NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pitolisant hydrochloride for treating excessive daytime sleepiness caused by obstructive sleep apnoea

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of pitolisant hydrochloride within its marketing authorisation for treating excessive daytime sleepiness caused by obstructive sleep apnoea.

Background

Excessive daytime sleepiness (EDS), also known as hypersomnia, means people struggle to stay awake and alert during the day (or equivalent waking hours), leading to an irrepressible need to sleep or unintended lapses into drowsiness or sleep. People with excessive sleepiness are likely to fall asleep during the day (often while eating or talking), regularly nap during the day but wake up feeling unrefreshed, and still sleep for long hours at night. One cause of excessive sleepiness is obstructive sleep apnoea (OSA).[1] Excessive sleepiness caused by OSA can affect many aspects of daily life, including education, employment, driving, relationships and emotional health and general health.

OSA is a condition in which a person stops breathing for a short time when they are asleep because of a closing or narrowing of the throat.[2] The blocking of the airway leads to breathing difficulties which causes people to wake suddenly and subsequently interrupts sleep. Interruption of normal sleeping patterns leads to excessive daytime sleepiness, and reduced concentration and alertness.[2] OSA is associated with neuropsychological impairment, metabolic and cardiovascular co-morbidities and increased mortality.[2]

OSA is the third most common respiratory disorder in the UK.[3] An estimated 1.5 million adults it in the UK have OSA, but up to 85% are undiagnosed and untreated.[4] The prevalence of OSA increases with age, with around 15 to 20% of people 70 years or older estimated to have OSA.[3,4]

Current clinical practice for treating excessive sleepiness caused by OSA is to treat the underlying condition. Managing OSA may involve lifestyle changes such as losing weight, stopping smoking and limiting alcohol consumption.[5] Continuous positive airway pressure (CPAP) is recommended as a treatment option for adults with moderate or severe symptomatic OSA, and for adults with mild OSA who have symptoms that affect their daily activities and have not responded to lifestyle changes (NICE technology appraisal 139). CPAP is

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not tolerated by all people with OSA. Other treatment options for OSA include mandibular advancement devices and surgery.[5]

The technology

Pitolisant hydrochloride (Tiprolisant, Lincoln Medical) binds to the histamine H_3 receptor, which activates histamine-releasing neurons in the brain and increases wakefulness. It is administered orally.

Pitolisant hydrochloride does not currently have a marketing authorisation in the UK for treating OSA. It has been studied in trials comparing the efficacy and safety of pitolisant hydrochloride with placebo in adults with OSA and have EDS who have inadequate response to CPAP or cannot use CPAP.

Intervention(s)	Pitolisant hydrochloride with or without primary obstructive sleep apnoea therapy
Population(s)	Adults with obstructive sleep apnoea whose excessive daytime sleepiness has not been satisfactorily treated by primary obstructive sleep apnoea therapy, such as continuous positive airway pressure.
Comparators	Established clinical management without pitolisant hydrochloride
Outcomes	The outcome measures to be considered include: • excessive daytime sleepiness • fatigue • length of life • adverse effects of treatment • 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.

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Other considerations	If the evidence allows, the following subgroups will be considered. These include: • mild, moderate and severe obstructive sleep apnoea • people who cannot have or have refused continuous positive airway pressure therapy • people not continuing primary obstructive sleep apnoea therapy, such as continuous positive airway pressure. 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 and NICE Pathways	**Related Technology Appraisals:** 'Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome' (2008) NICE technology appraisal guidance 139. **Appraisals in development:** Solriamfetol for treating excessive sleepiness caused by obstructive sleep apnoea. NICE technology appraisals guidance [ID1499]. Expected publication date, January 2021. **Guidelines in development:** Obstructive sleep apnoea/hypopnoea syndrome and obesity hypoventilation syndrome in over 16s. Expected publication date, November 2020. **Related Interventional Procedures:** Hypoglossal nerve stimulation for moderate to severe obstructive sleep apnoea. NICE interventional procedures guidance 598. 'Soft-palate implants for obstructive sleep apnoea' (2007) NICE interventional procedure guidance 241. **Related NICE Clinical Knowledge summary:** 'Obstructive sleep apnoea syndrome' (2015). NICE clinical knowledge summary. **Related NICE Pathways:** Chronic respiratory conditions: Sleep apnoea (2020) NICE pathway.

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Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2019) Manual for Prescribed Specialised Services 2018/19. Chapter 4, adult highly specialised respiratory services. Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1,2,4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1 NHS (2017) Excessive daytime sleepiness (hypersomnia). Accessed March 2020.

2 Mason M, Welsh EJ and Smith I. (2013) Drug therapy for obstructive sleep apnoea in adults (review). Cochrane Database of Systematic Reviews 5.

3 McMillan A, Bratton DJ, Faria R et al. (2015) A multicentre randomised controlled trial and economic evaluation of continuous positive airway pressure for the treatment of obstructive sleep apnoea syndrome in older people: PREDICT. Health Technology Assessment, No. 19(40): 1-188

4 Obstructive Sleep Apnoea (OSA) (2015). British Lung Foundation. Accessed March 2020.

5 NHS (2016) Obstructive sleep apnoea: treatment. Accessed March 2020.

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