NARCOLEPSY
Aintree University Hospital Sleep Service Pathway

GUIDELINE

Diagnosis of Narcolepsy made by Consultant Sleep Physician at Aintree University Hospital according to ICSD-3 criteria (*International Classification of Sleep Disorders. 3rd ed. (2014) American Academy of Sleep Medicine*)

Narcolepsy management in women of child-bearing potential

It is the responsibility of the specialist to consider and discuss the benefits and risks of drug treatment for narcolepsy with each patient, including use in pregnancy and breast feeding.

It is the responsibility of the initiating prescriber to ensure that, if indicated, the patient is using effective contraception prior to commencing treatment and is counselled appropriately. Confirmation that benefits, risks and contraception have been discussed and details of any action taken should be provided to primary care if primary care prescribing is requested.

Prescribers should refer to:

- FSRH CEU Statement: Contraception for women using known teratogenic drugs or drugs with potential teratogenic effects (01 February 2018)
- MHRA Drug Safety Update: Medicines with teratogenic potential: what is effective contraception and how often is pregnancy testing needed? (21 March 2019)

Pharmacological management of narcolepsy

The drugs in this pathway should be used sequentially based on clinical considerations (e.g, contraindications, tolerability). **The drugs in the pathway should not be used in combination.**

1st Line agent A Ret

Modafinil

- Stimulant therapy: Modafinil 100-600mg daily for excessive daytime sleepiness; Anti-depressant REM suppressant therapy for cataplexy: Clomipramine /imipramine/fluoxetine/venlafaxine which are titrated to response.
- If the patient's narcolepsy is well controlled i.e. improvement in daytime sleepiness and decreased frequency of cataplexy episodes and REM intrusion phenomena: Continue first line treatment of modafinil and REM suppressant anti-depressants. If ineffective then stop and change.
- Before prescribing for patients, they will be assessed for clinical suitability. Patients should have their blood pressure and heart rate monitored every at every clinic appointment following initiation, which is usually every three to 6 months depending on clinical stability.
- Modafinil potentially increases the risk of congenital malformations Women of childbearing potential must use effective contraception during treatment and for 2 months after stopping. As modafinil may reduce the effectiveness of oral contraception, alternative additional methods of contraception are required if the patient is using oral contraception.[1] See Modafinil (Provigil): increased risk of congenital malformations if used during pregnancy - GOV.UK (www.gov.uk) for further information.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

2nd Line agent RED

Methylphenidate or dexamfetamine

- If the patient's excessive daytime sleepiness is not controlled with modafinil therapy, a second line option may be the initiation of stimulants such as methylphenidate or dexamfetamine titrated to response. If ineffective then consider adding another agent which should allow down titrating of stimulants and/or anti-cataplexy drugs.
- Before prescribing for patients, they will be assessed for clinical suitability. Patients should have their blood pressure and heart rate monitored every at every clinic appointment following initiation, which is usually every 3 to 6 months depending on clinical stability.

If the patient's narcolepsy symptoms (excessive daytime sleepiness/cataplexy/REM intrusion phenomena) are poorly controlled with or intolerant / contraindicated to the above, then an assessment should be made considering the following variables:

- Comorbidity
- Psychiatric history
- Frequency of cataplexy
- Degree of REM intrusion phenomena
- History of nocturnal incontinence
- Whether there has been a previous adverse reaction to solriamfetol, sodium oxybate or pitolisant
- BMI
- Coexisting untreated OSA or hypoventilation (consider CPAP or NIV therapy)
- History of alcohol/sedative/illicit drug use
- History of coexisting insomnia

3rd Line agent RED

Solriamfetol (Sunosi®▼) – for narcolepsy with or without cataplexy

- Solriamfetol is recommended only if modafinil and either dexamfetamine or methylphenidate have not worked well enough or are not suitable, in accordance with NICE TA758 and the Pan Mersey APC prescribing statement.
- Before prescribing for patients they will be assessed for clinical suitability. Patients should have their blood pressure and heart rate monitored every at every clinic appointment following initiation which is usually every 3 to 6 months depending on clinical stability.
- Women of childbearing potential or their male partners must use effective method of contraception while taking solriamfetol.[2]

4th Line agent RED

Pitolisant (Wakix®▼) – for narcolepsy with or without cataplexy

- Pitosilant is recommended only if modafinil, either dexamfetamine or methylphenidate (+/- TCA / SSRI antidepressants), and solriamfetol have not provided an effective reduction in excessive daytime sleepiness or are not suitable (patient is intolerant of / contraindicated to these agents).
- Pitolisant is recommended ahead of solriamfetol if the patient also has cataplexy.
- Pitolisant should be prescribed in accordance with the Pan Mersey APC prescribing statement.
- Women of childbearing potential have to use effective contraception during treatment with pitolisant and for at least up to 21 days after treatment discontinuation. Pitolisant may reduce the effectiveness of hormonal contraceptives. Therefore, an alternative method of effective contraception should be used if the patient is using hormonal contraceptives.[2]

5th Line agent RED

Sodium oxybate (Schedule 2 Controlled Drug) – for narcolepsy with cataplexy

- Sodium oxybate is recommended only if modafinil, either dexamfetamine or methylphenidate (+/- TCA / SSRI antidepressants, solriamfetol and pitolisant have not provided an effective reduction in excessive daytime sleepiness or are not suitable (patient is intolerant of / contraindicated to these agents).
- Sodium oxybate should be prescribed in accordance with the Pan Mersey APC prescribing statement.

- Sodium oxybate is recommended in favour of solriamfetol or pitolisant in patients with cataplexy, where clinically appropriate:

    - Narcolepsy specific issues: Significant (i.e. multiple nightly) REM intrusion phenomena, greater frequency of cataplexy e.g. >15 episodes a week
    - Coexisting insomnia

All patients commenced on pitolisant, solriamfetol or sodium oxybate MUST be followed up every 3 months in the specific narcolepsy clinic.

References

1. Teva Pharma B.V. Summary of Product Characteristics; Modafinil Provigil 100 mg Tablets, 25 May 2021. Accessed 16 May 2022**.**

2. Jazz Pharmaceuticals. Summary of Product Characteristics; Sunosi 150 mg film-coated tablets, 10 March 2022. Accessed 16 May 2022.

3. Bioprojet UK Limited. Summary of Product Characteristics; Wakix 4.5 mg / 18mg film-coated tablets, 17 December 2020. Accessed 16 May 2022.