Sussex Health&Care

Local Shared Care Protocol:

Modafinil (≥18 years) Management of Narcolepsy (+/- Cataplexy) in adults for patients within adult services

Prescribing should be undertaken in accordance with the Sussex Partner Formulary

As well as these protocols, please ensure that summaries of product characteristics (SPCs), British national formulary (BNF) or the Medicines and Healthcare products Regulatory Agency (MHRA) or NICE websites are reviewed for up-to-date information on any medicine. Prescribing should be undertaken in accordance with the Sussex Partner Formulary.

Specialist responsibilities

- Ensuring patient fits criteria for use of stimulant +/- anti-cataplectic agents (e.g. no contraindications, cautions, fits local agreement for use of the drug).
- Baseline monitoring tests- Blood pressure, heart rate, weight, Epworth Sleep Score. ECG for initiation of modafinil, methylphenidate and dexamfetamine only.
- To initiate, stabilise and supply treatment for at least 3 months.
- To inform patients of practical issues related to the use of stimulant +/- anti-cataplectic agents, such as administration, storage and maximum dose.
- At the time of initiating, notify GP in writing that stimulant +/- anti-cataplectic agents has been prescribed.

The GP should ONLY be invited to share care once the patient is stable. Information provided to the GP should include:

- A copy of the shared care guidelines
- Information on when the patient will next be reviewed and by whom.
- A request that the GP continue prescribing the medication beyond the first 3 months on initiation of transfer.

- Any continuous monitoring that will remain under the specialist's responsibility.
- Review by specialist every 3-6 months. Regular follow-up in clinic or remotely by clinician.

- To review patient at the request of GP should any problems arise (side-effects / lack of efficacy) as soon as possible.

- To communicate promptly with the GP if patient does not attend clinic appointment or if treatment or management of condition is changed within 2 weeks.

To report any suspected adverse effects to the MHRA: http://www.yellowcard.gov.uk

Primary care responsibilities

- To consider shared care proposal within 2 weeks of receipt. If agree to request to continue prescribing as detailed in shared care guideline. Confirmation to the requesting specialist is required **within 2 weeks** of receipt of this guideline.

- If do not agree to shared care discuss with requesting specialist or local primary care medicines management team within 2 weeks of receipt of shared care request.

- To provide ongoing prescriptions for stimulant +/- anti-cataplectic agents after 3 months or once stable. To adjust the dose as advised by the specialist.

- To undertake monitoring requirements in accordance with the shared care guidance.

- To report and seek advice regarding any concerns, for example: side-effects, co-morbidities, pregnancy, or lack of efficacy to the specialist.

- To advise the specialist if non-compliance is suspected.

- To refer back to specialist if the patient's condition deteriorates.

- To stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.

  To report any suspected adverse effects to the MHRA via the Yellow Card scheme: http://www.yellowcard.gov.uk

Patient and/or carer responsibilities

- To contact the specialist or GP if they do not have a clear understanding of any aspect of the treatment.

- ***Narcolepsy and Driving:*** You are obliged by law to notify the Driver and Vehicle Licensing Agency (DVLA) of the diagnosis of Narcolepsy. Group one license holders (car, motorbike) must cease driving on the diagnosis of the narcolepsy. Driving will be permitted when satisfactory control of symptoms is achieved, then 1, 2 or 3 year license with medical review, till 70 years of age. License restored after several years of satisfactory control. Group two license holders (LGV/PCV) are generally considered unfit to drive this class of vehicle permanently. However, if a long period of symptom control has been established, licensing may be considered on an individual basis. Do not drive if feeling sleepy.

- To inform prescribing specialist, GP and other healthcare professionals of any other medication being taken, including over the counter products, alternative therapies or recreational drugs.

- To implement and maintain good sleep hygiene. Taking medication is not a replacement for a good sleep routine. It is still important to aim to get around seven to eight hours of sleep at night if possible. You should aim to go to bed when sleepy/tired and get up at about the same time each day.

- To inform community pharmacists that they are using stimulant +/- anti-cataplectic agents before purchasing medication over-the-counter.

- To attend all specialist and GP appointments.

- To take medicines as agreed and take steps to ensure that no doses are missed and not to share medicines with others.

- To read the patient information leaflet included with the medication.

- To report any adverse effects or warning symptoms to GP or specialist.

- To report to GP and specialist if planning pregnancy, pregnant or breastfeeding.

- To inform GP and specialist of any changes in addresses or telephone contact number

1. Background

Narcolepsy (+/- cataplexy) are long-term and debilitating sleep conditions which are similar in their clinical presentation, differ in their diagnosis but may be managed in a parallel manner.

Narcolepsy is a long-term condition that causes excessive sleepiness during the day and often disrupts your sleep at night. You can also have sleep attacks where you fall asleep at inappropriate times during the day without any warning. The Epworth Sleepiness Scale is a questionnaire intended to measure daytime sleepiness. Narcolepsy is generally associated with an ESS of >12, even after adequate nighttime sleep.

Cataplexy is a condition associated with narcolepsy that results in sudden muscle weakness triggered by strong emotions such as laughter, anger, fright or surprise. Muscle weakness can vary in severity and cataplexy attacks can differ in both nature and duration.

2. Indications

Modafinil promotes wakefulness by stimulating the brain to increase alertness and reduce excessive sleepiness during the day. Although there is no cure for narcolepsy, modafinil can help to control symptoms.

O = 'off-label' but considered routine treatment option

X = unlicensed and not currently considered a routine option

	Narcolepsy	Narcolepsy with Cataplexy
Modafinil	***Licensed***	***Licensed***
Methylphenidate XL	***O***	***O***
Methylphenidate IR	***O***	***O***
Dexamfetamine	***Licensed***	***Licensed***
Sodium Oxybate	***O***	***Licensed***
Venlafaxine XL	***X***	***O***
Clomipramine	***X***	***Licensed***
Fluoxetine	***X***	***O***
The agent below is coded as RED and is NOT included in this shared care arrangement. Prescribing will remain with the sleep centre.		
Pitolisant (NOT FOR SHARED CARE)	***Licensed***	***Licensed***

The information here is not exhaustive. Please also consult the current Summary of Product Characteristics (SPC) for stimulant +/- anti-cataplectic agents prior to prescribing for up to date prescribing information, including detailed information on adverse effects, drug interactions, cautions and contraindications (available via www.medicines.org.uk)

- Transfer of monitoring and prescribing to primary care is normally after the patient's dose has been optimised and with satisfactory investigation results.
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician
- Termination of treatment will be the responsibility of the specialist.

3. Locally agreed off-label use

To be agreed and completed locally (include supporting information)

4. Contraindications and cautions

This information does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it. Please see BNF & SPC for comprehensive information.

The list of contraindications and cautions is not exhaustive, please refer to the SPC for detail. https://www.medicines.org.uk/emc/product/4319/smpc

Contraindications:
Arrhythmia; history of clinically significant signs of CNS stimulant-induced mitral valve prolapse (including ischaemic ECG changes, chest pain and arrhythmias); history of cor pulmonale; history of left ventricular hypertrophy; moderate to severe uncontrolled hypertension.

Cautions:
Abuse, misuse and diversion. Patients should be carefully monitored for the risk of diversion, misuse and abuse of modafinil.

Effects on ability to drive or use machinery:
Modafinil can cause blurred vision or dizziness in some people therefore it may affect their ability to drive or use machines. Sleepiness associated with condition may also add to this.

5. Initiation and ongoing dose regime

- Transfer of monitoring and prescribing to General Practice is normally after at least 12 weeks, and when the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks.
- The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
- All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the General Practice clinician.
- Termination of treatment will be the responsibility of the specialist.

Initial stabilisation:

The initial stabilisation period must be prescribed by the initiating specialist.

- Oral: modafinil 50-100mg/day gradually increasing over 4 to 6 weeks to maintenance dose of 400mg/day.
- Hepatic impairment: Reduce dose by half in patients with severe hepatic impairment.
- Older People Limited data available but potential for lower clearance and increased systemic exposure, it is recommended that patients > 65 years of age commence therapy at 100 mg daily.

Maintenance dose (following initial stabilisation):

The initial maintenance dose must be prescribed by the initiating specialist.

Conditions requiring dose adjustment:

- Renal and hepatic impairment (see above under initial stabilisation).
- Older people (see above under initial stabilisation).
- GP to monitor blood pressure, heart rate. Inform the specialist of any reported adverse effects i.e. rash, headache urgently.

Duration of Treatment Indefinitely if patient is responding well to treatment and in absence of significant side effects.

6. Pharmaceutical aspects

Route of administration:	Oral
Formulation:	Modafinil 100mg tablets Modafinil 200mg tablets Modafinil Provigil 100mg tablets
Administration details:	For oral use. Tablets should be swallowed whole. The total daily dose may be taken as a single dose, one in the morning or as two doses in the morning and one at noon, according to physician assessment of the patient and the patient's response.
Other important information:	Physicians prescribing modafinil for an extended time should periodically re-evaluate the long-term use for the individual patients as the long-term efficacy of modafinil has not been evaluated (> 9 weeks).

7. Significant medicine interactions

The following list is not exhaustive. Please see BNF or SPC for comprehensive information and recommended management.

Clinically Significant Drug Interactions (refer to BNF/SPC for full list) - https://www.medicines.org.uk/emc/product/5412

Modafinil is a weak enzyme inducer.

Hormonal contraceptives including;

- combined hormonal contraception (CHC) pills
- rings
- patches;
- progestogen-only pill;
- progestogen-only implants

Ulipristal acetate emergency contraception may be less effective when used with modafinil and therefore should be avoided.

Advise to use copper intrauterine device (copper IUD), levonorgestrel-releasing intrauterine system (LNG-IUS), and depot progestogen-only injections.
For emergency contraception, if a copper IUD is not suitable, a double dose of oral levonorgestrel emergency contraception is advised. Refer to QVH Patient Leaflet for women of childbearing potential on modafinil.

8. Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist

Monitoring at baseline and during initiation is the responsibility of the specialist; only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to General Practice.

Baseline investigations:

- ECG, Blood pressure, heart rate, pregnancy test, if necessary, Epworth Sleep Score.
- Pregnancy Prevention: Women of childbearing potential must use effective contraception during treatment with modafinil and for 2 months after stopping (see MHRA Nov 2020 Update).

Ongoing monitoring (at 6 and 12 monthly clinic appointments):

- Blood pressure, Epworth Sleep Score. Ask patient about any rashes or change in mood and behaviour at each visit. Ask patient about side effects such as headache, chest pain.

Follow up:

- Subject to response to treatment: 6 monthly or 12 monthly if well controlled and stable.
- Send a letter/results notification to the GP after each clinic attendance indicating current dose, most recent blood pressure, Epworth Sleep Score and frequency of visits.

- Advise GP on review, duration and/or discontinuation of treatment when necessary. Inform GP of patients who do not attend clinic appointments. Advise GP to continue current plan until next reviewed in clinic.

9. Ongoing monitoring requirements to be undertaken by General Practice.

See section 10 for further guidance on management of adverse effects/ responding to monitoring results.

Monitoring	Frequency
Blood pressure and heart rate.	Annually and following any dose changes.

(If relevant) If monitoring results are forwarded to the specialist team, please include clear clinical information on the reason for sending, to inform action to be taken by secondary care.

10. Adverse effects and other management

Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme.
Visit https://yellowcard.mhra.gov.uk/
For information on incidence of ADRs see relevant summaries of product characteristics.

Result	Action for General Practice
As well as responding to absolute values in laboratory tests, a rapid change or a consistent trend in any value should prompt caution and extra vigilance.	
If rash develops breathlessness of unknown cause.	STOP and Inform specialist urgently.
Onset of chest pain.	STOP and Inform specialist urgently.
Palpitations.	STOP and Inform specialist urgently.
Arrhythmia.	STOP and Inform specialist urgently.

Moderate to severe hypertension.	STOP and Inform specialist urgently.
Changes in mood behaviour or thinking suicidal thoughts.	STOP and Inform specialist urgently.

11. Advice to patients and carers

The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.

The patient should be advised to report any of the signs or symptoms to their GP without delay:

- Changes in mood behaviour or thinking suicidal thoughts
- Moderate to severe hypertension
- Palpitations
- Arrhythmia
- If rash develops breathlessness of unknown cause
- Onset of chest pain

Reporting of side effects If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side-effects, you can help provide more information on the safety of this medicine.

Patient information (include links):

- General information:
  - https://www.narcolepsy.org.uk/
  - https://patient.info/mental-health/narcolepsy-and-cataplexy-leaflet

Patient information leaflets are also available from:

  - https://www.medicines.org.uk/emc/search?q=modafinil

12. Pregnancy, paternal exposure and breast feeding

It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review, but the ongoing responsibility for providing this advice rests with both the General Practice prescriber and the specialist.

Pregnancy:

Modafinil is not recommended for use in pregnancy or breastfeeding. Any patient considering becoming pregnant or has discovered they are pregnant should be referred back to their specialist immediately and shared care will no longer apply for the duration of the pregnancy and while breast feeding.

Breast Feeding:

Modafinil should not be used during breast feeding. Available pharmacodynamic/toxicological data in animals have shown excretion of modafinil/metabolites in milk.

Paternal exposure:

No studies reported regarding paternal exposure.

13. Specialist contact information

Name: *[insert name]*
Role and specialty: *[insert role and specialty]*
Daytime telephone number: *[insert daytime telephone number]*
Email address: *[insert email address]*
Alternative contact: *[insert contact information, e.g. for clinic or specialist nurse]* Out of hours contact details: *[insert contact information, e.g. for duty doctor]*

Consult information provided in appendix 1

14. Additional information

Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed. Ensure that the specialist is informed inwriting of any changes to the patient's GP or their contact details.

Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.

15. References

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16. Other relevant national guidance

- Shared Care Protocols. Available from https://www.england.nhs.uk/medicines-2/regional-medicines-optimisation-committees-advice/shared-care-protocols/#about
- NHSE policy – Responsibility for prescribing between primary & secondary/tertiary care. Available from https://www.england.nhs.uk/publication/responsibility-for-prescribing-between-primary-and-secondary-tertiary-care/
- General Medical Council. Good practice in prescribing and managing medicines and devices. Shared care. Available from https://www.gmc-uk.org/professional-standards/the-professional-standards/good-practice-in-prescribing-and-managing-medicines-and-devices
- NICE NG197: Shared decision making. Last updated June 2021. https://www.nice.org.uk/guidance/ng197/.

17. Local arrangement for referral

Define the referral procedure from hospital to General Practice prescriber & route of return should

the patient's condition change.

To be agreed and completed locally.

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