**Narcolepsy-Information for GPs and community pharmacists**

**What is narcolepsy?**

Narcolepsy is a long term neurological disorder where the brain is unable to regulate sleeping and waking patterns normally. The main characteristic is overwhelming daytime sleepiness so that the patient is unable to stay awake for >3 hours. Narcolepsy can significantly affect sleep cycles and decrease the quality of sleep. The Epworth Sleepiness Scale is a questionnaire intended to measure daytime sleepiness. Narcolepsy is generally associated with an ESS of >12, even after adequate night-time sleep. It is characterised by excessive daytime sleepiness but often several other symptoms. :

- **excessive daytime sleepiness** – feeling very drowsy throughout the day, and having difficulty concentrating and staying awake. Sometimes excessive daytime sleepiness can result in sleep attacks, falling asleep suddenly and without warning. These are more likely in monotonous situations but in extreme cases can occur during periods of activity.
- **cataplexy** – occurring in approximately half of patients, it is a temporary loss of muscle control, often in response to emotions such as laughter or anger.
- **sleep paralysis** – a temporary inability to move or speak when waking up or falling asleep
- **excessive dreaming** – dreams often come as you fall asleep (hypnogogic hallucinations) or just before or during waking (hypnopompic hallucinations)
- **disturbed night time sleep**

In addition, narcolepsy if commonly also associated with an increased body mass index, poor control of body temperature and blood pressure, binge-eating behaviour, automatic behaviour, low self-esteem, depression and suicidal thoughts.

**Click *here* to access the SEL APC Narcolepsy pathway**
**Click *here* to access the SEL APC cataplexy associated with narcolepsy pathway**

**What causes narcolepsy?**

Most cases of narcolepsy are caused by a lack of the brain chemical hypocretin (also known as orexin). In most of these patients, the loss of hypocretin neurons is thought to be caused by an autoimmune attack. In addition, head trauma can result in damage to the hypocretin cells, producing the same symptoms and in some cases (estimated at around 5%), there is a family history of the condition, suggesting a genetic basis. In very rare cases, it is possible for a patient to present with all the symptoms of narcolepsy but for their hypocretin levels to be normal and it is not yet understood why this should be.

There are a number of factors which have been identified as increasing a person's risk of narcolepsy or causing an autoimmune problem, including:

- age (there is a wide distribution to the onset of narcolepsy, but there is a clear peak at around age 15)
- an inherited genetic fault (in these cases, narcolepsy is often evident at a much younger age)
- hormonal changes, including those that occur during puberty or the menopause
- major psychological stress
- an infection, such as influenza or a streptococcal infection
- having the flu vaccine Pandemrix

Further research is required to confirm whether all of the above factors play a role in narcolepsy.

It is not yet possible to replace the hypocretin. Conseqeuently the symptoms must be managed through a combination of behavioural measures (such as strict sleep routine and sheduled naps) and medication. The patient's response to the available medications is wildly variable and it is very important that GPs support patients in their efforts to find the right combination of medications. By trying different medications, in different doses and with different timings is possible to improve sysmptoms for the patient. This can take many years of constant work to achieve.

Broadly speaking, there are two kinds of drugs that are prescribed for narcolepsy: those to counter the excessive daytime sleepiness and those to treat the cataplexy, sleep paralysis and dreaming. The hypnotic sodium oxybate can help both sleepiness and cataplexy and has the advantage of providing consolidated sleep at night.

**Drugs to combat sleepiness**

**Treatments, Half-lives and Side-effects**

| Drug | Starting dose | MAX recommended dosing | Time to therapeutic effect | Half-life | Side-effects |
|---|---|---|---|---|---|
| **Modafinil** | 100mg daily | 400mg daily | 2-4 hours | 15 hours | Headache, **rash**, GI disturbances, **changes to mood,** chest pain, dizziness/blurred vision, palpitations, nervousness, dry mouth. |
| **Methylphenidate XL** | 18mg daily | 72mg daily | 1-2 hours | 3.5 hours | Nausea, abdominal pain, indigestion, dry mouth, diarrhoea, headache, feeling sleepy, dizzy or tired, mood changes, fever, weight loss, sleeping problems. |
| **Methylphenidate** | 10mg daily (divided doses) | 60mg daily (divided doses) | 1-2 hours | 2 hours | Nausea, abdominal pain, indigestion, diarrhoea, headache, feeling sleepy, dizzy or tired, mood changes, fever, weight loss, sleeping problems. |
| **Dexamfetamine** | 10mg daily (divided doses) | 60mg daily (divided doses) | 1.5 hours | 10.2 hours | Nausea, decreased appetite, weight loss, stomach cramps, diarrhoea, dizziness, visual disturbances, headache, palpitations, mood changes |
| **Sodium Oxybate** | 2.25g BD (first dose at bedtime then second dose 3 hours later) | 4.5g BD (first dose at bedtime then second dose 3 hours later) | 0.5-1 hour | 6-8 hours | Sleep walking, bed wetting, nausea, electrolyte imbalance, decreased weight, blurred vision, sleepiness/drowsiness, tremor, slow/troubled breathing, changes in alertness. |

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| **Pitolisant** | 9mg daily (4.5mg in certain populations) | 36mg daily | 3 hours | 10-12 hours | Nausea, vomiting, dyspepsia, increased appetite, increased weight pain, headache, dizziness, tremor, vertigo, insomnia, anxiety, depression. |

**Pharmacological associated side effects of treatments for Narcolepsy**

| | Modafinil | Methylphenidate | Dexamfetamine | Sodium Oxybate | Pitolisant |
|---|---|---|---|---|---|
| **Headache** | +++ | ++ | ++ | ++ | ++ |
| **GI disturbances** | ++ | ++ | ++ | +++ | ++ |
| **Dizziness** | ++ | ++ | ++ | +++ | ++ |
| **Rash** | + | + | + | 0 | 0 |
| **Visual disturbances** | 0 | ++ | ++ | + | 0 |
| **Reduced appetite/weight loss** | ++ | +++ | +++ | ++ | 0 |
| **Palpitations** | ++ | ++ | ++ | 0 | 0 |
| **Chest pain** | + | + | + | 0 | 0/+ |
| **Mood changes** | + | ++ | ++ | ++ | + |

+ = mild
++ = moderate
+++ = severe

**Drugs to combat cataplexy, sleep paralysis and dreaming**

| Drug | Starting dose | MAX recommended dosing | Time to therapeutic effect | Half-life | Side-effects |
|---|---|---|---|---|---|

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| **Clomipramine** | 10mg ON | 75mg ON | 1-5 hours with full steady state concentration taking up to 2-3 weeks | 12-36 hours | Dry mouth, constipation, headache, dizziness, blurred vision, mood changes, restlessness, anxiety, forgetful, faint, light headedness, ECG changes, sweating, hot flushes, difficulty in passing urine, increased appetite, feeling confused, feeling anxious or restless, disturbed sleep, lack of concentration, feeling shaky, muscle weakness, itchy skin rash, weight changes, changes in sexual function, breast tenderness, changes in taste, ringing in ears, yawning |
| **Fluoxetine** | 20mg OM | 60mg OM | Steady state plasma concentrations are only achieved after continuous dosing for weeks. | 1-3 days after acute administration. Prolonged to 4-6 days after chronic administration | Nausea, vomiting, indigestion, diarrhoea, dry mouth, headache, mood changes; feeling anxious, nervous, agitated or forgetful, feeling restless or shaky, dizzy, tired, weak, flushing, sweating, difficulty sleeping, lack of appetite, loss of weight, aches and pains, reduced sexual drive or ability, urinary retention, yawning, palpitations, itching, changes in taste |
| **Venlafaxine XL** | 37.5mg | 150mg OM | 5.5-9 hours | 5-11 hours | Headache, dry mouth, nausea, sweating, dizziness, constipation, weight loss, sleeping problems, |

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| | | | | | tingling feelings, feeling nervous or confused, eyesight problems, lack of appetite, chills, yawning, hot flushes, difficulties having sex, increased cholesterol, menstrual problems |
| **Sodium Oxybate** | 2.25g BD (first dose at bedtime then second dose 3 hours later) | 4.5g BD (first dose at bedtime then second dose 3 hours later; patient advised to set an alarm) | 0.5-1 hour | 6-8 hours | Sleep walking, bed wetting, nausea, electrolyte imbalance, decreased weight, blurred vision, sleepiness/drowsiness, tremor, slow/troubled breathing, changes in alertness. |

**Driving and narcolepsy**

In the UK, a patient diagnosed with narcolepsy is required by law to inform the Driver and Vehicle Licensing Authority (DVLA). If cataplexy is not well controlled or sleep attacks are common then it may be too dangerous to drive again. But provided symptoms are well controlled with medication, it may be possible to drive again.

If your patient is a driver, please be aware that the above medication may affect their reactions and ability to drive. It is an offence to drive while reactions are impaired. Even if their driving ability is not impaired, should they drive, they are advised to carry some evidence that the medicine has been prescribed for them - a repeat prescription form or a patient information leaflet from the pack is generally considered sufficient.

****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

TCA = tricyclic antidepressant;
SNRI = serotonin and norepinephrine reuptake inhibitor;
SSRI = selective serotonin reuptake inhibitor