SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

ADCO-ZOLPIDEM HEMITARTRATE 5 mg film-coated tablets
ADCO-ZOLPIDEM HEMITARTRATE 10 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each **ADCO-ZOLPIDEM HEMITARTRATE 5 mg** tablet contains: 5 mg zolpidem hemitartrate.
Contains sugar: Lactose monohydrate 45,20 mg.

Each **ADCO-ZOLPIDEM HEMITARTRATE 10 mg** tablet contains: 10 mg zolpidem hemitartrate.
Contains sugar: Lactose monohydrate 90,40 mg.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.

ADCO-ZOLPIDEM HEMITARTRATE 5 mg: White, oval, biconvex, film-coated tablet, debossed with “ZIM” on one side and “5” on the other side.

ADCO-ZOLPIDEM HEMITARTRATE 10 mg: White, oval, biconvex, film-coated tablet, scored on both sides and debossed with “ZIM” and “10” on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ADCO-ZOLPIDEM HEMITARTRATE (zolpidem), a short-acting hypnotic, is indicated for the short- term treatment of insomnia which is disabling, severe, or subjecting the patient to extreme distress.

4.2 Posology and method of administration

Posology:
ADCO-ZOLPIDEM HEMITARTRATE should be taken just before bedtime.
The treatment period with **ADCO-ZOLPIDEM HEMITARTRATE** should be as limited as possible. In general, treatment duration varies from a few days to two weeks, with a maximum of 4 weeks (including the tapering off process).
It may be necessary to extend the duration of treatment in certain cases. However, this should not be done without re-assessing the status of the patient.

Dose:
Adults: The recommended daily dose is 10 mg immediately before going to bed.

Special populations
Elderly or debilitated patients, or patients with hepatic insufficiency in whom clearance of the drug is reduced: The recommended daily dose is 5 mg; this dose should not be exceeded except under special circumstances. (see section 4.8).
The maximum daily dose is 10 mg in any patient.
A dosage of 10 mg is equivalent to one tablet of **ADCO-ZOLPIDEM HEMITARTRATE 10 mg** or two tablets of **ADCO-ZOLPIDEM HEMITARTRATE 5 mg**. A dosage of 5 mg is equivalent to one tablet of **ADCO-ZOLPIDEM HEMITARTRATE 5 mg** or half a tablet of **ADCO-ZOLPIDEM HEMITARTRATE 10 mg.**

Paediatric population
Safety and effectiveness of **ADCO-ZOLPIDEM HEMITARTRATE** in paediatric patients under the age of 18 years have not been established. **ADCO-ZOLPIDEM HEMITARTRATE** should not be prescribed in this population. (see section 4.3).

Method of administration
Oral.

4.3 Contraindications
- **ADCO-ZOLPIDEM HEMITARTRATE** is contraindicated in patients with hypersensitivity to zolpidem or any of the excipients listed in section 6.1.
- It is contraindicated in patients who suffer from sleep apnoea, myasthenia gravis, severe hepatic insufficiency, acute and severe pulmonary insufficiency.
- **ADCO-ZOLPIDEM HEMITARTRATE** should not be used in children under the age of 18.
- Safety in pregnancy and lactation has not yet been established (see section 4.6).
- **ADCO-ZOLPIDEM HEMITARTRATE** should not be administered to lactating mothers as small quantities of zolpidem have been detected in breast milk.

4.4 Special warnings and precautions for use
The cause of insomnia should be identified wherever possible and the underlying factors treated before **ADCO-ZOLPIDEM HEMITARTRATE** is prescribed. The failure of insomnia to remit after a 7 – 14 days course of treatment may indicate the presence of a primary psychiatric or physical disorder, and the patient should be carefully re-evaluated at regular intervals.

Risks from concomitant use with opioids:
Concomitant use of opioids with benzodiazepines or other sedative-hypnotic medicines, including **ADCO-ZOLPIDEM HEMITARTRATE**, may result in sedation, respiratory depression, coma, and death. Because of these risks, reserve concomitant prescribing of

opioids and benzodiazepines for use in patients for whom alternative treatment options are inadequate.
If a decision is made to prescribe **ADCO-ZOLPIDEM HEMITARTRATE** concomitantly with opioids, prescribe the lowest effective dosages and minimum durations of concomitant use, and follow patients closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients to be aware of these symptoms (see section 4.5).

Pregnancy:
ADCO-ZOLPIDEM HEMITARTRATE may cause moderate respiratory depression, hypotonia and hypothermia in neonates if it is taken during the late phase of pregnancy or during labour. Moreover, physical dependence may develop in infants born to mothers who take **ADCO- ZOLPIDEM HEMITARTRATE** chronically during the last stages of pregnancy. The infant may also be at risk of developing withdrawal symptoms in the postnatal period.

Duration of treatment:
The treatment period with **ADCO-ZOLPIDEM HEMITARTRATE** should be as limited as possible and it should not extend beyond a maximum of 4 weeks, which includes the tapering off process. Extended periods of treatment should not occur without re-assessment of the patient's status.
When treatment is commencing, it may be helpful to inform the patient that treatment with **ADCO- ZOLPIDEM HEMITARTRATE** will be for a limited time period, and to explain exactly how the dosage will be gradually reduced.

Tolerance:
After repeated use for a few weeks, the hypnotic effects of **ADCO-ZOLPIDEM HEMITARTRATE** may be reduced.

Amnesia:
Anterograde amnesia may occur, most often several hours after ingestion of the product. Thus, to decrease the risk of this occurring, patients should make certain that they will be able to have an uninterrupted sleep of 7 to 8 hours (see section 4.8).

Rebound insomnia:
Rebound insomnia accompanied by restlessness, anxiety and mood changes may occur upon cessation of treatment with **ADCO-ZOLPIDEM HEMITARTRATE**.
Rebound insomnia is more likely to occur upon abrupt withdrawal of the product, thus treatment should be withdrawn gradually.
In order to reduce anxiety over possible rebound phenomena, the patient should be made aware that such symptoms could occur during the withdrawal period. There are indications that withdrawal effects can become evident within the dosage interval of short-acting hypnotics, especially when high dosages are used.

Psychiatric and "paradoxical"reactions:
Other psychiatric and paradoxical reactions like restlessness, exacerbated insomnia, agitation, irritability, aggression, delusion, anger, nightmares, hallucinations, abnormal behaviour and other adverse behavioural effects are known to occur when using **ADCO-ZOLPIDEM HEMITARTRATE**. Should this occur, use of **ADCO-ZOLPIDEM HEMITARTRATE** should be discontinued. These reactions are more likely to occur in the elderly (See section 4.8)

Somnambulism and associated behaviours:
Sleep walking and other associated behaviours such as “sleep driving”, preparing and eating food, making phone calls or having sex, with amnesia from the event, have been reported in patients who had taken **ADCO-ZOLPIDEM HEMITARTRATE** and were not fully awake.
The use of alcohol and other CNS-depressants with **ADCO-ZOLPIDEM HEMITARTRATE** appears to increase the risk of such behaviours, as does the use of **ADCO-ZOLPIDEM HEMITARTRATE** at doses exceeding the maximum recommended dose.
Discontinuation of **ADCO-ZOLPIDEM HEMITARTRATE** should strongly be considered for patients who report such behaviours.

Next-day psychomotor impairment:
ADCO-ZOLPIDEM HEMITARTRATE has CNS-depressant effects. The risk of psychomotor impairment, including impaired driving ability, is increased if: **ADCO-ZOLPIDEM HEMITARTRATE** is taken within less than 7 – 8 hours before performing activities that require mental alertness, a dose higher than the recommended dose is taken, or **ADCO-ZOLPIDEM HEMITARTRATE** is co-administered with other CNS depressants, alcohol, or with other medicines that increase the blood levels of **ADCO-ZOLPIDEM HEMITARTRATE** (see section 4.5).

Dependence and abuse:
Physical and psychological dependence may arise from the use of sedatives/hypnotics. The greater the dose and duration of therapy, the higher the risk of developing dependence. Patients with a history of alcohol or drug abuse are also at increased risk.
Withdrawal symptoms will occur in patients who are physically dependant on **ADCO-ZOLPIDEM HEMITARTRATE,** if treatment is discontinued abruptly. These symptoms include muscle pain or headaches, tension and extreme anxiety, irritability, confusion and restlessness. The following symptoms may occur in severe cases: depersonalisation, derealisation, hyperacusis, tingling of the extremities and numbness, hypersensitivity to noise, light and physical contact, epileptic seizures or hallucinations.
Withdrawal signs and symptoms have occurred as a result of abrupt termination of treatment with sedatives/hypnotics. Symptoms ranging from insomnia and mild dysphoria to a withdrawal syndrome that may include vomiting, abdominal and muscle cramps, tremors, convulsions and sweating have been reported.

Clear evidence for withdrawal syndrome is not evident from the U.S. clinical trial experience. Nonetheless , during U.S. clinical trials, the following adverse reactions, which occurred at an incidence of 1 % or less, were reported following placebo substitution within 48 hours after the last zolpidem dose: nausea, fatigue, light-headedness, flushing, stomach cramps, emesis, abdominal discomfort, uncontrolled crying, nervousness and panic attack. These adverse reactions are included in the DSM-111-R criteria for uncomplicated sedative/ hypnotic withdrawal.
However, a reliable estimate of the incidence, if any, of dependence during treatment at recommended doses of zolpidem cannot be provided by the available data. Less frequent post- marketing reports of dependence, abuse and withdrawal have been received.

History of alcohol and drug abuse:
People with a history of addiction to or abuse of drugs or alcohol, or those with a history of psychiatric disorders should take **ADCO-ZOLPIDEM HEMITARTRATE** under careful supervision, as they are at heightened risk of developing habituation and dependence.

Severe injuries:
Due to its pharmacological properties, **ADCO-ZOLPIDEM HEMITARTRATE** can cause drowsiness and a decreased level of consciousness, which may lead to falls and consequently to severe injuries.

Patients with long QT syndrome:
An *in vitro* cardiac electrophysiological study showed that under experimental conditions using very high concentration and pluripotent stem cells **ADCO-ZOLPIDEM HEMITARTRATE** may reduce the hERG (human ether-a-go-go-related gene) related potassium currents. The potential consequence in patients with congenital long QT syndrome is unknown. As a precaution, the benefit/risk ratio of **ADCO-ZOLPIDEM HEMITARTRATE** treatment in patients with known congenital long QT syndrome should be carefully considered.

Lactose intolerance:
Since **ADCO-ZOLPIDEM HEMITARTRATE** contains lactose, patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Special patient groups:

- **Elderly or geriatric patients**:

See section 4.2**.**

- **Respiratory insufficiency:**

ADCO-ZOLPIDEM HEMITARTRATE should be used with caution in patients with chronic respiratory insufficiency due to the risk of respiratory depression.

- **Suicidality and depression:**

Several epidemiological studies show an increased incidence of suicide and suicide attempt in patients with or without depression, treated with benzodiazepines and other hypnotics, including **ADCO-ZOLPIDEM HEMITARTRATE**. A causal relationship has not been established.

ADCO-ZOLPIDEM HEMITARTRATE should not be used as the primary treatment of depressive disorders. Patients showing symptoms of depression should use zolpidem and other hypnotics with caution. The least amount of drug that is required should be supplied to these patients as suicidal tendencies may be present and intentional overdosage by the patient is a possibility.

Pre-existing depression may be unmasked during use of **ADCO-ZOLPIDEM HEMITARTRATE**.

Since insomnia may be a symptom of depression, the patient should be re-evaluated if insomnia persists.

- **Psychotic illness**:

ADCO-ZOLPIDEM HEMITARTRATE is not recommended for the primary treatment of psychotic illness.

- **History of alcohol or drug abuse**:

Patients with a history of alcohol or drug abuse should not be treated with **ADCO-ZOLPIDEM HEMITARTRATE .**

- **Severe hepatic insufficiency**:

As hypnotics may precipitate encephalopathy, **ADCO-ZOLPIDEM HEMITARTRATE** is not indicated in the treatment of patients with severe hepatic insufficiency (see section 4.2 and section 4.3).

Paediatric patients:

ADCO-ZOLPIDEM HEMITARTRATE is contraindicated in patients under the age of 18 years due to increased occurrence of adverse effects including dizziness, headache and hallucinations.

4.5 Interactions with other medicines and other forms of interaction

Alcohol:

Enhanced sedation may occur when **ADCO-ZOLPIDEM HEMITARTRATE** is used in combination with alcohol and this will affect the ability to drive or use machines. Concomitant intake with alcohol is therefore not recommended.

Combination with CNS depressants:

Concurrent use of antipsychotics (neuroleptics), antidepressant agents, anxiolytics/sedatives, hypnotics, anti-epileptic drugs, narcotic analgesics, sedative

antihistamines and anaesthetics may enhance the central depressive effects of **ADCO-ZOLPIDEM HEMITARTRATE.** These medicines may increase drowsiness and psychomotor impairment, including impaired driving ability.
Co-administration of fluvoxamine may increase blood levels of **ADCO- ZOLPIDEM HEMITARTRATE**; concurrent use is not recommended (see CYP450 inhibitors and inducers).
Psychological dependence may be increased with the concurrent administration of narcotic analgesics due to their enhanced effect on the euphoria experienced with zolpidem.

Opioids:
The concomitant use of benzodiazepines and other sedative-hypnotic medicines, including **ADCO-ZOLPIDEM HEMITARTRATE**, and opioids increases the risk of sedation, respiratory depression, coma, and death because of additive CNS depressant effect. The dosage and duration of concomitant use should be limited (see section 4.4).

CYP450 inhibitors and inducers:
The activity of **ADCO-ZOLPIDEM HEMITARTRATE** may be increased by compounds which inhibit certain hepatic enzymes (particularly cytochrome P450), whereas components which induce hepatic enzymes (particularly cytochrome P450), such as rifampicin, carbamazepine, and phenytoin, may reduce the hypnotic effect of **ADCO-ZOLPIDEM HEMITARTRATE.**
ADCO-ZOLPIDEM HEMITARTRATE is metabolised via several hepatic cytochrome P450 enzymes: the main enzyme being CYP3A4 with the contribution of CYP1A2.

The pharmacodynamic effect of **ADCO-ZOLPIDEM HEMITARTRATE** is decreased when it is administered with a CYP3A4 inducer such as rifampicin and St John's Wort. Co-administration of St. John's Wort may decrease blood levels of **ADCO-ZOLPIDEM HEMITARTRATE**, concurrent use is not recommended.

However, when **ADCO-ZOLPIDEM HEMITARTRATE** was administered with itraconazole (a CYP3A4 inhibitor) its pharmacokinetics and pharmacodynamics were not significantly modified. The clinical relevance of these results is unknown.

Co-administration of **ADCO-ZOLPIDEM HEMITARTRATE** with ketoconazole (200 mg twice daily), a potent CYP3A4 inhibitor, prolonged **ADCO-ZOLPIDEM HEMITARTRATE** elimination half-life, increased total AUC, and decreased apparent total clearance when compared to **ADCO-ZOLPIDEM HEMITARTRATE** plus placebo. The total AUC for **ADCO-ZOLPIDEM HEMITARTRATE**, when co-administered with ketoconazole, increased by a factor of 1,83 when compared to **ADCO-ZOLPIDEM HEMITARTRATE** alone. A routine dosage adjustment is not considered necessary, but patients should be advised that use of **ADCO-ZOLPIDEM HEMITARTRATE** with ketoconazole may enhance the sedative effects.

Fluvoxamine is a strong inhibitor of CYP1A2 and a moderate to weak inhibitor of CYP2C9 and CYP3A4. Co-administration of fluvoxamine may increase blood levels of **ADCO-ZOLPIDEM HEMITARTRATE**, concurrent use is not recommended.

Ciprofloxacin has been shown to be a moderate inhibitor of CYP1A2 and CYP3A4. Co-administration of ciprofloxacin may increase blood levels of **ADCO-ZOLPIDEM HEMITARTRATE**, concurrent use is not recommended.

Other medicines:
When **ADCO-ZOLPIDEM HEMITARTRATE** was administered with warfarin, digoxin, ranitidine or cimetidine, no significant pharmacokinetic interactions were observed.

4.6 Fertility, pregnancy and lactation
Safety in pregnancy and lactation has not been demonstrated (see section 4.3).

Pregnancy:
The use of **ADCO-ZOLPIDEM HEMITARTRATE** in pregnancy and breastfeeding should be avoided.
Zolpidem crosses the placenta.
A large amount of data on pregnant women (more than 1 000 pregnancy outcomes) collected from cohort studies has not demonstrated evidence of the occurrence of malformations following exposure to benzodiazepines or benzodiazepine-like substances during the first trimester of pregnancy. However, certain case-control studies reported an increased incidence of cleft lip and palate associated with use of benzodiazepines during pregnancy.
Cases of reduced fetal movement and fetal heart rate variability have been described after administration of benzodiazepines or benzodiazepine-like substances during the second and/or third trimester of pregnancy.
Administration of **ADCO-ZOLPIDEM HEMITARTRATE** during the late phase of pregnancy, or during labour, has been associated with effects on the neonate such as hypothermia, hypotonia, feeding difficulties (‘floppy infant syndrome’) and respiratory depression, due to the pharmacological action of **ADCO-ZOLPIDEM HEMITARTRATE**.
Cases of severe neonatal respiratory depression have been reported.
Infants born to mothers who took **ADCO-ZOLPIDEM HEMITARTRATE** chronically during the latter stages of pregnancy may have developed physical dependence and may be at risk of developing withdrawal symptoms in the postnatal period. Appropriate monitoring of the newborn in the postnatal period is recommended.
If **ADCO-ZOLPIDEM HEMITARTRATE** is prescribed to a woman of childbearing potential, she should be warned to contact her doctor about stopping the product if she intends to become pregnant or suspects that she is pregnant.

Lactation:
Small quantities of zolpidem appear in breast milk. The use of **ADCO-ZOLPIDEM HEMITARTRATE** in breastfeeding mothers is, therefore not recommended (see section 4.3).

4.7 Effects on ability to drive and use machines
Patients taking **ADCO-ZOLPIDEM HEMITARTRATE** may experience drowsiness, sedation, vertigo and dizziness, and this may adversely affect their ability to drive or use machinery. They may also experience a decreased level of alertness if they sleep for an insufficient duration of time.
In order to minimise this risk a resting period of at least 8 hours is recommended between taking **ADCO-ZOLPIDEM HEMITARTRATE** and driving, using machinery and working at heights.
Driving ability impairment and behaviours such as 'sleep-driving' have occurred with **ADCO-ZOLPIDEM HEMITARTRATE** alone at therapeutic doses.
Furthermore, the co-administration of **ADCO-ZOLPIDEM HEMITARTRATE** with alcohol and other CNS depressants increases the risk of such effects. Patients should be warned not to use alcohol or other psychoactive medicines when taking **ADCO-ZOLPIDEM HEMITARTRATE**.

4.8 Undesirable effects
a. Summary of the safety profile
The side effects which occur primarily at the onset of therapy but usually disappear after repeated administrations are: day-time drowsiness , reduced alertness, numbed emotions, fatigue, confusion, dizziness, headache, ataxia, muscle weakness or double vision. The above side effects also occur most often in elderly patients.
Occasionally, other side effects such as gastrointestinal disturbances , skin reactions or changes in libido have been reported.

b. Tabulated list of adverse reactions

MedDRA System Organ Class	**Frequency**	**Side effects**
Infections and infestations	Frequent	Upper respiratory tract infection, lower respiratory tract infection
Immune system disorders	Frequency unknown	Angioedema
Metabolism and nutrition disorders	Less frequent	Appetite disorder
Psychiatric disorders	Frequent	Hallucinations, agitation, nightmare, depression (see section 4.4)

	Less frequent	Confusional state, irritability, restlessness, aggression, somnambulism (see section 4.4), euphoric mood, libido disorder, delusion, dependence (withdrawal symptoms, or rebound effects may occur after treatment discontinuation)
	Frequency unknown	Anger, psychosis, abnormal behaviour Most of these psychiatric side effects are related to paradoxical reactions.
Nervous system disorders	Frequent	Somnolence, headache, dizziness, exacerbated insomnia, cognitive disorders such as anterograde amnesia (amnestic effects may be associated with inappropriate behaviour)
	Less frequent	Paraesthesia, tremor, disturbance in attention, speech disorder, depressed level of consciousness
Eye disorders	Less frequent	Diplopia, blurred vision, visual impairment
Respiratory, thoracic and mediastinal disorders	Less frequent	Respiratory depression (see section 4.4)
Gastrointestinal disorders	Frequent	Diarrhoea, nausea, vomiting, abdominal pain
Hepato-biliary disorders	Less frequent	Elevated liver enzymes, hepatocellular, cholestatic or mixed liver injury (see sections 4.2, 4.3 and 4.4)
Skin and subcutaneous tissue disorders	Less frequent	Rash, pruritus, hyperhidrosis, urticaria
Musculoskeletal and connective tissue disorders	Frequent	Back pain
	Less frequent	Arthralgia, myalgia, muscle spasms, neck pain, muscular weakness
General disorders and administration site conditions:	Frequent	Fatigue
	Less frequent	Gait disturbances, fall (predominantly in elderly patients and when **ADCO-ZOLPIDEM HEMITARTRATE** was not taken in accordance with prescribing recommendation) (see section 4.4).
	Frequency unknown	Drug tolerance

c. Description of selected adverse reactions

Amnesia:

At therapeutic doses of **ADCO-ZOLPIDEM HEMITARTRATE**, anterograde amnesia may be experienced. An increased risk is expected at higher dosages and inappropriate behaviour may accompany the amnesia.

***Depression*:**

The use of **ADCO-ZOLPIDEM HEMITARTRATE** may reveal pre-existing depression.

Psychiatric and "paradoxical" reactions:

Should the following reactions occur, use of **ADCO-ZOLPIDEM HEMITARTRATE** should be discontinued: agitation, restlessness, aggressiveness, irritability, rages, delusion, hallucinations, nightmares, inappropriate behaviour, psychoses and other adverse behavioural effects. The occurrence of such reactions is more probable in children (see section 4.3) and the elderly.

Dependence:

Physical dependence may develop with the use of therapeutic doses of **ADCO-ZOLPIDEM HEMITARTRATE**. Withdrawal or rebound symptoms may occur upon discontinuation of treatment (see section 4.4). Psychological dependence may also develop. Polydrug users have been known to abuse zolpidem.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Symptoms and signs

Impairment of consciousness ranging from somnolence to light coma has occurred following an overdose of zolpidem alone. Individuals ingesting doses of up to 400 mg of zolpidem have fully recovered.

More severe symptomatology, including fatal outcomes, has occurred following overdose cases involving zolpidem in combination with CNS-depressant agents (e.g. alcohol).

Treatment:

Treatment is generally symptomatic and supportive. Administration of intravenous fluids may be necessary. Sedative drugs should not be used even if excitation occurs.

It is not yet known whether dialysis is of any value in the treatment of overdose. However, haemodialysis studies have shown that zolpidem cannot be dialysed in patients with renal failure receiving therapeutic doses of the drug.
If serious symptoms occur, the use of benzodiazepine-antagonists (e.g. flumazenil) may be considered.
Flumazenil is reported to have an elimination half-life of about 40 – 80 minutes. Patients should be kept under close observation because of this short duration of action; further doses of flumazenil may be necessary.
However, flumazenil administration may contribute to the appearance of neurological symptoms (convulsions).
It must be borne in mind that multiple agents may have been ingested when managing an overdose with a medicinal product.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 2.2 Sedatives, hypnotics
Pharmacotherapeutic groups: Nervous system, Psycholeptics, Hypnotics and sedatives, Benzodiazepine related drugs
ATC code: N05CF02

Mechanism of action:
ADCO-ZOLPIDEM HEMITARTRATE (zolpidem), an imidazopyridine, is a non-benzodiazepine sedative/hypnotic medicine. The sedative and hypnotic effects are exerted due to an agonist action specifically at central receptors belonging to GABA-omega benzodiazepine-1 and benzodiazepine-2 macromolecular receptor complex, regulating the opening of the chloride ion channel. Zolpidem acts predominantly on the omega-1 (benzodiazepine-1) receptor subtypes. The clinical significance of this affinity is unknown.

5.2 Pharmacokinetics properties

Absorption:
Zolpidem is absorbed readily from the gastrointestinal tract and first-pass hepatic metabolism results in an oral bioavailability of about 70 %. Peak plasma concentrations are reached between 0,5 and 3 hours after dosing.

Distribution:
Zolpidem displays linear pharmacokinetic behaviour at therapeutic dose levels. Zolpidem has a plasma elimination half-life of about 2,5 hours (1,4 to 3,8 hours) and is approximately 92 % bound to plasma proteins. In adults the volume of distribution is 0,54 ± 0,02 L/kg, which decreases to 0,34 ± 0,05 L/kg in the elderly.

Excretion:
Zolpidem is excreted mainly in the urine (56 %) and faeces (37 %) in the form of inactive metabolites (hepatic metabolism). Zolpidem is not a hepatic enzyme inducer. In the elderly, the peak concentration is increased by approximately 50 % and the elimination half-life is increased by 32 %, due to a reduced clearance.
There is a moderate reduction in clearance in patients with renal insufficiency, whether they are dialysed or not. Other pharmacokinetic parameters remain unchanged.

Bioavailability:
Clearance of the medicine is reduced in patients with hepatic insufficiency and the elimination half-life is prolonged (about 10 hours). The bioavailability of zolpidem is therefore increased in these patients.

5.3 Preclinical safety data
No data available.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Lactose Monohydrate
Microcrystalline Cellulose (Avicel PH101)
Sodium Starch Glycolate
Hypromellose
Magnesium Stearate

Film coating
Opadry Y-1-7000 White containing:
Hypromellose
Titanium dioxide (E 171)
Macrogol

6.2 Incompatibilities
Not applicable

6.3 Shelf life
36 months

6.4 Special precautions for storage
Store in the original package at or below 25 °C.
Protect from light and moisture.
Keep the container well-closed.

6.5 Nature and contents of container:
ADCO-ZOLPIDEM HEMITARTRATE 5 mg & 10 mg tablets:
Carton boxes with 1, 2, 3 or 10 white, opaque PVC/PE/PVDC/Al-blisters with 10 tablets each or carton boxes with 1 or 2 white, opaque PVC/PE/PVDC/Al-blisters with 14 tablets each.
Primary packaging material specification aluminium lidding foil (20 µm):
The aluminium blister foil consists of the following layers (from the layer in contact with drug product to the outside layer):
- Heat seal lacquer
- Aluminium (20 µm)
- Primer

Primary packaging material specification PVC/PE/PVDC (250/25/90) blister foil system:
PVDC is the inner layer; this side of the plastic foil is in contact with the tablets.

Pack sizes:
10, 14, 20, 28, 30 and / or 100's
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
No special requirements.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION
Adcock Ingram Limited
1 New Road
Erand Gardens
Midrand
1685
Customer Care: 0860 ADCOCK / 232625

8. REGISTRATION NUMBER:
ADCO-ZOLPIDEM HEMITARTRATE 5 mg: 36/2.2/0131
ADCO-ZOLPIDEM HEMITARTRATE 10 mg: 36/2.2/0132

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION
03 July 2003

10. DATE OF REVISION OF THE TEXT
25 March 2025

Product name	Registration number
Botswana	
ADCO-ZOLPIDEM HEMITARTRATE 10 mg	1C BOT0801427
Namibia	
ADCO-ZOLPIDEM HEMITARTRATE 10 mg	NS5 05/2.2/0138

adcock ingram

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05/2025