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New advice to minimise risk of next-morning impaired driving ability and mental alertness with zolpidem

On 24 April 2014, the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh)[1] endorsed by majority new recommendations for zolpidem-containing medicines, used for the short-term treatment of insomnia (difficulty sleeping). The CMDh agreed that the benefit-risk balance of these medicines remains positive; however, some changes have been made to the product information to minimise the known risk of reduced mental alertness and impaired ability to drive and use machinery the morning after use.

These recommendations followed a review by the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) of available data on the safety of zolpidem with regards to the risk of impaired driving, somnambulism, and reduced mental alertness (such as drowsiness and slower reactions) after taking the medicine, and information on its effectiveness at lower doses.

Changes made to the product information of zolpidem-containing medicines include strengthened warnings and precautions. The normal recommended daily dose in adults, which must not be exceeded, remains at 10 mg, and for older patients and patients with reduced liver function it remains at 5 mg. Patients should take the lowest effective dose of zolpidem in a single intake just before going to bed and should not take another dose during the same night. Furthermore, patients should not drive or perform activities that require mental alertness for at least 8 hours after taking zolpidem. Since the risk of impaired driving seems to increase if zolpidem is taken together with other medicines that have an effect on the central nervous system (brain and spinal cord), or with alcohol or illicit drugs, these substances should not be used when taking zolpidem.

As the CMDh position on zolpidem was adopted by majority vote, it was sent to the European Commission, which endorsed it and adopted an EU-wide legally binding decision on 23 June 2014.

[1] The CMDh is a medicines regulatory body representing the European Union (EU) Member States

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Information to patients

- Zolpidem-containing medicines are used for the short-term treatment of insomnia (difficulty sleeping). Zolpidem may cause drowsiness and slower reactions the day after taking the medicine, which could cause impaired driving ability and increase the risk of road accidents; a warning of these risks is included in the package leaflet.
- It is important that patients do not exceed the recommended dose of zolpidem, which is 10 mg by mouth once a day; a lower dose may be prescribed to some adults. In older patients and patients with reduced liver function a lower dose of 5 mg is recommended. Zolpidem should be taken just before going to bed, and it should not be taken again during the same night.
- Patients taking zolpidem should make sure there is a period of at least 8 hours between taking the medicine and driving or operating other machinery.
- Since the risk of reduced mental alertness and driving ability seems to increase if zolpidem is taken together with other medicines that cause drowsiness or lack of alertness, or with alcohol or illicit drugs, these substances should not be used when taking zolpidem.
- Patients who have any concerns about their treatment should speak to their doctor or pharmacist.

Information to healthcare professionals

- A review of the available data confirmed that the benefit-risk balance of zolpidem-containing medicines remains positive but changes have been introduced to the product information of these medicines, aimed at further minimising the known risks of next-morning reduced mental alertness and impaired driving ability.
- The daily dose of zolpidem remains 10 mg a day in adults and 5 mg a day in the elderly and in patients with hepatic impairment; this dose must not be exceeded. The data analysed during the review showed that, while most cases of impaired driving were linked to the intake of a 10 mg daily dose of zolpidem, lower doses were not shown to significantly reduce the risk of impaired driving and were not consistently shown to be effective at population level.
- Patients should take the lowest effective dose, in a single intake just before bedtime. Some studies showed an association between intake of zolpidem in the middle of the night and impaired driving ability the next day. In order to minimise this risk, zolpidem should not be re-taken during the same night.
- The risk of impaired mental alertness is higher if zolpidem is taken with less than a full night of sleep remaining; therefore, a period of at least 8 hours is recommended between taking zolpidem and performing activities such as driving or operating other machinery.
- The risk of impaired mental alertness also increases if zolpidem is taken at higher than recommended doses, or if it is co-administered with other CNS depressants, alcohol, or illicit drugs. Warnings have been introduced to the product information to highlight these risks.

These recommendations are based on a careful assessment of the available data on the safety and efficacy of zolpidem from clinical studies, post-marketing reports and the published literature.

More about the medicine

Zolpidem is a medicine used for the short-term treatment of insomnia. It acts by attaching to and stimulating a particular type of receptor on nerve cells called the alpha-1 GABA-A receptor (also called the omega-1 receptor). This receptor is part of a system in the brain that normally responds to a neurotransmitter called gamma-aminobutyric acid (GABA) and which reduces the activity of the brain, causing relaxation and sleepiness. A neurotransmitter is a chemical that carries signals between nerve cells. By stimulating the receptor, zolpidem is able to enhance this effect, helping patients to sleep.

Zolpidem has been authorised via national procedures in all Member States of the EU.

More about the procedure

The review of zolpidem-containing medicines was initiated on 4 July 2013 at the request of the Italian Medicines Agency (AIFA) under Article 31 of Directive 2001/83/EC.

A review of these data was first conducted by the Pharmacovigilance Risk Assessment Committee (PRAC). As zolpidem-containing medicines are all authorised nationally, the PRAC recommendations were sent to Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which adopted a final position on 24 April 2014. The CMDh, a body representing EU Member States, is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.

As the CMDh position was adopted by majority vote, it was sent to the European Commission, which endorsed it and adopted an EU-wide legally binding decision on 23 June 2014.

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