Pathway for the pharmacological management of cataplexy associated with narcolepsy

Note: Treatments noted in this pathway are **IMOC Amber 3 category** – initiation and minimum **3 months**' supply by the sleep centre (specialising in narcolepsy with cataplexy). GPs are **not** expected to initiate these treatments but may be asked to take on prescribing in line with IMOC recommendations under the **shared care guideline**. Pitolisant is IMOC RED category (hospital only) for cataplexy – initiation and ongoing prescribing will be by the sleep service.

Cataplexy associated with Narcolepsy

Initiate **(specialist initiation):**

- Clomipramine 10-75mg nocte (***TCA)*** **or**
- Venlafaxine XL 75-150mg mane ***(SNRI)*** **or**
- Venlafaxine IR 75mg-150mg mane, or in two divided doses*

Review by specialist in 3-6 months
Regular follow up in clinic or via telephone by the sleep pharmacist between consultant appointments.

If not tolerated or effective, stop TCA/SNRI and initiate **(specialist initiation):**

- Fluoxetine: 20-60mg mane ***(SSRI)*****

Review by specialist in 3-6 months
Regular follow up in clinic or via telephone by the sleep pharmacist between consultant appointments.

If the TCA, SNRI, SSRI*** are not tolerated or effective, consider **(specialist initiation)**:

- Pitolisant 4.5mg-36mg mane
- Sodium oxybate (Xyrem®) 4.5-9.0g nocte in TWO divided doses

red - for secondary or tertiary care initiation and long-term maintenance of prescribing.

May be adjuvant or monotherapy
Review by specialist in 3-6 months
Regular follow up in clinic or via telephone by the sleep pharmacist between consultant appointments.

*****Important: Abrupt cessation of antidepressants can result in status-cataplecticus (particularly cessation of venlafaxine). They should be withdrawn slowly and overlapped with next treatment option.**

*Once/twice daily dosing of venlafaxine (IR) as agreed with specialist and with close monitoring of symptoms.

** Fluoxetine would only be trialled if there is a co-morbidity which would benefit from management with fluoxetine e.g. neuropathic pain. Without the presence of a co-morbidity, pitolisant or sodium oxybate would be trialled next.

- Consider pitolisant when ongoing cataplexy events are frequent, affect patient's normal functioning, or entail safety concerns due to their presentation, despite previous anti-cataplectic options.

TCA = tricyclic antidepressant
SNRI = serotonin and norephinephrine reuptake inhibitor
SSRI = selective serotonin reuptake inhibitor

South East London Integrated Medicines Optimisation Committee (SEL IMOC). A partnership between NHS organisations in South East London Integrated Care System: SEL Integrated Care Board (covering the boroughs of Bexley/Bromley/Greenwich/ Lambeth/Lewisham and Southwark) and GSTFT/KCH /SLaM/ Oxleas NHS Foundation Trusts and Lewisham & Greenwich NHS Trust

Appendix 1:
Important Administration Instructions
Patients should take the first dose of sodium oxybate (Xyrem®) at least 2 hours after eating because food significantly reduces the bioavailability of sodium oxybate.
Patients should prepare both doses of sodium oxybate prior to bedtime. Prior to ingestion, each dose of sodium oxybate should be diluted with approximately approximately 60 mL of water in the empty pharmacy vials provided.
Patients should take both doses of sodium oxybate while in bed and lie down immediately after dosing as sodium oxybate may cause them to fall asleep abruptly without first feeling drowsy. Patients will often fall asleep within 5 minutes of taking sodium oxybate, and will usually fall asleep within 15 minutes, though the time it takes any individual patient to fall asleep may vary from night to night.
Patients should remain in bed following ingestion of the first and second doses, and should not take the second dose until 2.5 to 4 hours after the first dose.
Patients may need to set an alarm to awaken for the second dose. Rarely, patients may take up to 2 hours to fall asleep.

Appendix 2:
The weaning and cross tapering of anti-depressants will be initiated and supervised by the sleep clinic.

The presence or history of mental health co-morbidities to be discussed with patients, which may guide the choice of a preferable anti-cataplectic treatment.

Appendix 3:
Please note that there are no specific criteria which can be applied to the use of pitolisant and in the management of cataplexy. This includes initiation and cessation of treatment. This is because the indication would not only rely on number of events but also their severity and characteristics, as well as personal circumstances in which these arise, and other matters such as patients' profession or driving status.
The best practice is to include the following information (in the clinic letter and the referral to the pharmacist): number of cataplexy events per week, whether they are spontaneous/triggered, partial/generalised, personal patient's circumstances that might affect cataplexy, and safety concerns linked to cataplexy, to justify the indication of going to the next step (pitolisant or sodium oxybate) in the clinical pathway. It is very much an individualised decision.

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