Daridorexant

Traffic light classification- Amber 3
Information sheet for Primary Care Prescribers

Licensed Indication

Adult patients with insomnia characterised by symptoms present for at least three months and considerable impact on daytime functioning.

Therapeutic summary

Insomnia is difficulty in getting to sleep, difficulty maintaining sleep, early wakening, or non-restorative sleep which occurs despite adequate opportunity for sleep and 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. Long-term (or chronic) insomnia is that which lasts for three months or longer.

When diagnosing chronic insomnia, completion of a sleep diary should be requested - eg. sleepdiary.pdf (www.nhs.uk). This can be helpful identifying sleeping patterns and lifestyle factors that may exacerbate or maintain insomnia. The diary should be kept for at least two weeks. Good sleep hygiene should be established. Other strategies that may aid sleep should also be encouraged, eg. mindfulness, smoking cessation, exercise, reducing alcohol consumption.

Daridorexant is a dual orexin receptor(s) antagonist. These block the binding of wake-promoting orexin-A and -B to receptors to suppress the wake drive, allowing sleep to occur. Daridorexant is recommended by NICE for treating insomnia in adults with symptoms lasting for three nights or more per week for at least three 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.*

Patients with co-existing mental health conditions should first be considered for referral to Nottinghamshire Talking Therapies (notts-talk.co.uk) with an initial aim to focus on sleep. Some non-medication options are suggested in the Choice and medication leaflet. www.sleepful.me is available free of charge.

Clinical trials have compared daridorexant to placebo for up to twelve months. Improvements in sleep have been observed which include a reduction in time to fall asleep (LPS) and time awake during the night (WASO). Improvements seen with daridorexant 50mg in addition to placebo were a reduction in LPS of approximately 11 minutes and a 20-minute reduction in WASO. Subjective improvements in sleep and daytime functioning were seen within three months of taking the medication.

Products Available

Daridorexant is available as 25 mg and 50 mg film-coated tablets.

Cost= £42 per pack of 30 tablets.

Dosages and route of administration

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. This should be reduced to 25mg in those with moderate hepatic dysfunction or when taking moderate CYP3A4 inhibitors (see below).

Taking daridorexant soon after a large meal may reduce the effect on sleep onset.

When initiating treatment with daridorexant, treatment expectations, requirements for review and trials without medication should be outlined.

Duration of treatment and requirements for review

The length of treatment should be as short as possible. Treatment with daridorexant should be reviewed within the first month, with a further assessment within three months of treatment initiation. It should be stopped in people who do not experience a significant improvement. If treatment is continued, regular assessments and trials without medication should be conducted e.g. every 3-6 months. Lifestyle factors should be addressed at each review.

Clinical data are available for up to twelve months of continuous treatment. Treatment can be stopped without down-titration.

Contraindications and precautions:

Daridorexant is contraindicated in those with:

- Hypersensitivity to the active substance or to any of the excipients
- Narcolepsy
- Concomitant use with strong CYP3A4 inhibitors (see below)

Precautions include:

Elderly- use with caution. Limited data is available in those >75 years and no data >85 years.

Patients with psychiatric co-morbidities-
In primarily depressed patients treated with hypnotics, worsening of depression and suicidal thoughts and actions have been reported. As with other hypnotics, daridorexant should be administered with caution in patients exhibiting symptoms of depression. There is limited data in patients with psychiatric co-morbidities.

Severe obstructive sleep apnoea (OSA) and severe COPD (FEV1 < 40% of predicted)- a lack of data in this patient population.

Potential for abuse and dependence
There was no evidence of abuse or withdrawal symptoms indicative of physical dependence upon treatment discontinuation in clinical studies with daridorexant in subjects with insomnia. However, individuals with a history of abuse or addiction to alcohol or other substances may be at increased risk for abuse of daridorexant.

Pregnancy/ lactation- lack of data, seek specialist advice.

Clinically relevant medicine interactions and their management

- CYP3A4 inhibitors: contraindicated in combination with strong CYP3A4 inhbitors (eg. itraconazole, clarithromycin, ritonavir). In patients taking moderate CYP3A4 inhibitors (eg. erythromycin, ciprofloxacin, cyclosporine), the recommended dose is 25 mg daily.

  The consumption of grapefruit or grapefruit juice in the evening should be avoided.

- CYP3A4 inducers: concomitant use with a moderate or strong CYP3A4 inducer substantially decreases exposure to daridorexant, which may reduce efficacy.

- CNS-depressant medicinal products- dose adjustments of daridorexant and/or the other medicinal products may be required, based on clinical evaluation, due to potentially additive effects.

For further information on contraindications, precautions and interactions refer to the BNF or Summary of Product Characteristics.

Side effects

The most frequently reported adverse reactions to daridorexant in clinical trials were headache and somnolence.

Sleep paralysis, an inability to move or speak for up to several minutes during sleep wake transitions, and hypnagogic/hypnopompic hallucinations, including vivid and disturbing perceptions, can occur with daridorexant, mainly during the first weeks of treatment. Symptoms similar to mild cataplexy have also been reported with dual orexin receptor antagonists. Prescribers should explain the nature of these events to patients when prescribing daridorexant. Should such events occur, patients need to be further evaluated and, depending on the nature and severity of the events, discontinuation of treatment should be considered.

Daridorexant is a black triangle medication and any suspected adverse reactions should be reported to the MHRA via the Yellow Card scheme- Yellow Card | Making medicines and medical devices safer (mhra.gov.uk).

For a full list of side effects and information on incidence of ADRs, refer to the BNF or Summary of Product Characteristics (SPC).

Information given to patient

Sleep hygiene advice should be given. Useful resources include:
How to sleep better | Mental Health Foundation
Insomnia - NHS (www.nhs.uk)
Sleeping well | Royal College of Psychiatrists (rcpsych.ac.uk)
Insomnia (choiceandmedication.org)

Some non-medication treatment options are suggested in the Choice and Medication daridorexant leaflet www.sleepful.me is available free of charge.

When treatment with daridorexant is being considered, goals of treatment and expectations for review should be set with the patient at the outset. Lifestyle factors that may affect sleep should be re-visited at every review.

Because daridorexant acts by reducing wakefulness, patients should be cautioned about engaging in potentially hazardous activities, driving, or operating heavy machinery unless they feel fully alert, especially in the first few days of treatment. **In order to minimise this risk, a period of approximately 9 hours is recommended between taking daridorexant and driving or using machines**.

Patients should be advised that the consumption of grapefruit or grapefruit juice in the evening should be avoided.

References

QUVIVIQ Summary of Product characteristics. Last updated 25th October 2023. Accessed via MHRA Products | Home.
NICE TA922- Daridorexant for treating long-term insomnia. October 2023.
NICE CKS insomnia, last revised May 2022.
Mignot E et al. (2022) Safety and efficacy of daridorexant in patients with insomnia disorder: results from two multicentre, randomised, double-blind, placebo-controlled, phase 3 trials. Lancet Neurol 2022; 21: 125–39