NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Oveporexton for treating type 1 narcolepsy

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of oveporexton within its marketing authorisation for treating type 1 narcolepsy.

Background

Narcolepsy is a chronic neurological condition affecting the brain's ability to regulate normal sleep/wake cycles. It is often caused by a lack of the brain chemical hypocretin (also known as orexin), but this is not true in all cases and the exact cause of the condition is often unclear.[1] Symptoms of narcolepsy can include excessive daytime sleepiness, cataplexy (temporary loss of muscle control resulting in weakness and possible collapse), sleep attacks (falling asleep suddenly and without warning), sleep paralysis, excessive dreaming, waking in the night and disturbed nocturnal sleep.[1,2] Narcolepsy may lead to cognitive, psychiatric, and metabolic problems, as well as substantial social, occupational, and educational impairment.

The two main types of narcolepsy are primarily distinguished by the presence of cataplexy symptoms and by orexin levels:

- Type 1 narcolepsy (previously known as narcolepsy with cataplexy). People with type 1 narcolepsy have cataplexy (in addition to other symptoms listed above) and usually have low orexin levels.[2]

- Type 2 narcolepsy (previously known as narcolepsy without cataplexy). People with type 2 narcolepsy do not have cataplexy, typically have fewer symptoms, and usually have normal orexin levels.[2]

Distinguishing between type 1 and type 2 can be complicated by the emergence of cataplexy over time in people with type 2 narcolepsy.

A UK study estimates that the prevalence of all narcolepsy in England is 0.02%, or approximately 11,000 people.[3] This estimate is lower than previous estimates of symptomatic frequency,[4] and may be an underestimate due to underdiagnosis. Initial symptoms often occur before the age of 18, but the condition is usually diagnosed between the ages of 20 and 40.[1] The prevalence of type 1 and type 2 narcolepsy is broadly similar.[4]

There are no UK-specific treatment guidelines for narcolepsy and practice can vary between centres. NICE guidance TA758 recommends solriamfetol for treating excessive daytime sleepiness caused by narcolepsy, only if modafinil and either dexamfetamine or methylphenidate have not worked well enough or are not suitable. In TA758, the clinical experts explained that modafinil is the established first-line treatment in the NHS for excessive daytime sleepiness caused by narcolepsy. Second-line treatment includes other wake-promoting agents such as methylphenidate and dexamphetamine. At first- and second-line, people with type 1

narcolepsy may also have antidepressants such as venlafaxine, clomipramine, or fluoxetine as an adjunct to treat cataplexy. Other treatments, including solriamfetol, pitolisant and sodium oxybate are typically used for patients with persistent symptoms, problematic cataplexy, stimulant intolerance or complex disease requiring combination therapy. There is geographic variability in the use of sodium oxybate and pitolisant across the NHS.

The technology

Oveporexton (Orzeyful, Takeda) does not currently have a marketing authorisation in the UK for type 1 narcolepsy. It has been studied in clinical trials compared with placebo in people aged 16 years or older with type 1 narcolepsy.

Intervention(s)	Oveporexton
Population(s)	People aged 16 years or older with type 1 narcolepsy
Subgroup(s)	If evidence allows, subgroups based on the number of previous treatments received may be considered.

Comparators	Established clinical management without oveporexton, which may include:
	• First-line:
	  ○ modafinil with or without antidepressants (such as venlafaxine, clomipramine, or fluoxetine)
	• Second-line:
	  ○ methylphenidate or dexamphetamine, with or without antidepressants
	• Third-line:
	  ○ sodium oxybate
	  ○ pitolisant
	  ○ solriamfetol with or without antidepressants

Outcomes	The outcome measures to be considered include: • excessive daytime sleepiness • number of cataplectic episodes • adverse effects of treatment • mortality • health-related quality of life

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals:** Solriamfetol for treating excessive daytime sleepiness caused by narcolepsy (2022) NICE technology appraisal guidance 758.

References

1. NHS (2022) Narcolepsy. Available from: https://www.nhs.uk/conditions/narcolepsy/ [Accessed June 2026]

2. National Institute of Neurological Disorders and Stroke (2026) Narcolepsy. Available from: https://www.ninds.nih.gov/health-information/disorders/narcolepsy [Accessed June 2026]

3. Strongman H, Sykorova M, Yu YTN, et al. (2026) Incidence and prevalence of obstructive sleep apnoea and narcolepsy in the UK: a population-based descriptive study. Thorax. Available from: https://doi.org/10.1136/thorax-2025-223863

4. Ohayon MM, Dave S, Crawford S, et al. (2025) Prevalence of narcolepsy in representative samples of the general population of North America, Europe, and South Korea. *Psychiatry Research* 347. Available from: https://doi.org/10.1016/j.psychres.2025.116390

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