Daridorexant Prescribing Support Document

This document provides summary information on daridorexant (Quviviq®) to support appropriate and safe prescribing by primary care clinicians.

Background

Daridorexant is a dual orexin receptor antagonist, acting on both orexin 1 and orexin 2 receptors. The orexin neuropeptides (orexin A and orexin B) act on orexin receptors to promote wakefulness. Daridorexant antagonises the activation of orexin receptors by the orexin neuropeptides and consequently decreases the wake drive, allowing sleep to occur, without altering the proportion of sleep stages.

Local/National Institute for Health and Care Excellence (NICE) approved indication for use

NICE Technology Appraisal 922 recommends daridorexant as an option 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, assessment should be undertaken to determine whether it is still working at regular intervals.

General Practitioner/Primary Care prescriber responsibilities

GPs/primary care prescribers can prescribe daridorexant in accordance with the recommendations in NICE TA922 (see section on NICE guidance above).
Prescribers should refer to NICE Clinical Knowledge Summary on insomnia for further information about the assessment, diagnosis, and management of insomnia before considering daridorexant.

Before considering daridorexant ensure:

- Any circumstances/stressors associated with onset of insomnia have been addressed
- Insomnia related to other conditions such as sleep apnoea, restless legs have been explored
- Information has been provided to patients on insomnia and sleep hygiene (see below)
- Sleep hygiene measures have been implemented and failed
- Symptoms are lasting for 3 nights or more per week for at least 3 months
- Daytime functioning is considerably affected
- Cognitive behavioural therapy for insomnia has been tried but not worked, or is not available, or is unsuitable.
- Medications are reviewed to ensure any pharmacological causes of insomnia are identified.

Sleep hygiene measures to advise patients:

Do's

- Go to bed and wake up at the same time every day
- Relax for at least an hour before bed, for example take a bath or read a book
- Make sure your bedroom is dark and quiet – use curtains, blinds and an eye mask and ear plug if needed
- Exercise regularly during the day but avoid within four hours of bedtime
- Make sure your mattress, pillows and covers are comfortable

Don’ts

- Do not smoke, use nicotine containing products, drink alcohol/tea/coffee/energy drinks at least 6 hours before going to bed.
- Do not eat a big meal late at night
- Do not watch television or use devices right before going to bed due to the bright light which makes you more awake
- Avoid napping in the day
- Do not drive when you feel sleepy
- Do not sleep in after a bad night’s sleep and stick to your regular sleeping hours instead

Sleep diary

Ask patients to keep a sleep diary to help identify what is keeping them awake. This is a useful tool which will help to pinpoint if there are any patterns affecting sleep. This is best completed over a two-week period and can be used as evidence of patient’s sleep-wake pattern which can help with diagnosis.

An example can be found here https://thesleepcharity.org.uk/information-support/adults/sleep-diary

*Talking therapies and Cognitive Behavioural therapy for Insomnia – CBT-I

Signpost patients to talking therapies websites which have self-help videos and drop-in sessions which address sleep problems.

Hertfordshire patients: How to sleep better | HPFT IAPT Services (hpft-talkingtherapies.nhs.uk)

To access help for primary insomnia, people aged 16 or over who are registered with a GP in Hertfordshire can self-refer for CBT-I via the HPFT Talking Therapies website: https://www.hpft-talkingtherapies.nhs.uk/referral. GPs and other Healthcare Professionals can also refer someone to the service directly by using the clinical referral form. This will be reviewed by administrators and patients will then be contacted for initial appointments.

West Essex patients: West Essex - Vita (vitahealthgroup.co.uk)

The ICB is currently reviewing options for provision of CBT-I for patients in West Essex. As soon as information is available, local guidance will be updated.

Sleep hygiene resources

- https://www.nhs.uk/every-mind-matters/mental-health-issues/sleep/
- https://www.nhs.uk/conditions/insomnia/
- https://cks.nice.org.uk/topics/insomnia/management/managing-short-term-insomnia-less-3-months/#good-sleep-hygiene
- https://www.ageuk.org.uk/information-advice/health-wellbeing/mind-body/getting-a-good-nights-sleep/
- https://www.headspace.com/sleep/sleep-hygiene

Daridorexant

Pharmaceutical form

25mg and 50mg film-coated tablets

Dosing advice

50mg once per night, taken orally in the evening within 30 minutes before going to bed. Tablets may be taken with or without food; however, administration soon after a large meal may reduce the effect on sleep onset.

Reduce dose to 25mg once per night in the following circumstances:

- Moderate hepatic impairment
- Concomitant use with moderate CYP3A4 inhibitors e.g. ciclosporin, ciprofloxacin, erythromycin (NB: consumption of grapefruit or grapefruit juice in the evening should be avoided).
- Caution should be exercised when prescribing with CNS-depressant medicinal products due to potentially additive effects, and a dose adjustment of either daridorexant or the concomitant CNS depressants may be required.

Missed doses

If a patient forgets to take daridorexant at bedtime, that dose should not be taken during the night.

Reviewing treatment

Treatment duration should be as short as possible. The need for continued treatment should be assessed within 3 months of starting daridorexant and at regular intervals thereafter. Treatment should be stopped in people whose long-term insomnia has not responded adequately. Clinical data is available for up to 12 months of continuous treatment.

It is important to note that sleep hygiene measures and behavioural changes for people with insomnia are essential to maximise the treatment effect for daridorexant. Therefore, when reviewing treatment ask for a sleep diary and more details about patients' symptoms and ensure sleep hygiene measures are being taken before agreeing to continue treatment.

In clinical trials not all the benefits of daridorexant found at 3 months were found after 12 months of treatment therefore having regular reviews is important to ensure the medicines is still appropriate for prescribing.

Stopping treatment

Treatment can be stopped without down-titration.

Special patient populations

Renal impairment

No dose adjustment required (including severe renal impairment)

Hepatic impairment

Mild hepatic impairment – no dose adjustment required.
Moderate hepatic impairment – reduce dose to 25mg once per night.
Severe hepatic impairment – not recommended.

Elderly (>65 years)

No dose adjustment required. Limited data available in patients >75 years. No data available in patients >85 years.

Children

Not recommended. Safety and efficacy in paediatric patients have not yet been established. No data are available.

Contraindications:

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

Cautions (see SPC for full details)

- Elderly patients (limited data on efficacy/safety in people aged >75 years; potential for increased risk of falls).
- Depression (worsening of symptoms including suicidal ideation) and psychiatric co-morbidities (efficacy and safety data in this patient population are limited). These patients would benefit from additional consideration, monitoring and possible dose adjustment before initiating treatment.
- CNS depressant effects: caution engaging in potentially hazardous activities, driving, or operating heavy machinery unless the patient feels fully alert, especially in the first few days of treatment.
- Potential additive effects when co-prescribing daridorexant and CNS depressant medicines – dose adjustment of either daridorexant (to 25mg at night) or the concomitant CNS depressant(s) should be considered. Other hypnotic medicines should be reviewed prior to starting daridorexant and, if they are to be stopped or reduced, this should be done in accordance with clinical recommendations e.g. Clinical Knowledge Summary - Benzodiazepine and z-drug withdrawal.
- Severe obstructive sleep apnoea and/or severe COPD.
- Consumption of alcohol (additive effects on psychomotor performance). Patients with a history of abuse or addiction to alcohol or other substances.

Adverse effects

- Headache (common)
- Somnolence (common)
- Dizziness (common)
- Fatigue (common)
- Nausea (common)
- Hallucinations (occurs mainly in the first weeks of treatment, uncommon)
- Sleep paralysis (occurs mainly in the first weeks of treatment, uncommon)

Pregnancy, lactation and fertility (see SPC for full details)

Pregnancy

There is no data on the use of daridorexant in pregnant women. Animal studies did not indicate harmful effects with respect to reproductive toxicity. Daridorexant should be used during pregnancy only if the clinical condition of the pregnant woman requires treatment with daridorexant (avoid unless essential).

Breast feeding

It is unknown whether daridorexant or its metabolites are excreted in human milk. Available data in animals have shown excretion of daridorexant and its metabolites in milk. As a risk of excessive somnolence to the breastfed infant cannot be excluded, daridorexant should be used with caution on a risk-benefit basis. If used, monitor the breast-fed infant for sedation, poor feeding, and poor weight gain (amount in milk likely to be small as daridorexant is about 99.7% bound to plasma proteins). Consider alternative drug, particularly if breast-feeding a neonate (pre- or full-term).

Fertility

There is no data concerning the effect of exposure to daridorexant on human fertility. Animal studies indicate no impact on male or female fertility.

Interactions (see SPC for full details)

The effects of alcohol and other CNS depressants is enhanced when taken in combination with daridorexant.

Potential additive effects when co-prescribing daridorexant and CNS depressant medicines – dose adjustment of either daridorexant (to 25mg at night) or the concomitant CNS depressant(s) should be considered. Other hypnotic medicines should be reviewed prior to starting daridorexant and, if they are to be stopped or reduced, this should be done in accordance with clinical recommendations e.g. Clinical Knowledge Summary - Benzodiazepine and z-drug withdrawal.

Daridorexant should not be used in patients taking strong inhibitors of CYP3A4 (e.g. itraconazole, clarithromycin, ritonavir). Reduce the dose to 25mg in patients taking moderate CYP3A4 inhibitors (e.g. erythromycin, ciprofloxacin, ciclosporin). Consumption of grapefruit or grapefruit juice in the evening should be avoided.

Concomitant use of daridorexant with a moderate or strong CYP3A4 inducer (e.g. rifampicin, carbamazepine, phenytoin, topiramate, ritonavir, efavirenz, St John's Wort) substantially decreases exposure to daridorexant, which may reduce efficacy.

Caution is required when co-administering CYP3A4 substrates with a narrow therapeutic index (e.g. high-dose simvastatin, tacrolimus) and P-gp substrates with a narrow therapeutic index (e.g. digoxin).

Counselling points

- Emphasise the importance of good sleep hygiene (see resources below).
- Take daridorexant 30 minutes before going to bed. If forgotten, the dose should not be taken during the night.
- May be taken with or without food, but eating a large meal soon before taking the dose may reduce the effects.
- Drowsiness may persist the next day, especially in the first few days of treatment – leave about 9 hours between taking daridorexant and performing skilled tasks (e.g. driving or operating machinery).
- Long-term treatment is not recommended and treatment duration should be as short as possible. Treatment will be assessed within 3 months of starting and regularly thereafter.
- Report adverse effects, including mood changes, sleep paralysis, hallucinations and cataplexy-like symptoms.

Training provided by Idorsia Pharmaceuticals (manufacturers of Daridorexant (Quviviq®)

- Introduction to insomnia: https://www.idorsia.uk/documents/uk/edu/intro-to-insomnia-UK.pdf
- Medical education on daridorexant: https://www.idorsia.uk/documents/uk/edu/UK-smPC-education.pdf

References

1. Summary of product characteristics Microsoft Word - 8866650923336198830_spc-doc.doc (windows.net) accessed 21/12/23

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