Surrey Heartlands Integrated Care System
Area Prescribing Committee (APC)

Integrated Care Partnership - Surrey Downs, Guildford & Waverley, North-West Surrey, and East Surrey Places & associated partner organisations.

NICE Technology Appraisals (TA) briefing paper for local implementation After Consultation

NICE TA Guidance name and number	Daridorexant for treating long-term insomnia Technology appraisal guidance [TA922]		
Available at	https://www.nice.org.uk/guidance/ta922		
Date of issue	18 October 2023	**Implementation deadline**	3 months

Medicine details[1]	
Name and brand name	Daridorexant (Quviviq)
Manufacturer	Idorsia Pharmaceuticals UK Ltd
Mode of action	Daridorexant is a selective and potent Dual Orexin Receptor Antagonist (DORA), acting as an equipotent orthosteric antagonist at both orexin 1 and orexin 2 receptors. The orexin neuropeptides (orexin A and orexin B) act on orexin receptors to promote wakefulness. Daridorexant blocks the binding of orexin neuropeptides to the receptors and consequently decreases the wake-drive, allowing sleep to occur. As a DORA, daridorexant acts by decreasing wakefulness, which contrasts with the mechanism of action of sedative/hypnotic medications (such as benzodiazepines and Z-drugs) that induce sleep through general suppression of the CNS via GABA-A receptor agonism.
Licenced indicatio daridorexant (Quviviq) n	For the treatment of adult patients with insomnia characterised by symptoms present for at least 3 months and considerable impact on daytime functioning.
Formulation	SPC formulation 25mg and 50mg film-coated tablets
Dosage	The recommended dose for adults is one tablet of 50 mg once per night, taken orally in the evening within 30 minutes before going to bed. Based on clinical judgement, some patients may be treated with 25 mg once per night. The maximum daily dose is 50 mg. The treatment duration should be as short as possible. The appropriateness of continued treatment should be assessed within 3 months and periodically thereafter. Clinical data are available for up to 12 months of continuous treatment. Treatment can be stopped without down-titration.
Comparison of NICE TA with Summary of Product Characteristics (SmPC)[2]	The NICE TA is more specific about patient eligibility and about actions to review treatment than the SPC

NICE TA recommendations[2]

Recommendations

Daridorexant is recommended for treating insomnia in adults with symptoms lasting for 3 nights or more per week for at least 3 months, and whose daytime functioning is considerably affected, only if:

• cognitive behavioural therapy for insomnia (CBTi) has been tried but not worked, or

• CBTi is not available or is unsuitable.

The length of treatment should be as short as possible. Treatment with daridorexant should be assessed within 3 months of starting and should be stopped in people whose long-term insomnia has not responded adequately. If treatment is continued, assess whether it is still working at regular intervals.

Decision making framework (DMF)

National guidance and priorities

The ICS has a legal obligation to commission this medicine in line with the NICE TA.

- This NICE TA has been assigned an implementation deadline of 3 months
- The implementation deadline is 18 January 2024

Clinical effectiveness

CBTi is the standard first treatment for people with long-term insomnia after sleep hygiene advice is offered. But access to CBTi varies across the UK, and for some people it does not work or is unsuitable. For this evaluation, the company asked for daridorexant to be considered as a first treatment when CBTi is not available or is unsuitable, and as a second treatment when CBTi has been tried but not worked. This does not include everyone who it is licensed for. The APC consultation highlighted the high value of CBTi for chronic insomnia, that there are in-person CBTi services in the specialist units and that there is a national commissioning of a digital CBTI solution. It is clear that further work is required to maximise patients' access to CBTi,

Clinical trial evidence shows that daridorexant improves symptoms of insomnia compared with placebo for 12 months. The effects if it's taken for longer than this are unknown. A condition of the marketing authorisation is that treatment with daridorexant should be reviewed within 3 months and regularly after that..The APC consultation highlighted that there is a lack of experience around reviewing efficacy and making decisions as to whether to stop or continue treatment, and therefore the recommendation is for diagnosis and initiation in specialist centres before discharge. Further feedback will be given to the APC after 1 year. Specialists highlighted the importance of CBTi even while taking the medication

The most likely cost-effectiveness estimate is within what NICE considers an acceptable use of NHS resources. So, daridorexant is recommended for routine use in the NHS.

Patient safety

- The product should be used within the NICE restrictions which is more restrictive than its product licence.
- As for all new medicines, this is a Black Triangle drug and requires that all suspected reactions be reported to MHRA, not just those which might be considered rare or serious. The triangle is usually in place for 5 years (but can be longer if needed).
- all suspected adverse reactions should be reported in order to identify rare adverse effects.
- Phase 3 trials showed that daridorexant 25 mg and 50 mg improved sleep outcomes, and daridorexant 50 mg also improved daytime functioning, in people with insomnia disorder, with a favourable safety profile5.
- Interacts at CYP3A4: Give a dose of 25 mg once daily with concurrent use of moderate CYP3A4 inhibitors, ciclosporin, or ciprofloxacin6.
- Cautions: Depression (worsening of symptoms including suicidal ideation); elderly (limited information available in patients older than 75 years); psychiatric illness (suicidal ideation reported in those with pre-existing disorders) [6]

- Lack of long term experience in use

Patient factors

- Access to CBTi is poor in Surrey Heartlands [7] Although the National commissioning of a digital solution and better signposting of local services will be helpful
- Long-term insomnia has both night-time symptoms and an effect on daytime functioning. This affects subjective and objective dimensions of health. The patient expert described how insomnia negatively affects mental and physical health and emotional wellbeing. They explained that insomnia is more than struggling to sleep, it also affects daytime functioning and social relationships. The patient expert explained that people with insomnia may have different care depending on where they live. They said that people with the condition would benefit from a longer-term treatment option, because current medicines can only be used for a short time. The committee concluded that long-term insomnia can substantially affect people's quality of life, and there is an unmet need for longer-term treatment options.

- An additional treatment option would be valued by patients. It is important that accurate diagnosis of chronic insomnia is made with differentiation between chronic insomnia and other underlying conditions such as restless leg syndrome, or sleep apnoea, which is why it is important that this diagnosis is carried out in a specialist setting

- Patients would need to be reviewed on a regular basis by the prescribing clinician to ensure concordance, monitor for adverse effects and efficacy.

Environmental impact

- Another oral tablet pack

Equality & diversity

Equality Impact Assessment:

This has been assessed by NICEas follows:

The company noted that that CBTi is recommended as first-line treatment for long-term insomnia but may not be suitable for or accessible to all people. The committee recognised this and understood that care varied, with people having different standards of care for long-term insomnia depending on where they live in the country. But the committee noted that access to treatments is an implementation issue that cannot be addressed by a NICE technology appraisal recommendation. No other equality or social value issues were identified.

Note 1: Drugs approved by NICE for adult conditions will be commissioned in children at specialised paediatric centres if the patient meets the NICE criteria and there is evidence to suggest that the drug is safe and clinically appropriate to use in children as per the NHS England Medicines for Children Policy (see https://www.england.nhs.uk/publication/commissioning-medicines-for-children-specialised-services/ and a Blueteq form is available.

Place in therapy relative to available treatments

Clinical Knowledge Summary (CKS): Insomnia https://cks.nice.org.uk/topics/insomnia/
Last revised in May 2022 (will not yet include daridorexant)

Stakeholder views

Cost-effectiveness

The drug cost per Place according to NICE resources does exceed £100,000 but only after year 3*

**NICE Costing calculator indicates that cost may exceed £100,000 per place after year 4 of implementation. Whether this materialises will depend on real life experience of efficacy, safety. If CBTi does not become available in Surrey Heartlands, costs may be higher*

Section 1: cost of the technology

a. Annual cost per patient (or complete course if shorter)

Costs in primary care: Up to £504 per annum (if taken for full 12 months)
Costs in secondary care:

b. Availability of CAP/PAS price:

c. Price relative to comparable medicines:
   a. Cost for 2 weeks: zopiclone £0.90* *maximum recommended duration*
   b. Cost for 13 weeks: melatonin £20
   c. Cost for 13 weeks: daridorexant £126

Section 2: NICE resource impact statement and template
Number of patients Year 1 and Year 5:

Potential patient numbers per 100,000:

a. NICE resource impact statement

b. NICE resource impact template

	Year 1	Year 2	Year 3	Year 4	Year 5
Number of patients receiving daridorexant	**368**	**739**	**1151**	**1647**	**2145**
Cost caculations provided in NICE template ('000)	**£100**	**£201**	**£313**	**£447**	**£583**
Cost caculations provided if treatment continous (not stopped) ('000)*	**£186**	**£373**	**£580**	**£830**	**£1,081**

**Calculation carried out by author based on the number of patients identified in the NICE template, but where all patients were prescribed the treatment for an entire year*

Commentary:

There has been concern expressed regarding the assumption of long term safety of this medicine in view of experience with previous treatments for insomnia.
Specialist initiation is likely to ensure that only appropriate prescribing is initiated, with growing expertise around treatment evaluation and continuation/ cessation as required.
Specialist cessation is likely to introduce delays in access to treatment
Technology should be able to increase access to CBTi but issues around commissioning and information governance to these new technologies remain.

The Surrey Heartlands Director of Pharmacy and Medicines Optimisation has delegated authority to enable the Committee to be a decision-making committee providing the impact of any single decision does not exceed £100,000 within an individual Place per annum. Decisions with a cost impact of over £100,000 within an individual Place per annum require authorisation from Surrey Heartlands Health & Care Professionals Committee at their next meeting. Exception to this will be for any decision made in relation to a NICE Technology Appraisal (which are subject to requiring mandatory funding by commissioners) and other urgent items. The exceptions will be taken to the next Executive Meeting (which meets weekly) for authorisation.

Traffic light recommendation to APC

NHS Payment Scheme (NHSPS) excluded high-cost drug: see NHS England » 2023-25 NHS

Payment Scheme
No

Recommended traffic light status and rationale:
BLUE initiation by specialist services
NICE identifies this treatment to be provided by Primary Care

PAD definitions, available at:

FINAL April 2023
Colour classification g

Implementation

NICE TA implementation must be within 90 days of publication.

Actions to implement:

- Recommend pursuing pathway to increase access to CBTi – this would be useful for both preventing the need for medication, but also ensure that medication is used for a shorter duration.
- Consider recommending further work on advice on repeated use of treatment –
- Consider developing an insomnia treatment pathway
- Continue to follow evidence regarding long term safety

a. Primary care

Diagnosis of chronic insomnia is complex and takes a considerable amoing of time, requiring accurat diagnosis of chronic insomnia, and differentiation between chronic insomnia and other underlying conditions such as restless leg syndrome, or sleep apnoea
There is a lack of experience around decision making on efficacy and duration of treatment
The medicine itself is not complex and does not require monitoring

b. Secondary care

As this treatment is only appropriate for long term insomnia, it should only be initiated in specialist sleep clinics. Specialist clinics will need to provide the medicines for the first 4 months (if clinicially indicated), providing a review after the first 3 months to review whether treatment should be continued. Transfer of care should be made in a timely manner after the 3-month review to allow prescribing in primary care. Specialists will continue to arrange regular reviews to advise on treatment continuation.

c. ICS

The ICS should liaise with the specialist centres to optimise access between existing face-to-face CBTi and the nationally commissioned CBTi digital tools

d. PAD and Joint Formulary

- The manufacturers have provided educational support (NHS letter) and patient information at the point of initiation, attached with this paper

- New PAD profile will be required

Proposed tick box forms

References:

1 Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/quviviq-epar-product-information_en.pdf , accessed January 2024

2 NICE Technology Appraisal Guidance: Daridorexant for treating long-term insomnia, Technology appraisal guidance [TA922], Published: 18 October 2023 . Available at: https://www.nice.org.uk/guidance/ta922 Accessed January 2024

3 NICE Resource Impact Report: Resource impact report: Daridorexant for treating long-term insomnia (TA922), Available at: https://www.nice.org.uk/guidance/ta922/resources/resource-impact-report-pdf-13195163053 Accessed January 2024

4 NICE Resource Impact Template: Available at: https://www.nice.org.uk/guidance/ta922/resources/resource-impact-template-excel-13195164349 Accessed January 2024

5 Safety and efficacy of daridorexant in patients with insomnia disorder: results from two multicentre, randomised, double-blind, placebo-controlled, phase 3 trials, Feb 2022, https://www.thelancet.com/journals/laneur/article/PIIS1474-44222100436-1/fulltext

6 BNF, accessed January 2024, https://bnf.nice.org.uk/drugs/daridorexant/#indications-and-dose

7 Verbal communication, Mr Jayesh Shah, Lead Primary Care Pharmacist for Mental Health,SHICB

8 Surrey Heartlands Prescribing Advisory Database, https://surreyccg.res-systems.net/PAD/Search/DrugConditionProfile/4488, accessed January 2024