Loprazolam 1mg Tablets

Summary of Product Characteristics Updated 26-Jun-2020 | Zentiva

1. Name of the medicinal product

Loprazolam 1mg Tablets

Dormonoct

2. Qualitative and quantitative composition

Each tablet contains loprazolam mesylate equivalent to 1mg loprazolam.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Light yellow, biconvex, round tablets, 7mm in diameter marked with an 'A' and '026' separated by a score line on one side. The other side is blank.

4. Clinical particulars

4.1 Therapeutic indications

Loprazolam is indicated for the short-term treatment of insomnia including difficulty in falling asleep and/or frequent nocturnal awakenings. Benzodiazepines should be used to treat insomnia only when it is severe, disabling or subjecting the individual to extreme distress. An underlying cause of insomnia should be sought before deciding upon the use of benzodiazepines for symptomatic relief.

4.2 Posology and method of administration

***Adults*:** The recommended dose is 1mg at bedtime. This may be increased to 1.5mg or 2mg if necessary.

***Elderly*:** Dosage in the elderly should be limited to 1mg at bedtime.

***Frail, debilitated or aged patients*:** A starting dose of a half tablet may be appropriate. Dosage should not exceed 1mg.

Treatment should if possible be intermittent.

The lowest dose to control symptoms should be used. Treatment should not normally be continued beyond 4 weeks.

Long term chronic use is not recommended.

Treatment should always be tapered off gradually.

Patients who have taken benzodiazepines for a long time may require a longer period during which doses are reduced.

***Children*:** There is insufficient evidence to recommend the use of Loprazolam in children.

4.3 Contraindications

Sensitivity to benzodiazepines, acute pulmonary insufficiency, severe respiratory insufficiency, myasthenia gravis, phobic or obsessional states and sleep apnoea syndrome. Monotherapy in depression or anxiety associated with depression and chronic psychosis and alcohol intake.

4.4 Special warnings and precautions for use

Disinhibiting effects may be manifested in various ways. Suicide may be precipitated in patients who are depressed and who exhibit aggressive behaviour towards self and others. Extreme caution should therefore be used in prescribing benzodiazepines in patients with personality disorders.

In general, the dependence potential of benzodiazepines is low but this increases when high doses are attained, especially when given over long periods and particularly in patients with a history of alcoholism or drug abuse. However, withdrawal symptoms occur even with normal therapeutic doses given for short periods of time. Withdrawal from benzodiazepines may be associated with physiological and psychological symptoms of withdrawal including depression, anxiety, tension, restlessness, confusion, irritability and headaches. Patients receiving benzodiazepines should be regularly monitored.

Rebound insomnia may also occur. It may be accompanied by other reactions such as changes in mood, anxiety, sleep disturbances and restlessness.

Loprazolam should be used with caution in chronic pulmonary insufficiency, cerebrovascular disease and chronic renal or hepatic impairment.

Risks from concomitant use of benzodiazepines and opioids

Concomitant use of benzodiazepines, including loprazolam, and opioids may result in sedation, respiratory depression, coma, and death. Because of these risks, reserve concomitant prescribing of benzodiazepines and opioids for use in patients for whom alternative treatment options are inadequate.

If a decision is made to prescribe loprazolam 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. (See Section 4.5)

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 loprazolam. A causal relationship has not been established.

Fall

Due to its pharmacological properties, loprazolam can cause drowsiness and a decreased level of consciousness, which may lead to falls and consequently to severe injuries, especially in elderly (see section 4.8).

4.5 Interaction with other medicinal products and other forms of interaction

Loprazolam may be potentiated by alcohol or other drugs acting on the CNS or with Cisapride. Additive synergy has been observed with neuromuscular depressants (curare-like drugs and muscle relaxants).

Combination with CNS depressants e.g. antipsychotics, hypnotics, anxiolytics/sedatives, antidepressant agents, narcotic analgesics, anti-epileptic drugs, anaesthetics and sedative antihistamines, causes enhancement of the central depressive effects of Loprazolam.

Concommitant intake with alcohol is not recommended. The sedative effects may be enhanced when the product is used in combination with alcohol. This affects the ability to drive or use machinery.

The risk of a withdrawal syndrome occurring is increased when loprazolam is combined with other benzodiazepines prescribed as anxiolytics or hypnotics.

Benzodiazepines and Opioids

The concomitant use of benzodiazepines and opioids increases the risk of sedation, respiratory depression, coma, and death, because of additive CNS depressant effect. Limit dosage and duration of concomitant use of benzodiazepines and opioids (see section 4.4).

4.6 Fertility, pregnancy and lactation

If the product is prescribed to a woman of childbearing potential, she should be warned to contact her physician regarding discontinuance of the product if she intends to become or suspects that she is pregnant.

If, for compelling medical reasons, the product is administered during the late phase of pregnancy, or during labour at high doses, effects on the neonate, such as hypothermia, hypotonia and moderate respiratory depression can be expected due to the pharmacological action of the compound.

Moreover, infants born to mothers who took benzodiazepines chronically during the latter stages of pregnancy may have developed physical dependency and may be at some risk for developing withdrawal symptoms in the postnatal period.

Since benzodiazepines are found in the breast milk, they should not be given to breast feeding mothers.

4.7 Effects on ability to drive and use machines

Attention should be drawn to the risk of drowsiness, sedation, amnesia, impaired concentration and muscular weakness, especially in drivers of vehicles and operators of machines, when taking the product (see also “Interactions”).

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

• The medicine is likely to affect your ability to drive

• Do not drive until you know how the medicine affects you

• It is an offence to drive while under the influence of this medicine

• However, you would not be committing an offence (called 'statutory defence') if:

- The medicine has been prescribed to treat a medical or dental problem and

- You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and

- It was not affecting your ability to drive safely

4.8 Undesirable effects

In general, Loprazolam is very well tolerated. However, the common side effects of benzodiazepines, including headaches, nausea, drowsiness, hypotonia, blurring of vision, dizziness and ataxia may occur on the following day, particularly in unusually sensitive patients or when dosage has been excessive.

Rare behavioural adverse effects of benzodiazepines include paradoxical aggressive outbursts, excitement, confusion and the uncovering of depression with suicidal tendencies. If these reactions should occur, use of the drug should be discontinued. Even more rare side effects reported with some benzodiazepines have been hypotension, gastro-intestinal and visual disturbances, skin rashes, urinary retention, changes in libido, blood dyscrasias and jaundice.

Frequency not known: speech disorders

Benzodiazepines may induce cognitive disorders (anterograde amnesia). In cases of loss or bereavement, psychological adjustment may be inhibited by benzodiazepines.

Injury poisoning and procedural complications

Fall (see Section 4.4)

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 Yellow Card Scheme at :www.mhra.gov.uk/yellowcard.

4.9 Overdose

As with other benzodiazepines, overdosage does not usually present a threat to life. Treatment is symptomatic and gastric lavage may be of use if performed shortly after ingestion. Use of a specific antidote such as flumazenil in association with symptomatic treatment in hospital should be considered.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Benzodiazepines have a widespread action as a result of their enhancing the release of gamma-aminobutyric acid (GABA). They are effective as anti-convulsants, muscle relaxants, anti-anxiety agents, pre-medications and sedative hypnotics.

5.2 Pharmacokinetic properties

The pharmacokinetics of oral Loprazolam given in a single dose or in repeated doses on 7 consecutive nights were studied in a balanced cross-over trial in six healthy male subjects aged 22-37 years. The subjects were allocated randomly to the treatment phases which were separated by 2-week drug-free intervals. Loprazolam was administered as 1mg tablets.

On the night of administration of the single dose and the seventh repeated dose, venous blood samples were taken before and at intervals after treatment. Serum Loprazolam concentrations were measured using both a radioimmunoassay (RIA) and the more specific high pressure liquid chromatography and gas chromatography (HPLC/GC) technique. Maximum serum levels (C_{max}) and the time taken to achieve them (T_{max}) were measured, and the half-life ($t_{1/2}$) was calculated. The area under the serum concentration-time curve (AUC) was determined using the trapezoidal rule. The ratios of AUC and C_{max} after repeated doses to AUC and C_{max} after single doses were used to assess possible accumulation of Loprazolam.

	MEAN (SD)	

SINGLE DOSES	**RIA data**	**HPLC/GC data**
C_{max} (mcg/litre)	4.0 (1.2)	4.1 (2.2)
t_{max} (hours)	4.0 (2.1)	5.0 (3.6)
$t_{1/2}$ (hours)	11.7 (4.7)	8.0 (3.4)*
AUC (mcg/litre hour)	60.0 (20.9)	35.5 (22.2)
REPEATED DOSES	**RIA data**	**HPLC/GC data**
C_{max} (mcg/litre)	5.1 (1.2)	4.6 (2.1)
t_{max} (hours)	5.3 (3.7)	5.5 (2.7)
$t_{1/2}$ (hours)	12.8 (4.9)	3.5 (0.2)**
AUC (mcg/litre hour)	75.6 (21.1)	50.0 (26.9)

n = 6 subjects, except for *n = 5, **n = 3.

5.3 Preclinical safety data

No additional data of relevance to the prescriber.

6. Pharmaceutical particulars

6.1 List of excipients

Povidone, Lactose, Colloidal silicon dioxide, Maize starch, Microcrystalline cellulose and Magnesium stearate.

6.2 Incompatibilities

None.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 25°C in a dry place. Protect from light.

6.5 Nature and contents of container

UPVC/aluminium foil blisters, packaged in cartons of 10, 28 or 30 tablets.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorisation holder

Zentiva Pharma UK Limited

12 New Fetter Lane

London

EC4A 1JP

United Kingdom

8. Marketing authorisation number(s)

PL 17780/0306

9. Date of first authorisation/renewal of the authorisation

17 March 2009

10. Date of revision of the text

24 June 2020

LEGAL CLASSIFICATION

POM

Company Contact Details

Zentiva

Address
12 New Fetter Lane, LONDON, EC4A 1JP, UK

E-mail
gfd-customerservices@zentiva.com

Medical Information Direct Line
+44 (0)800 090 2408

Medical Information e-mail
UKMedInfo@zentiva.com

Customer Care direct line
+44 (0)844 8793 188