. **If symptoms are suspected, modafinil should be discontinued.**

Dependence and abuse potential - the possibility of dependence with long-term use cannot be entirely excluded.

Other reactions- headache, dizziness, somnolence, paraesthesia, blurred vision.

For full list see SPC at [www.medicines.org.uk/EMC](http://www.medicines.org.uk/EMC)

### Responsibilities of the specialist initiating treatment:

- To assess the suitability of the patient for treatment.
- To ensure that the patient/carer has received counselling and understands the therapy, its benefits, limitations, continued monitoring (where applicable), adverse effects, and is aware of actions to take if adverse effects are suspected.
- Inform the GP of the information provided to the patient.
- To review the patient at agreed intervals and copy all relevant results to the GP.
- Carry out disease and drug monitoring as listed below.
- Formally hand over to GP by letter and patient informed - send a copy (either electronically or paper copy) of the shared care guideline to the GP and ask whether they are willing to participate in shared care.
Prescribing:
- The first prescription will be issued by the Consultant, and subsequent prescriptions will be supplied by the GP once they have agreed to accept shared care.

Disease & drug monitoring:
- Monitoring according to the following schedule:

<table>
<thead>
<tr>
<th>Baseline</th>
<th>ECG - abnormal findings will be further evaluated by specialists before modafinil treatment is started</th>
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<tbody>
<tr>
<td></td>
<td>Blood pressure and heart rate</td>
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<tr>
<td></td>
<td>Liver function</td>
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<tr>
<td></td>
<td>Assessment of overall wellbeing including any psychiatric symptoms or suspected adverse behaviours and thoughts.</td>
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</tbody>
</table>

- Discuss shared care arrangement with patient.
- Support and advise GPs as required.
- Assess response to treatment and initiate any dose changes as clinically appropriate including discontinuation of treatment.

Responsibilities of other prescribers (GP):

General and Prescribing:
- To reply to the request for shared care within 2 weeks of receipt of the consultant letter.
- Monitor and prescribe as recommended by the specialist. The GP will be typically asked to take up the monitoring and prescribing of modafinil approximately one month after treatment has been initiated. Notify consultant if treatment with modafinil is discontinued.
- Ensure there are no drug interactions with any other medications initiated in primary care.

Disease & drug monitoring:
- Carry out drug monitoring as listed – and communicate abnormal results to the specialist.
- Urgent drug discontinuation/ referral to specialist as clinically appropriate
- To stop treatment on the advice of the specialist.
- To refer back to the specialist if the patient’s condition deteriorates.
- To identify adverse effects if the patient presents with any signs and liaise with the hospital specialist where necessary. To report adverse effects to the specialist and where appropriate to the Commission on Human Medicines/MHRA (Yellow Card scheme).

Unless otherwise stated by the secondary care specialist, apply the following monitoring frequencies following handover from secondary care:
Responsibilities of the Patient / Carer:

At one month then every six months thereafter.

- Assess efficacy and tolerability. Dose may be adjusted as detailed in “Dosage and administration section”, above.
- Blood pressure and heart rate.
- Assessment of overall wellbeing including any psychiatric symptoms or suspected adverse behaviours and thoughts.
- LFTs.

One month after a dose increase

- Blood pressure and heart rate.
- LFTs.

Discontinue modafinil and seek advice from initiating team if arrhythmia’s or moderate to severe hypertension develops. Do not restart until the condition has been adequately evaluated and treated.

General:

- Women of child bearing age must ensure adequate effective methods of contraception are maintained during treatment and for 2 months after treatment is stopped.
- Modafinil is not a replacement for sleep/good sleep hygiene/.
- Report any possible side effects to their GP.
- Ensure they have an adequate supply of medication.
- Attend appointments.

Disease & drug monitoring:
As above – contact GP or initiating team if side effects develop (see adverse effects) and attend appointments including those for routine blood tests/investigations.

Communication:

Specialist to GP:

- The specialist will inform the GP when they have initiated modafinil – standard clinic letter.
- Send a link or copy (either electronically or paper copy) of the shared care guideline to the GP and ask whether they are willing to participate in shared care.
- Inform the GP of the information provided to the patient

GP to Specialist:

- To reply to the request for shared care within 2 weeks of receipt of the consultant letter.
- Irrespective of whether you accept prescribing responsibility or not, you should inform the consultant of relevant medical information regarding the patient and changes to the patient’s medication regime irrespective of indication.
- Notify consultant if treatment with modafinil is discontinued.
## Contact names & details:
If you have any concerns regarding individual patients, see consultant letter for medical contact details or contact one of the following:

<table>
<thead>
<tr>
<th>Name</th>
<th>Title/Location</th>
<th>Telephone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr P Duffey</td>
<td>Consultant Neurologist</td>
<td>Sec 01904 725755</td>
</tr>
<tr>
<td>Dr A Heald</td>
<td>Consultant Neurologist</td>
<td>Sec 01904 725602</td>
</tr>
<tr>
<td>Dr C Johnston</td>
<td>Consultant Neurologist</td>
<td>Sec 01904 725754</td>
</tr>
</tbody>
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## Cost:

- 100mg tablets £6.92 for 30 tablets
- 200mg tablets £24.09 for 30 tablets

100mg twice a day for 30 days = £13.84
200mg twice a day for 30 days = £27.68 (using least expensive 100mg tabs)

Drug Tariff November 2015

## References:


This information is not inclusive of all prescribing information and potential adverse effects. Please refer to the SPC (data sheet) or BNF for further prescribing information.

The original Microsoft Word file of this document is located on:

York Teaching Hospital NHS Foundation Trust Pharmacy Department X:\MEDICINES INFORMATION\Shared Care Guidelines\Approved Shared Care Guidelines

Shared Care Guidelines are also available electronically via [http://www.yorkandscarboroughformulary.nhs.uk/](http://www.yorkandscarboroughformulary.nhs.uk/)

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