NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Daridorexant for treating insomnia

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of daridorexant within its marketing authorisation for treating insomnia.

Background

Insomnia is difficulty in getting to sleep, difficulty maintaining sleep, early wakening, or non-restorative sleep which occurs despite adequate opportunity for sleep. It results in impaired daytime functioning. Daytime symptoms typically include poor concentration, mood disturbance, and fatigue. Sleep disturbance in the absence of daytime impairment is not considered to be insomnia disorder. Insomnia is classed as short-term when symptoms occur for less than 3 months and chronic when symptoms persist for more than 3 months.

Identifying sleep patterns in the UK is difficult due to the lack of regular, high quality surveys. However, one study in the UK, found that the prevalence of people reporting sleep difficulties increased slightly from 35% to 39% between 1993 and 2007.[1] Although, a systematic literature review noted that only 6% of people met the criteria for an insomnia diagnosis.[2] Prevalence of insomnia is 1.5 to 2 times higher in females than males and is most common in older adults.[3] In addition, insomnia is associated with comorbid conditions such as chronic obstructive pulmonary disease, heart failure, chronic pain, and psychiatric conditions (depression, anxiety, substance abuse, and post-traumatic stress disorder).

NICE Clinical Knowledge Summary (CKS) for insomnia recommends sleep hygiene, which is increasing awareness of factors that may be detrimental or beneficial to sleep, for both acute and chronic insomnia. Cognitive behavioural therapy for insomnia (CBT-I) is recommended as first-line treatment for people with chronic or acute insomnia for whom sleep hygiene measures have failed and insomnia is not likely to resolve soon. Short-term pharmacotherapy with non-benzodiazepine hypnotic medication can be considered as a temporary adjunct to behavioural and cognitive treatments for people with chronic insomnia who have severe symptoms or an acute exacerbation. Short term pharmacotherapy can also be an option for people with acute insomnia if sleep hygiene measures fail and daytime impairment is severe causing significant distress. NICE technology appraisal 77 recommends hypnotic drugs zolpidem or zopiclone as treatment options for insomnia in adults. Benzodiazepines (including nitrazepam, loprazolam, lormetazepam and temazepam) or melatonin for those aged 55 or older may also be used.

The technology

Daridorexant (brand name unknown, Idorsia) is a dual orexin receptor antagonist (DORA). In contrast to treatments of insomnia that act via broad sedation of the central nervous system, DORAs specifically target excessive alertness. Daridorexant is administered orally.

Daridorexant does not currently have a marketing authorisation in the UK for insomnia. It has been studied in randomised controlled trials in adults with insomnia disorder, compared with placebo.

Intervention	Daridorexant
Population	Adults with insomnia
Comparators	• Established clinical management (including sleep hygiene and CBT-I) • Zolpidem and zopiclone • Melatonin (for those aged 55 and over) • Benzodiazepines (for example nitrazepam, loprazolam, lormetazepam, temazepam).
Outcomes	The outcome measures to be considered include: • Resolution of symptoms • Changes in sleep patterns and architecture • Sleep quality • Daytime alertness • Recurrence of insomnia • Adverse effects of treatment (including residual daytime sedation and memory impairment) • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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	The availability and cost of biosimilar and generic products should be taken into account. 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:** 'Guidance on the use of zaleplon, zolpidem and zopiclone for the short-term management of insomnia' (2004). NICE Technology Appraisal TA77. **Related Guidelines:** 'Scenario: Managing short-term insomnia (less than 3 months)' (2020). NICE CKS. 'Scenario: Managing long-term insomnia (3 months or more)' (2020). NICE CKS. 'Scenario: Benzodiazepine and z-drug withdrawal' (2019). NICE CKS.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 78: Neuropsychiatry services (adults and children). Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2 and 4 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for daridorexant been included in the scope? Which treatments are considered to be established clinical managment in the NHS for insomnia? Are benzodiazepines used in clinical practice in the NHS? If yes, please specify where in the pathway benzodiazepines are currently used.

Is daridorexant likely to be used alone or as an add-on to existing treatments for insomnia?

Are the outcomes listed appropriate?

What is the potential for dependence or misuse of daridorexant?

Is it anticipated that there will be a demonstrable QALY gain for people having daridorexant versus the comparators listed in the scope?

What do you consider the size of the eligible population for daridorexant to be?

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

Where do you consider daridorexant will fit into the clinical pathway for insomnia? Do you consider daridorexant to be an option for acute insomnia, chronic insomnia or both?

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 daridorexant 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 daridorexant 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 daridorexant 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1 Calem M, Bisla J, Begum A et al. (2012) Increased Prevalence of Insomnia and Changes in Hypnotics Use in England over 15 Years: Analysis of the 1993, 2000, and 2007 National Psychiatric Morbidity Surveys. Sleep 35(3): 377-384.

2 Ohayon M (2002) Epidemiology of insomnia: what we know and what we still need to learn. Sleep Medicine Reviews 6(2), 97-111.

3 Wilson S, Anderson K, Baldwin D et al. (2019) British Association for Psychopharmacology consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders: An update. Journal of Psychopharmacology 33(8), 923-947.