Medicines & Healthcare products
Regulatory Agency

Public Assessment Report

National Procedure

Zolpidem 5 mg film-coated tablet
Zolpidem 10 mg film-coated tablet

zolpidem tartrate

PL 55863/0102 - 0103

NOVUMGEN LIMITED

LAY SUMMARY

Zolpidem 5 mg and 10 mg film-coated tablets
zolpidem tartrate

This is a summary of the Public Assessment Report (PAR) for Zolpidem 5 mg and 10 mg film-coated tablets. It explains how these products were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use these products.

These products have been authorised by Medicines and Healthcare products Regulatory Agency (MHRA) for the United Kingdom. These procedures take into account the outcome of decentralised (DC) procedures in European Union Member States (and/or Iceland, Liechtenstein, Norway) on 2 October 2014 (DK/H/2309/001-002/DC). This is known as the MR/DC Reliance Procedure.

These applications were approved under Regulation 51B of the Human Medicines Regulation 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended).

For practical information about using Zolpidem 5 mg and 10 mg film-coated tablets, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What are Zolpidem 5 mg and 10 mg film-coated tablets and what are they used for?
These products are generic medicines. This means that these medicines are the same as, and considered interchangeable with, reference medicines already authorised, called Stilnoct 10 mg film-coated tablet.

Zolpidem 5 mg and 10 mg film-coated tablets are used for temporary sleep problems in adults that are causing severe distress or that are affecting everyday life. This includes sleep problems in adults such as:

- difficulty falling asleep
- waking in the middle of the night
- waking too early

The person’s doctor will identify sleep problem wherever possible and the underlying factors before prescribing this medicine. The failure of sleep problems to stop after a 7 to 14 day course of treatment may indicate that patients have an underlying disorder, which the patient’s doctor will assess at regular intervals.

These medicines are used for short-term treatment of insomnia in adults. They should not be used long-term. Treatment should be as short as possible, because the risk of dependence increases with the duration of treatment. Patients should ask their doctor for advice if they are unsure.

How do Zolpidem 5 mg and 10 mg film-coated tablets work?
Zolpidem contains a medicine called zolpidem tartrate. This belongs to a group of medicines called hypnotics. It works by acting on the brain to help people to sleep.

How are Zolpidem 5 mg and 10 mg film-coated tablets used?
The pharmaceutical form of these medicines is film-coated tablets and the route of administration is oral (by mouth). The tablets should be swallowed whole with a drink of water and should be taken as a single intake just before bedtime.

The recommended dose per 24 hours is 10 mg of Zolpidem. A lower dose may be prescribed to some patients.

Patients should make sure they have a period of at least 8 hours after taking this medicine before performing activities that require alertness.

Do not exceed 10 mg per 24 hours.

The usual length of treatment is 2 days to 4 weeks.

For adults, the usual dose is one Zolpidem tablet 10 mg just before bedtime.

In older patients, people who are elderly or have liver problems, the usual dose is 5 mg just before bedtime. For patients with liver problems, the doctor may decide to increase this to 10 mg if it is safe to do so.

Zolpidem should not be used in people under 18 years old.

For further information on how Zolpidem 5 mg and 10 mg film-coated tablets are used, refer to the PIL and Summaries of Product Characteristics (SmPCs) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

These medicines can only be obtained with a prescription.

The patient should always take the medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Zolpidem 5 mg and 10 mg film-coated tablets have been shown in studies?
Because Zolpidem 5 mg and 10 mg film-coated tablets are generic medicines, studies in healthy volunteers have been limited to tests to determine that they are bioequivalent to the reference medicines. Two medicines are bioequivalent when they produce the same levels of the active substance in the body.

What are the possible side effects of Zolpidem 5 mg and 10 mg film-coated tablets?
For the full list of all side effects reported with these medicines, see Section 4 of the PIL or the SmPCs available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card

scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Why were Zolpidem 5 mg and 10 mg film-coated tablets approved?
MHRA decided that the benefits are greater than the risks and recommended that these medicines can be approved for use.

What measures are being taken to ensure the safe and effective use of Zolpidem 5 mg and 10 mg film-coated tablets?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Zolpidem 5 mg and 10 mg film-coated tablets. The RMP details the important risks of Zolpidem 5 mg and 10 mg film-coated tablets, how these risks can be minimised, any uncertainties about Zolpidem 5 mg and 10 mg film-coated tablets (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Zolpidem 5 mg and 10 mg film-coated tablets:

Important identified risks	• Dependence and withdrawal symptoms/Rebound effect • Psychiatric and paradoxical reactions • Additive CNS depressant effects when administered with alcohol or CNS depressant • Coma/respiratory depression during overdose • Drug abuse • Suicidality in patients with depression, severe depression or suicidal ideation
Important potential risks	• None
Missing information	• Use in children and adolescents under 18 years of age • Use during pregnancy • Use during nursing/breastfeeding

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Zolpidem 5 mg and 10 mg film-coated tablets are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Other information about Zolpidem 5 mg and 10 mg film-coated tablets
Marketing authorisations were granted in the United Kingdom on 21 May 2024.

The full PAR for Zolpidem 5 mg and 10 mg film-coated tablets follows this summary. This summary was last updated in September 2024.

TABLE OF CONTENTS

I. INTRODUCTION 6
II. PRODUCT INFORMATION 6
III. QUALITY ASPECTS 7
IV. NON-CLINICAL ASPECTS 7
V. CLINICAL ASPECTS 7
VI. RISK MANAGEMENT PLAN (RMP) 7
VII. USER CONSULTATION 7
VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION 7
TABLE OF CONTENT OF THE PAR UPDATE 8

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the applications for Zolpidem 5 mg and 10 mg film-coated tablets (PL 55863/0102 - 0103) could be approved.

The products are approved for short-term treatment of insomnia in adults in situations where the insomnia is severe, disabling or subjecting the individual to extreme distress.

The active ingredient in this medicine is zolpidem tartrate. Zolpidem is an imidazopyridine, which binds selectively to omega-1 receptors which constitute the alpha unit in the GABA-A receptor complex. Whereas benzodiazepines non-selectively binds to all three omega-subtype receptors, zolpidem binds preferentially to the alpha-1 subunit.

The modulation of the chloride anion channel via this receptor leads to the specific sedative effects demonstrated by zolpidem. The selective binding of zolpidem tartrate to omega-1 receptors may explain the virtual absence at hypnotic doses of myorelaxant and anti-convulsant effects in animals which are normally exhibited by benzodiazepines which are not selective for omega-1 sites. The preservation of deep sleep (stages 3 and 4 - slow-wave sleep) may be explained by the selective omega-1 binding by zolpidem.

These products have been authorised by Medicines and Healthcare products Regulatory Agency (MHRA) for the United Kingdom. These procedures take into account the outcome of decentralised (DC) procedures in European Union Member States (and/or Iceland, Liechtenstein, Norway) on 2 October 2014 (DK/H/2309/001-002/DC). This is known as the MR/DC Reliance Procedure.

For the scientific discussion of the quality, non-clinical and clinical assessment conducted during the DC procedures, please refer to the Reference Member State (RMS) Public Assessment Report, available on the RMS regulatory agency website or on the Heads of Medicines Agencies website.

These applications were approved under Regulation 51B of the Human Medicines Regulation 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended).

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these products at all sites responsible for the manufacture, assembly and batch release of these products.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with these applications and are satisfactory.

Marketing authorisations were granted on 21 May 2024.

II. PRODUCT INFORMATION

Summaries of Product Characteristics (SmPCs)

The SmPCs are in line with current guidelines and are satisfactory.

PATIENT INFORMATION LEAFLET (PIL)

The PIL is in line with current guidelines and is satisfactory.

LABEL
The labelling is in line with current guidelines and is satisfactory.

III. QUALITY ASPECTS
MHRA considered that the quality data submitted for these applications is satisfactory. The grant of marketing authorisations was recommended.

IV. NON-CLINICAL ASPECTS
MHRA considered that the non-clinical data submitted for these applications is satisfactory. The grant of marketing authorisations was recommended.

V. CLINICAL ASPECTS
MHRA considered that the clinical data submitted for these applications is satisfactory. The grant of marketing authorisations was recommended.

VI. RISK MANAGEMENT PLAN (RMP)
The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

VII. USER CONSULTATION
A full colour mock-up of the Patient Information Leaflet (PIL) was provided with the application in accordance with legal requirements, including user consultation.

VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The benefit/risk balance is, therefore, considered to be positive.

The Summaries of Product Characteristics (SmPCs), Patient Information Leaflet (PIL) and labelling are satisfactory.

In accordance with legal requirements, the current approved UK versions of the SmPCs and PIL for these products are available on the MHRA website.

IX. TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPCs and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**