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New Approved Treatment for Insomnia

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Abstract

Insomnia is a common health condition which can affect any age group, being more common in women, elderly and is a common presentation in primary care. It can have a short term or a chronic presentation with associated physical and psychological risks and increased morbidity. It is a complex sleeping condition affecting many lives worldwide. Recently, National Institute for Health and Care Excellence, United Kingdom (NICE-UK) has approved a new medicine for long term treatment of insomnia. This article will summarise the new guidance along with relevant clinical evidence.

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Keywords

Insomnia, Cognitive Behavioural Therapy for Insomnia (CBT-I), Dual Orexin Receptor Antagonists (DORAs), Daridorexant (Quviviq), Orexin, Wake time after sleep onset (WASO) Latency to persist sleep (LPS).

1.Introduction

Insomnia is defined as having problems with sleep. This include either having problem falling asleep or staying asleep or it can be not getting good quality sleep or early morning waking up. This can be the case even when present in right and comfortable environment and it can affect the day time activities, mood, memory and performance (*Insomnia - What Is Insomnia?*, 2022). In other words it is the dissatisfaction with either the quality of sleep or the quantity of sleep or both (Brasure et al., 2015). The prevalence is around 10-20% with 50% having a chronic course (Buysse, 2013).

Short term Insomnia is when it's for few days or weeks only (under 3 months), while chronic insomnia is when lasting for more than 3 months and happening 3 or more nights a week. Chronic insomnia has various negative impacts on health including poor concentration, low mood, high blood pressure, diabetes, coronary heart disease, respiratory disease, cerebral vascular disease and increased morbidity (*Insomnia - What Is Insomnia?*, 2022) (Brasure et al., 2015). Short term insomnia is usually caused by stress while chronic insomnia has a variety of risk factors including increasing age, but can happen at any age, working pattern (night shifts, loud noises), life style, environment, stress and female gender (*Insomnia - What Is Insomnia?*, 2022) (*Patient Education: Insomnia (Beyond the Basics) - UpToDate*, n.d.). As per Robinson et al, the prevalence is higher in elderly, disabled, female, population and those with shift work pattern, substance misuse, alcohol abuse along with social factors like

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unemployment, poor marital status and co-existing mental health conditions (Robinson et al., n.d.).

Insomnia is a very common complaint for adults in primary care and is linked with a decline in general well-being, higher anxiety levels, with a negative impact on personal and social life (Brasure et al., 2015). It can be approached and managed by various means including medications, cognitive behavioural therapy for insomnia (CBT-I), sleep education, life style changes, diet, exercise and so on (*Patient Education: Insomnia Treatments (Beyond the Basics) - UpToDate*, n.d.).

2.Main Guideline Review

The first line therapy for insomnia is CBT-I. If CBT-I and other general measures have not helped and insomnia is affecting daytime functioning, then pharmacotherapy can be tried. Pharmacotherapy falls under four classes of medications and include Benzodiazepine receptor agonists (BZRAs), Histamine receptor antagonists, Melatonin receptor agonists and Dual Orexin receptor antagonists (DORAs) (*Patient Education: Insomnia Treatments (Beyond the Basics) - UpToDate*, n.d.), (Robinson et al., n.d.) .

Traditionally, BZRAs and Histamine receptor agonists have been the mainstay treatment for insomnia but discouraged for their long-term use given dependency issues, risk of abuse and side effects. Newer treatment option like DORAs offer better symptomatic relief without any severe side effects and dependency issues (Robinson et al., n.d.).

Recently Daridorexant (brand name: Quviviq) from DORAs family has been approved by National Institute for Health and Care Excellence, United Kingdom (NICE-UK) for the long-term treatment of insomnia. Daridorexant belongs to Dual Orexin Receptor Antagonists (DORAs) family. These medicines work by blocking a chemical in brain called Orexin,

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which normally helps to keep awake. The other medicines in this group include Lemborexant and Suvorexant (*Patient Education: Insomnia Treatments (Beyond the Basics) - UpToDate*, n.d.).

Daridorexant (Quviviq) has been provisionally approved by NICE-UK very recently for chronic insomnia. It blocks both Orexin 1 and Orexin 2 receptors, helping sleep and decreasing waking effect (September 2023, n.d.). NICE-UK recommends using Daridorexant for long term insomnia in adults with symptoms for at least 3 nights every week for at least 3 months, only if CBT-I has either failed or is not available and insomnia is affecting daytime functioning. The duration of treatment should be minimal, with a review in 3 months' time after starting the treatment and discontinue the treatment if has not responded well in 3 months' time period. As CBT-I which is the recommended first line treatment for long term insomnia is not available all across UK, the committee has made the recommendations (*674.Pdf*, n.d.). NICE recommends GPs in primary care to prescribe it but the committee also emphasised GPs to always offer CBT-I as first line. It is estimated by NICE-UK that around 20,000 people in England only could get this medicine prescribed during first year (Parr, 2023)

It was patented in 2013 and got its first approval for insomnia treatment in USA in January 2022. It helps by inducing sleep quicker and also helping in staying asleep longer (Robinson et al., n.d.).

3.Clinical Evidence

A total of 1854 adults were randomised in a multicentre double blind, phase 3 trial at 156 sites in 18 countries. Participants were randomised to receive Daridorexant vs placebo over 3 months period. Primary end points were changes in baseline wake time after sleep onset (WASO) and latency to persist sleep (LPS), measured through polysomnography at 1st and 3rd

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months. The secondary endpoints were self-reported day time functioning and total sleep time, measured through questionnaire (IDSIQ). The trial showed significant improvement in WASO and LPS from baseline at 1st and 3rd months among those who received Daridorexant 50mg vs placebo. The common side effects were headaches and somnolence with no evidence of any abuse or physical dependency or withdrawal (September 2023, n.d.) (Mignot et al., 2022).

4.Dosage, Administration and Contraindication

The recommended dose is 25mg to 50mg once at night, to be taken around 30 minutes before bedtime, with minimum 7 hours of planned sleep time. It is contraindicated in patients with narcolepsy and should be used with caution in patients with hepatic impairment and those on cytochrome P450 inducer or inhibitor medications. So far there is no available data for safe use in pregnant women (*214985s000lbl.Pdf*, n.d.)

5.Conclusion

Insomnia is a complex condition affecting people physically and psychologically worldwide. There are four approved medicine groups to help treat insomnia. Among these, Daridorexant (Quviviq) from DORAs family is the first dual orexin receptor antagonist to get approved recently for the treatment of chronic insomnia by NICE-UK. In phase 3 clinical trials it has improved wake time after sleep onset and latency to persist sleep and has been tolerated well at a 50mg dose. CBT-I is the recommended first line treatment for long term insomnia, but if it doesn't help or if it is not available then Daridorexant is the recommended. It should be offered only when symptoms are for more than 3 months and affecting daytime functioning. NICE recommends GPs in primary care to prescribe it but the committee also emphasised GPs to always offer CBT-I as first line.

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