NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

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

Draft scope (pre-referral)

Draft 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

Obstructive sleep apnoea (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.[1] 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 (EDS), reduced concentration and alertness.[1] OSA is associated with neuropsychological impairment, metabolic and cardiovascular co-morbidities and increased mortality.[1]

OSA is the third most common respiratory disorder in the UK.[2] An estimated 1.5 million adults it in the UK are affected by OSA, but up to 85% are undiagnosed and untreated.[3] The prevalence of OSA increases with age, with around 15 to 20% of people 70 years or estimated to have OSA[2,3]

First line treatment for people with mild OSA involves targeting known risk factors through improving lifestyle behaviours (such as, improving diet, increasing exercise, and reducing cigarette, alcohol, and drug consumption). NICE technology appraisal guidance 139 recommends continuous positive airway pressure (CPAP) for those with moderate to severe OSA. It also recommends CPAP for people with mild OSA when symptoms affect quality of life and improvements in lifestyle behaviours and other relevant treatment options are not possible or have not been successful. CPAP is not tolerated by all people with OSA. In some cases, intra-oral devices or pharyngeal surgery can be considered as alternative an to CPAP.[4,5] People suffering from EDS may be prescribed stimulants to reduce daytime sleepiness.[6]

The technology

Pitolisant hydrochloride (Tiprolisant, Bioprojet) 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 randomised controlled trials that compared the efficacy and safety of pitolisant hydrochloride with placebo in adults with OSA who are treated with CPAP, or are refusing CPAP and have EDS.

Intervention(s)	Pitolisant hydrochloride
Population(s)	Adults with obstructive sleep apnoea who are treated with CPAP, or are refusing CPAP and have excessive daytime sleepiness
Comparators	Stimulants with or without nasal continuous positive airway pressure: • modafinil • dexamphetamine • methylphenidate • sodium oxybate
Outcomes	The outcome measures to be considered include: • daytime sleepiness (e.g. Epworth sleepiness scale) • mortality • 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.

Other considerations	If the evidence allows, the following subgroups will be considered. These include mild, moderate and severe obstructive sleep apnoea. 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. Reviewed 2012, on static list. **Guidelines in development:** 'Sleep disordered breathing'. Expected publication date, August 2020. **Related Interventional Procedures:** 'Soft-palate implants for obstructive sleep apnoea' (2007) NICE interventional procedure guidance 241 **Interventional Procedure guidance in development:** 'Hypoglossal nerve stimulation for moderate to severe obstructive sleep apnoea'. Publication date to be confirmed. **Related NICE Evidence Summary:** 'Narcolepsy with or without cataplexy in adults: pitolisant' (2017). NICE evidence summary 8. **Related NICE Clinical Knowledge summary:** 'Obstructive sleep apnoea syndrome' (2015). NICE clinical knowledge summary **Related NICE Pathways:** Respiratory conditions (2016) NICE pathway
Related National Policy	NHS England (2017) Manual for Prescribed Specialised Services 2017/18. 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

Questions for consultation

Have all relevant comparators for pitolisant hydrochloride been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for EDS in people with OSA who are treated by CPAP, or in people with OSA who cannot tolerate CPAP?

Are stimulants prescribed for narcolepsy appropriate alternatives to pitolisant hydrochloride for treating excessive daytime sleepiness in people with obstructive sleep apnoea? Are the stimulants listed in the comparators used in current NHS clinical practice to treat EDS in people with OSA?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate?

Are there any other subgroups of people in whom pitolisant hydrochloride is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider pitolisant hydrochloride will fit into the existing NICE pathway, Respiratory conditions?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which pitolisant hydrochloride will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider pitolisant hydrochloride to be innovative in its potential to make a significant and substantial impact on health-related benefits and how

it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of pitolisant hydrochloride can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

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

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

3. Obstructive Sleep Apnoea (OSA) (2015). British Lung Foundation. Accessed July 2018.

4. Service Specification for Investigation and treatment of Obstructive Sleep Apnoea Syndrome (2009). British thoracic society. Accessed July 2018.

5. Management of Obstructive Sleep Apnoea/Hypopnoea Syndrome in Adults (2003). Scottish Intercollegiate Guidelines Network. Accessed July 2018.

6. Narcolepsy (2016). NHS choices. Accessed July 2018.