SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Delipam 5 mg tablets
Delipam 10 mg tablets
Delipam 15 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 tablet contains 5 mg, 10 mg, 15 mg of oxazepam, respectively.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

5 mg: White to yellowish, round, bevelled-edged, convex tablet, with ‘5’ debossed on one side and ‘score line’ on the other side. The tablet is 6 mm in diameter, and can be divided into equal doses.
10 mg: White to yellowish, round, bevelled-edged, convex tablet, with ‘10’ debossed on one side and ‘score line’ on the other side. The tablet is 8 mm in diameter, and can be divided into equal doses.
15 mg: White to yellowish, round, bevelled-edged, convex tablet, with ‘15’ debossed on one side, and plain on the other side. The tablet is 9 mm in diameter.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[Product name] has an effect on the common symptoms of the anxiety syndrome: fear, anxiety, restlessness and sleeping difficulties. In case of a depression with the just mentioned symptoms, [Product name] can be used together with usual antidepressants.

Delirium tremens, pre-delirious conditions and acute withdrawal symptoms such as anxiety, agitation, and excitation in connection with alcohol abuse.

4.2 Posology and method of administration

Dosage and duration of treatment should be adjusted individually. The risk of dependence may increase with dose and duration of treatment. Therefore, the lowest effective dose should be prescribed for the shortest possible duration of treatment, and the need for continued treatment should be evaluated regularly (see section 4.4).

Abrupt withdrawal or rapid dose reduction of oxazepam after longer-term use may lead to withdrawal symptoms, which can be life-threatening, and/or withdrawal phenomena (rebound phenomena).
The medicinal product should be discontinued gradually or the dose should be reduced (see section 4.4).

Pharmaceutical treatment of anxiety should take place within the settings of a carefully considered treatment plan. If possible, treatment should be initiated, followed, and withdrawn by the same physician.

<u>Posology</u>

Usual dosing: 15 mg 3-4 times daily. If needed, this may be increased to 25 mg 3-4 times daily.

Elderly/sensitive patients: 10 mg 2-3 times daily. If needed, this may be cautiously increased to 15 mg 3-4 times daily.

Mild agitation: 10 mg 3-4 times daily
Anxiety and agitation in connection with depressions: 25 mg 3-4 times daily.
In case of concomitant sleeping difficulties, 15-25 mg of the daily dose is administered 1 hour before bedtime.

Premedication before surgery: 25-50 mg in the evening on the day before surgery.

Premedication before dental treatment: 15 mg in the evening on the day before dental treatment and 1 hour before the dental treatment.

Delirium tremens, pre-delirious conditions and acute withdrawal symptoms: 15-25 mg 3-4 times daily.

Method of administration
Oral administration.

The tablets should be swallowed with a glass of water.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Sleep apnoea.

4.4 Special warnings and precautions for use

In general, caution is advised when treating elderly patients, patients with hepatic and renal impairment, myasthenia gravis, respiratory insufficiency, impaired general condition, and substance abuse.

Caution is also advised in case of concomitant treatment with other psychopharmaceuticals and in case of intake of alcohol (see section 4.5).

Risk with concomitant use of opioids:
Concomitant use of [Product name] and opioids may lead to sedation, respiratory depression, coma, and death. Due to these risks, concomitant prescription of benzodiazepines and opioids should be limited to patients in whom there are no other treatments options. If a decision is made to prescribe benzodiazepines concomitantly with opioids, the lowest dose should be used, and the treatment duration should be as short as possible. Patients should be monitored closely for signs and symptoms of respiratory depression and sedation (see section 4.5).

Treatment duration should be agreed with the patient, and the patient should be informed of the usual initial side effects.

Sleeping difficulties may be due to psychiatric or somatic disease. Therefore, prolonged sleeping difficulties should be evaluated with this in mind.

Tolerance
There is evidence that tolerance develops to the sedative effects of benzodiazepines.

Dependence
Due to the risk of dependence, this medicinal product should be prescribed for a limited duration.

The risk of dependence increases with higher doses and longer-term use. The risk is also greater in patients with a history of alcohol and/or drug abuse, or who are predisposed to drug abuse. The risk for dependence is reduced when oxazepam is used in an appropriate dose for short-term treatment.

Withdrawal symptoms
Abrupt withdrawal or rapid dose reduction of oxazepam after continuous use may lead to withdrawal symptoms, which can be life-threatening. These may range from headache, mild dysphoria and insomnia to more severe reactions like abdominal and muscle cramps, muscle pain, vomiting, sweating, extreme anxiety, tension, restlessness, irritability, tremor and convulsions. More severe acute signs and symptoms of withdrawal, also life-threatening reactions, include disorientation, depersonalization, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact , delirium tremens, depression, hallucinations, mania, psychoses, epileptic seizures and suicidal tendencies. Convulsions/seizures may be more common in patients with pre-existing seizure disorders, or who are taking other medicinal products that lower the convulsive threshold such as antidepressants.

Withdrawal symptoms, especially the severe, are more common in patients who have used higher doses for a longer period. Withdrawal symptoms have also been reported after discontinued treatment when benzodiazepines have been used continuously at therapeutic doses. Since the risk of withdrawal symptoms / rebound phenomena is greater after abrupt discontinuation of treatment, it is recommended that the dosage is decreased gradually.

Rebound phenomena: a transient syndrome whereby the symptoms that led to treatment with a benzodiazepine recur in an enhanced form, may occur on withdrawal of treatment. These symptoms may be difficult to distinguish from the original symptoms for which the medicinal product was prescribed.

Drug abuse
Drug abuse is a known risk when using benzodiazepines, and patients prescribed with oxazepam should be monitored closely. Benzodiazepines may be subject to dissemination for other uses (illegal trade). Deaths related to overdose have been reported with concomitant use of benzodiazepines and other CNS depressants, including opioids, other benzodiazepines, alcohol and/or illegal substances. These risks should be considered when prescribing or dispensing oxazepam. To minimise these risks, the lowest effective dose should be used, and the patient should be informed about the correct storage and disposal of unused medicine in order to avoid other uses / illegal trade (e.g. through friends and relatives).

In elderly, a state of confusion may occur with too high doses.

Paediatric population
The safety and efficacy of [Product name] in children below 18 years of age have not been established. Benzodiazepines should not be given to children without a careful evaluation of the treatment need. The total treatment period should be as short as possible.

Excipients
[Product name] contains sodium:
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

Opioids
Concomitant use of benzodiazepines and opioids increases the risk of sedation, respiratory depression, coma and death due to additive CNS depressant effects. The dosage and duration of concomitant use should be limited (see section 4.4).

The effects of oxazepam and alcohol may be enhanced with concomitant use; thus, combination should be avoided.

Oxazepam interacts with *contraceptives*. A number of studies show that oral contraceptives may interfere with the metabolism of some benzodiazepines. There are reports of inhibiting effects on the oxidation of diazepam, chlordiazepoxide, midazolam and alprazolam, probably via slight inhibition of CYP 3A4. Inducing effects on the glucuronidation of oxazepam and lorazepam have been observed. In view of the wide therapeutic window of benzodiazepines, these metabolic drug interactions are probably not of clinical relevance.

4.6 Fertility, pregnancy and lactation

Pregnancy
Oxazepam crosses the placenta and reaches the foetus, and continous administration for prolonged periods during pregnancy may cause hypotonia, effects on the respiratory function and hypothermia in the newborn child. Isolated cases of withdrawal symptoms in the child have also been reported. Cleft palate, CNS malformations and persistent behavioural disturbances in the offspring were reported in animal studies with administration of benzodiazepines during pregnancy. Therefore, benzodiazepines should only be given on compelling indication during pregnancy, and only after weighing the need of the mother against the risks for the foetus.

Breastfeeding
Oxazepam is excreted in breast milk, but a risk of effects on the child is considered to be unlikely with therapeutic doses.

4.7 Effects on ability to drive and use machines

[Product name] has moderate influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions are dose dependant, and elderly patients are more sensitive. The most common adverse reaction is drowsiness (10-15 %), which usually subsides after a few days of treatment.

In the table below, all adverse reactions are presented by organ system and frequency; very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

Tabulated list of adverse reactions

Organ system	Very Common	Common	Uncommon	Rare	Not known
Psychiatric disorders				Paradoxical reactions such as excitation, aggression and hallucinations, insomnia, nightmares	Drug abuse, Dependence
Nervous system disorders[±]		Drowsiness	Ataxia Dizziness Headache Anterograde amnesia		

			following high doses		
Respiratory, thoracic and mediastinal disorders				Respiratory depression[β]	
Musculoskeletal and connective tissue disorders			Muscle weakness		
Skin and subcutaneous tissue disorders				Allergic reactions	
General disorders and administration site conditions					Withdrawal symptoms

[±] The effects of benzodiazepines on the central nervous system (CNS) are dose-dependent, with more severe CNS depression occurring with high doses.
[β] The extent of respiratory depression with benzodiazepines is dose-dependent, with more severe depression occurring with high doses.

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
Some development of tolerance and individual sensitivity. 15 mg to a 2½-year-old caused mild intoxication. 50 mg to a 3-year-old caused mild intoxication after gastric emptying; 75 mg to a 3-year-old who underwent gastric emptying and 250 mg to a 5-year-old caused moderate intoxication.
120 mg to elderly caused moderate to severe intoxication.

Symptoms of overdosing
Ataxia, dizziness, dysarthria, muscle weakness, somnolence/unconsciousness, but also paradoxical reactions such as agitation, aggression and hallucinations. Possibly mydriasis or miosis. At high doses, respiratory depression, possibly hypotension. Tachycardia. Hypothermia. Nausea, vomiting.

Treatment
If necessary, gastric emptying, charcoal. In case of hypotension, intravenous fluid administration, in severe cases (uncommon), inotropic support. Controlled ventilation, if needed. In most cases, symptomatic treatment is sufficient. However, flumazeil reverses the central nervous effects and is indicated in some situations. In adults, IV administration of 0.3 mg, followed by repeated doses, as needed, at intervals of one minute until effect is reached. (2-3 doses are often enough, and in general, the total dose is maximum 2 mg).

NOTE! The duration of effect is shorter than for benzodiazepine derivatives. Thus, continuous infusion may be of value, eg. 0.3-1 mg/hour. In case of severe hallucinations, physostigmin may be tried (1-2 mg via slow IV administration in adults and 0.02-0.04 mg/kg in children. The dose is titrated, and atropin kept ready for reversal of possible adverse reactions).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: anxiolytics, sedatives with muscle relaxant properties. ATC code: N05BA04

Oxazepam is a benzodiazepine derivative which is chemically different from clopoxide, diazepam, chlorazepate and nitrazepam due to an active OH group, inducing quick glucuronic acid binding, resulting in significantly reduced toxicity.

Mechanism of action
The effect of oxazepam is related to receptors in CNS linked to the GABA complex.

Pharmacodynamic effects
Administration of oxazepam is believed to increase the GABA effect. Oxazepam does not seem to affect REM sleep, neither during treatment, nor following withdrawal.

Clinical efficacy and safety
There is a risk of development of tolerance.

5.2 Pharmacokinetic properties

Absorption
Oxazepam is absorbed more slowly than diazepam, and peak plasma concentrations are reached after approximately 2 hours.

Distribution
The volume of distribution is estimated to 0.6-2.0 l/kg bodyweight and clearance to 0.9-2.0 ml/min/kg bodyweight. Plasma protein binding for oxazepam is 97 %.

Biotransformation
Oxazepam does not produce any active metabolites. Enzyme induction for oxazepam is low.

Elimination
Oxazepam is eliminated quickly, primarily via the kidneys, with a half-life of approximately 10 hours.

Other special populations
Elderly and patients with hepatic impairment:
Age and hepatic disease have no significant effect on the pharmakokinetics of oxazepam.

Renal impairment:
Protein binding of oxazepam is reduced in patients with renal impairment to a plasma protein binding of 94 %. Thus, renal disease may be associated with prolonged half-life and increased volume of distribution.

5.3 Preclinical safety data

There are no preclinical data of relevance to the safety evaluation besides those already mentioned in this summary of product characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose
Pregelatinised starch
Calcium hydrogen phosphate dihydrate (E341ii)
Anhydrous collodial silica

Sodium laurilsulfate (E487)
Croscarmellose sodium (E468)
Magnesium stearate (E470b)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Blisters: 3 years
Bottles: 3 years

6.4 Special precautions for storage

Blisters: Do not store above 30°C.
Bottles: This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

[Product name] are packed in Al/PVC/PVDC blisters and white HDPE bottles with PE screw cap.

Pack sizes:
25, 30, 50 and 100 tablets in blisters.
49x1 and 50x1 tablets in unit-dose blisters.
250 and 500 tablets in bottles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local 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:
2025-09-23