

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Zopiclone Orifarm 5 mg film-coated tablets
Zopiclone Orifarm 7.5 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 5 mg and 7.5 mg zopiclone, respectively.

Excipients with known effect:

Each 5 mg film-coated tablet contains lactose monohydrate 22.3 mg.
Each 7.5 mg film-coated tablet contains lactose monohydrate 33.5 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet (tablet).

[Invented name] 5 mg are white to off white, round biconvex film-coated tablets, debossed with 'Z3' on one side and plain on the other side and with a diameter of approximately 6 mm.

[Invented name] 7.5 mg are light blue to blue, scored oval biconvex film-coated tablets, debossed with 'Z' on one side of the breakline and '1' on the other side of the breakline and plain on the other side of the tablets and with a length of approximately 10 mm and width of approximately 5 mm.
The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Zopiclone is indicated for the short-term treatment of insomnia in adults.

Benzodiazepines and benzodiazepine-like substances are only indicated when the disorder is severe, disabling or subjecting the individual to extreme distress.

4.2 Posology and method of administration

Posology

Adults

The treatment duration should be as short as possible. The lowest effective dose should be used.
The usual initial dose is 5 mg as a single dose at bedtime and should not be re-taken during the same night. For patients who do not respond to this dose, the dose can be increased to 7.5 mg.
The dose should not exceed 7.5 mg per day.

Treatment duration

The treatment time should be as short as possible (a few days to 2 weeks) and no longer than 4 weeks, including the tapering off. In some cases, it may be necessary to extend treatment beyond the maximum treatment period; however, this should not take place without re-evaluation of the patient's

status since the risk of dependence or abuse increases with dose and duration of treatment (see also section 4.4).

Special populations

Elderly

The usual initial dose is 3.75 mg for elderly. The dose may later be increased to 5 mg and, if necessary, up to 7.5 mg.

Renal impairment

Although no accumulation of zopiclone or its metabolites have been found in patients with renal insufficiency, it is advisable to begin treatment of patients with reduced renal function at 3.75 mg.

Hepatic impairment or chronic respiratory failure

Treatment should be started with a dose of 3.75 mg. The dose may later be increased to 5 mg and, if necessary, up to 7.5 mg.

Paediatric population

[Invented name] should not be administered in children and adolescents aged less than 18 years. The safety and efficacy of zopiclone in this age group have not been established.

Method of administration

For oral use.

The tablet should be taken before bedtime at night.

The tablets should be taken in an upright position as the absorption might be delayed in the lying position.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Severe hepatic insufficiency
- Sleep apnoea syndrome
- Myasthenia gravis
- Severe respiratory insufficiency
- Previously experienced complex sleep behaviours after taking zopiclone (see section 4.4).

4.4 Special warnings and precautions for use

Before starting treatment with zopiclone any underlying cause of insomnia should be addressed carefully.

[Invented name] should also be used with caution in patients with a history of alcohol or drug abuse. Concomitant alcohol consumption should be avoided.

Dependence

Treatment with sedative/hypnotic agents, such as zopiclone, may lead to physical or psychological dependence or abuse on these agents.

The risk of dependence or abuse increases with dose and duration of treatment. The risk of dependence or abuse is also greater in patients with a history of alcohol or drug abuse and if zopiclone is taken in combination with alcohol or other psychotropic drugs.

If a physical dependence occur, sudden discontinuation of treatment may lead to withdrawal symptoms, which may include insomnia, headaches, muscle pain, severe anxiety, tension, agitation, confusion, and irritability. In severe cases, the following symptoms may occur: depersonalization, derealisation, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures.

Withdrawal symptoms may appear within days of stopping treatment. For short-acting benzodiazepines, and especially if given at high doses, symptoms may even appear during the interval between doses.

Rebound insomnia

A transient syndrome where the symptoms that led to treatment with sedative/hypnotic agents recur in an enhanced form on discontinuation of therapy. The risk of these symptoms occurring is greater with an abrupt discontinuation, especially after prolonged treatment with sleeping pills. Therefore, it is recommended that the patient be informed of this and advised to gradually reduce the dose (see also section 4.8). Treatment with sleeping pills should be temporary or intermittent to reduce the risk of withdrawal problems.

Treatment duration

The duration of treatment should be as short as possible (see section 4.2) but not longer than 4 weeks including the tapering off process. This period should only be exceeded after re-evaluation of the patient's status. It may be of benefit to inform the patient at the beginning of treatment that the treatment will be of short duration, and to explain precisely how to reduce the dose gradually. It is also important to draw attention to the possibility of a rebound effect, so the patient does not worry unduly about these symptoms during the treatment withdrawal.

Psychomotor impairment

Like any other sedative/hypnotic medicine, zopiclone has CNS-depressant effects. Alterations in psychomotor functions are likely to appear within hours of administration. The risk of psychomotor impairment, including the ability to drive, increases in the following situations:

- Taking this medicine less than 12 hours before carrying out an activity requiring alertness (see section 4.7),
- Exceeding the recommended dose,

Co-administration with other CNS depressants, alcohol, illegal substances or other medicinal products that increase zopiclone blood concentrations (see section 4.5). Patients should be cautioned against engaging in dangerous activities requiring full alertness or motor coordination (e.g. operating machinery or driving) after taking zopiclone, and especially during the first 12 hours after administration.

Anterograde amnesia

Anterograde amnesia may occur, especially if sleep is interrupted or if bedtime is delayed after taking [Invented name]. Anterograde amnesia could appear within hours of administration.

To reduce the risk of anterograde amnesia, the patient should be advised to:

- take the tablet immediately before bedtime or when already in bed,
- create the most favourable conditions for a full night's sleep (7-8 hours).

Tolerance

The hypnotic effect of short-acting benzodiazepines and benzodiazepine-like agents may diminish after repeated use for a few weeks. For zopiclone however, no pronounced tolerance has occurred during a treatment period of up to 4 weeks.

Somnambulism and associated behaviours

Sleepwalking and other associated complex sleep behaviours such as 'sleep driving', cooking and eating, having sex or making phone calls in sleep, with amnesia for the event, have been reported in patients who have taken the first or any subsequent dose of zopiclone and have not been awoken enough. Patients usually do not remember these events.

Patients can be seriously injured or injure others during complex sleep behaviors. Such injuries may result in a fatal outcome.

The use of alcohol and other CNS depressants with zopiclone may increase the risk of such behaviour or when the maximum recommended dose is exceeded. Discontinuation of treatment should be strongly considered for patients who reports such behaviour (see section 4.5).

Other psychiatric and paradoxical reactions

Reactions like restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychosis, inappropriate behavior and other behavioral disturbances may occur during treatment with benzodiazepines and benzodiazepine-like agents. In this case, the medicinal product must be discontinued. These reactions occur more often in the elderly.

Suicide / Depression / Major depressive episode

Some epidemiological studies show an increased incidence of suicidal ideation, suicide attempts and suicides in patients with or without depression, and treated with benzodiazepines and other hypnotics, including zopiclone. However, a causal relationship has not been established.

As with other hypnotics, zopiclone does not constitute a treatment for depression and may even mask its symptoms (suicide may be precipitated in such patients).

In persons with major depressive episode

Benzodiazepines and benzodiazepine-like medicinal products should not be prescribed as monotherapy as this may allow the underlying depression to evolve and become persistent, leading to an increased risk of suicide.

Because of the suicidal risk in these patients, the lowest possible dose of zopiclone should be used to these patients to avoid the possibility of intentional overdose.

Risks of concomitant use of opioids

Concomitant use of [Invented name] and opioids may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing of sedative medicines such as benzodiazepines or related drugs such as [Invented name] with opioids should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe [Invented name] concomitantly with opioids, the lowest effective dose should be used, and the duration of treatment should be as short as possible (see also general dose recommendation in section 4.2).

The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their caregivers (where applicable) to be aware of these symptoms (see section 4.5).

Special populations

Hepatic impairment

A reduced dosage is recommended, see section 4.2. Benzodiazepines are not indicated to treat patients with severe hepatic insufficiency as they may precipitate encephalopathy (see section 4.3).

Respiratory impairment

A lower dose is recommended for patients with chronic respiratory insufficiency due to the risk of respiratory depression.

Renal impairment

A reduced dosage is recommended (see section 4.2).

Elderly

Elderly should be given a reduced dose (see section 4.2). There is a risk of fall, particularly in the elderly when they get up during the night due to the muscle relaxing effect of zopiclone.

Paediatric population

[Invented name] should not be administered in children and adolescents under 18 years of age. The safety and efficacy of zopiclone in this group have not been established.

Excipients

[Invented name] contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use is not recommended

Alcohol

Concomitant intake with alcohol is not recommended. The sedative effect of [Invented name] can be enhanced when the drug is combined with alcohol. This affects the ability to drive and use machines.

Interaction has to be taken with caution

CNS depressants

Combination with other CNS depressants, such as neuroleptics, hypnotics, anxiolytics / sedatives, antidepressants, narcotic analgesics, antiepileptics, anaesthetics and sedative antihistamines should be carefully considered as the suppressive effect of zopiclone on the central nervous system may be increased in combination with these agents.

In the case of narcotic analgesics potentiation of euphoria may also occur, which can lead to increased psychological dependence.

Opioids

The concomitant use of sedative medicines such as benzodiazepines or related drugs such as [Invented name] with 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).

CYP3A4 inhibitors/ CYP3A4 inducers

Since zopiclone is metabolised via CYP3A4, plasma levels of zopiclone may increase if co-administered with CYP3A4 inhibitors such as macrolide antibiotics, azoles, HIV protease inhibitors and grapefruit juice. The dose reduction of zopiclone may be required during concomitant treatment with CYP3A4 inhibitors.

Conversely, plasma levels of zopiclone may decrease if co-administered with CYP3A4 inducers such as phenobarbital, phenytoin, carbamazepine, rifampicin and products containing St. John's wort. A dose of zopiclone might need to be increased.

Erythromycin

The effect of erythromycin on the pharmacokinetics of zopiclone has been studied in healthy subjects. The AUC of zopiclone increases by 80% in the presence of erythromycin, probably due to erythromycin inhibiting the metabolism of drugs metabolised by CYP 3A4. As a consequence, the hypnotic effect of zopiclone may be enhanced.

Itraconazole

If co-administered with itraconazole (which inhibits CYP 3A4-mediated metabolism) the bioavailability of zopiclone is increased by approximately 70%.

Rifampicin

Rifampicin strongly induces the metabolism of zopiclone likely via CYP 3A4. Its plasma concentration decreases by about 80% and its effects in psychomotor tests are significantly reduced.

4.6 Fertility, pregnancy and lactation

Pregnancy

The use of zopiclone is not recommended during pregnancy.

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

Zopiclone 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 benzodiazepines or benzodiazepine-like substances, including zopiclone, during the late phase of pregnancy or during labour have 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 the product. Cases of severe neonatal respiratory depression have been reported.

Moreover, infants born to mothers who took sedative/hypnotic agents 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 [Invented name] is prescribed to women of childbearing potential, she should be informed to consult a physician to discuss discontinuation of the medicine if she intends to become or suspects that she is pregnant.

Breast-feeding

Zopiclone is excreted in breast milk, although the concentration of zopiclone in the breast milk is low, use in nursing mothers must be avoided.

4.7 Effects on ability to drive and use machines

Zopiclone may have a major influence on the ability to drive and use machines.

During treatment with zopiclone, the reactivity may be reduced. This should be considered when alertness is required, e.g., when driving or performing precision work, especially in the first 12 hours following zopiclone administration. To minimise these risks, an uninterrupted rest period of at least 12 hours is recommended between taking zopiclone and driving, using machines or working at heights.

In addition, the risk is increased with concomitant alcohol intake or other CNS depressants. The risk is even higher when sleep duration is insufficient. Patients should be warned to avoid alcohol or other psychoactive substances when taking zopiclone.

4.8 Undesirable effects

Summary of the safety profile

About 10% of treated patients experience some form of side effect. The most common side effect is a bitter taste, often transient, which occurs in about 4% of patients in clinical trials, followed by drowsiness, which is dose dependent.

Tabulated list of adverse reactions

The frequencies of undesirable effects are ranked in the table below according to the following: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$), very rare ($< 1/10,000$) and not known (cannot be estimated from the available data).

These effects are related both to the dose taken and the patient's individual sensitivity.

System organ class	Common	Uncommon	Rare	Very rare	Not known
Immune system disorders				Angioedema, anaphylactic reactions	
Psychiatric disorders		Agitation, nightmares	Confusional state, libido disorders, irritability, aggression, hallucinations, depression*		Restlessness, delusions, anger, abnormal behaviour (possibly associated with amnesia) and complex sleep behaviours including somnambulism (see section 4.4), psychosis, physical and psychological dependence, withdrawal syndrome**
Nervous system disorders	Dysgeusia (bitter/metallic taste), drowsiness	Decreased alertness, headache, dizziness	Anterograde amnesia		Ataxia, paraesthesia, cognitive disorders such as memory impairment, disturbance in attention, speech disorder
Eye disorders					Diplopia
Respiratory, thoracic and mediastinal disorders			Dyspnoea		Respiratory depression
Gastrointestinal disorders	Dry mouth	Nausea, malaise, abdominal pain			Dyspepsia, vomiting
Hepatobiliary disorders				Increases in serum transaminases and/or blood alkaline phosphatase (mild or moderate)	
Skin and subcutaneous tissue disorders			Allergic skin reactions (including rash, itching, urticaria)		
Musculoskeletal and connective tissue disorders					Muscular weakness
General disorders and administration site conditions		Difficulty getting up in the morning, fatigue (asthenia)			

System organ class	Common	Uncommon	Rare	Very rare	Not known
System organ class	Common	Uncommon	Rare	Very rare	Not known
Injury, poisoning and procedural complications			Fall (mainly in the elderly, see section 4.4)		

* Existing depression may manifest itself during use of benzodiazepines and benzodiazepine-like substances.

** Use of zopiclone may lead to physical dependence even at therapeutic doses, and discontinuation of treatment may cause withdrawal symptoms or rebound effect (see section 4.4). Psychological dependence may also occur. Abuse has occurred.

Description of selected adverse reactions

Withdrawal syndrome have been reported upon discontinuation of zopiclone (see section 4.4).

Withdrawal symptoms vary and include difficulty sleeping, anxiety, tremor, sweating, agitation, confusion, headache, palpitations, tachycardia, delirium, nightmares, hallucinations and irritability. In very rare cases, seizures have also occurred.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in [Appendix V](#).

4.9 Overdose

Toxicity

Great individual variations. 5 mg caused mild intoxication in 1½-year-old children.

Approximately 30 mg caused moderate intoxication in 6-year-old children. 22.5-50 mg for adults and 40 mg for the elderly caused mild intoxication. >50->100 mg caused mild to moderate intoxication in adults. 100 mg caused deep unconsciousness in adults. 187 mg and alcohol caused severe intoxication for adults.

Symptoms

Overdose is usually manifested by varying degrees of central nervous system depression (in the elderly sometimes very prolonged) ranging from drowsiness to coma. In mild cases, symptoms include fatigue, drowsiness, somnolence, confusion, lethargy, unconsciousness which are sometimes preceded or followed by agitation and hallucinations; in more serious cases, symptoms include ataxia, muscle weakness (hypotonia), hypotension, methaemoglobinaemia, respiratory depression (mainly in combination with alcohol or CNS depressants) and coma.

Other risk factors, such as the presence of concomitant illness or the debilitated condition of the patient, may contribute to the severity of the symptoms and in very rare cases may lead to fatal outcome.

Treatment

Symptomatic and supportive treatment in adequate clinical environment is recommended, attention should be paid to the respiratory and cardiovascular functions. Gastric lavage or activated charcoal is only useful when performed soon after digestion. Flumazenil as an antidote may be useful to relieve CNS and respiratory depression and is mainly indicated in severe poisoning to avoid intubation and respiratory care. Note that the effect duration of flumazenil is shorter than that of zopiclone.

Haemodialysis is not useful in treating overdose due to the large volume of distribution of zopiclone.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Hypnotics and sedatives; benzodiazepine related drugs, ATC code: N05CF01

Zopiclone is a benzodiazepine-like hypnotic agent which belongs to the group of cyclopyrrolones. Its pharmacological properties are: hypnosis, sedation, anxiolysis, anticonvulsion, muscle relaxation. Zopiclone has a high affinity for the binding site within the macromolecular GABA_A receptor complex, where it induces specific conformational changes and enhances the normal transmission of the neurotransmitter GABA in the CNS. Zopiclone has a rapid onset of action (within about 30 minutes), shortens the sleep time, prolongs sleep duration, and reduces the number of awakenings during the night. The amount of REM sleep and deep sleep (stages III and IV) is maintained at the recommended dose.

5.2 Pharmacokinetic properties

Absorption

The bioavailability of zopiclone is about 80%. Maximum plasma concentrations are reached within 1.5-2 hours and are approximately 30 ng/ml and 60 ng/ml after a dose of 3.75 mg and 7.5 mg, respectively. The absorption is the same in women and men and is not affected by simultaneous food intake. Absorption may be delayed if zopiclone is ingested horizontally.

Distribution

Zopiclone is rapidly distributed from the vascular compartment. The volume of distribution is 1.3 l/kg and the protein binding levels is about 45% and is not saturable. Less than 1% of the dose ingested by the mother can be expected to reach a breast-feeding infant via breast milk.

Biotransformation

There is no accumulation after repeated administration and inter-individual variations appear to be minor. Zopiclone is extensively metabolized in the liver by decarboxylation. About 11% is converted to N-oxide zopiclone, which is less active than the parent substance, and of no clinical significance, and about 15% are transformed into the inactive N-desmethyl-zopiclone. The apparent half-lives are approximately 4.5 and 7.4 hours, respectively.

Elimination

The low renal clearance of zopiclone (mean 8.4 ml/min) compared to plasma clearance (232 ml/minute) indicates that zopiclone is essentially eliminated by metabolism.

The half-life is 5 hours, increased to 7 hours in the elderly. In various trials with elderly patients, no accumulation of zopiclone was observed in the plasma after repeated doses. Plasma clearance is reduced by approximately 40% in patients with liver cirrhosis, due to the slower methylation process and therefore the dose should be adjusted for these patients. In patients with renal insufficiency, no accumulation of zopiclone, which also crosses the dialysis membrane, or its metabolites has been detected after prolonged administration.

About 80% of all zopiclone is excreted in the urine, mainly in the form of unconjugated metabolites (N-oxide and N-dimethyl derivatives). About 16% is excreted in the faeces.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SmPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium hydrogen phosphate dihydrate
Lactose monohydrate
Sodium starch glycolate (type A)
Maize starch
Magnesium stearate

Film-coating:

5 mg:

Hypromellose
Talc
Titanium dioxide (E171)
Propylene glycol (E1520)

7.5 mg:

Hypromellose
Talc
Titanium dioxide (E171)
Propylene glycol (E1520)
Brilliant blue FCF Aluminum Lake (E133)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

[Invented name] 5 mg film-coated tablets:

Carton containing Alu-PVC/PVDC blisters in packs containing: 10, 30 (3×10), 100 (10×10) film-coated tablets.

Carton containing HDPE bottle with PP screw cap containing: 250 film-coated tablets.

[Invented name] 7.5 mg film-coated tablets:

Carton containing Alu-PVC/PVDC blisters in packs containing: 10, 20 (2×10), 30 (3×10), 100 (10×10) film-coated tablets.

Carton containing HDPE bottle with PP screw cap containing: 250 film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

2026-03-18