IRISH MEDICINES BOARD ACT 1995

MEDICINAL PRODUCTS(LICENSING AND SALE)REGULATIONS, 1998

(S.I. No.142 of 1998)

PA0012/051/001
Case No: 2020344

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

HE Clissmann T/A Schering

44 Dartmouth Square, , **Dublin 6**, **Ireland**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Noctamid Tablets 0.5mg

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **06/03/2006** until **31/10/2007** .

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Noctamid Tablets 0.5mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains lormetazepam 0.5mg

For excipients, see 6.1

3 PHARMACEUTICAL FORM

Tablets

Round, white, flat tablets with a beveled edge, imprinted ‘CG’ in a regular hexagon on one face and a breakline on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Short-term treatment of insomnia.

Benzodiazepines are only indicated when the disorder is severe, disabling or subjecting the individual to extreme distress.

4.2 Posology and method of adminstration

Treatment should be as short as possible. Generally the duration of treatment varies from a few days to two weeks with a maximum, including tapering off period, of four weeks.

In certain cases extension beyond the maximum treatment period may be necessary; if so, it should not take place without re-evaluation of the patient’s status.

Treatment should be started with the lowest recommended dose. The maximum dose should not be exceeded.

Dose:

Adults take 0.5-1mg before bedtime, depending on the severity of the condition.

Elderly patients may be better on lower dosage (0.25-0.5mg) and less frequent use. Duration of treatment should be as short as possible.

Children: Lormetazepam has not been evaluated for the treatment of children.

The tablets should be taken with some liquid before bedtime.

4.3 Contraindications

Myasthenia gravis, hypersensitivity to benzodiazepines, severe respiratory insufficiency (e.g. severe chronic obstructive pulmonary disease), sleep apnoea syndrome, severe hepatic insufficiency.

Acute intoxication with alcohol, hypnotics, analgesics or psychotropic drugs (neuroleptics, antidepressants, lithium).

Patients with rare hereditary problems of galactose intolerance, the Lapp
lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.4 Special warnings and precautions for use

As a precaution, Noctamid must not be used in patients under eighteen years of age.

Tolerance:
Some loss of efficacy to the hypnotic effects of benzodiazepines may develop after repeated use for a few weeks.

Dependence:
Use of benzodiazepines may lead to the development of physical and psychic dependence upon these products. The risk of dependence increases with dose and duration of treatment; it is also greater in patients with a history of alcohol or drug abuse.

Once physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms. These may consist of headaches, muscle pain, extreme anxiety, tension, restlessness, confusion and irritability. In severe cases the following symptoms may occur: derealisation, depersonalisation, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, hallucinations and epileptic seizures.

Rebound insomnia and anxiety:
A transient syndrome whereby the symptoms that led to treatment with a benzodiazepine recur in enhanced form, may occur on withdrawal of treatment. It may be accompanied by other reactions including mood changes, anxiety or sleep disturbances and restlessness.

Since the risk of withdrawal phenomena/rebound phenomena is greater after abrupt discontinuation of treatment, it is recommended that the dosage is decreased gradually. Moreover, it is important that the patient should be aware of the possibility of rebound phenomena thereby minimising anxiety over such symptoms should they occur while Noctamid is being discontinued.

Duration of treatment:
The duration of treatment should be as short as possible (see Posology) depending on the indication but should not exceed 4 weeks for insomnia including tapering off process. Extension beyond these periods should not take place without re-evaluation of the situation.

It may be useful to inform the patient when treatment is started that it will be of limited duration and to explain precisely how the dosage will be progressively decreased. Moreover it is important that the patient should be aware of the possibility of rebound phenomena, thereby minimising anxiety over such symptoms should they occur while the medicinal product is being discontinued.

When benzodiazepines with a long duration of action are being used it is important to warn against changing to a benzodiazepine with a short duration of action, as withdrawal symptoms may develop.

Amnesia:
Benzodiazepines may induce anterograde amnesia. The condition occurs most often several hours after ingesting the product and therefore to reduce the risk patients should ensure that they will be able to have an uninterrupted sleep of 7 - 8 hours (see also Undesirable Effects).

Psychiatric and "paradoxical" reactions:
Reactions like restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour and other adverse behavioural effects are known to occur when using benzodiazepines. Should this occur, use of the product should be discontinued.

They are more likely to occur in children and the elderly (cf. also "4.8 Undesirable Effects").

Specific patient groups:
Benzodiazepines should not be given to children without careful assessment of the need to do so: the duration of treatment must be kept to a minimum.

Elderly should be given a reduced dose (see Posology). A lower dose is also recommended for patients with chronic respiratory insufficiency due to the risk of respiratory depression.

Benzodiazepines are not indicated to treat patients with severe hepatic insufficiency as they may precipitate encephalopathy.

Benzodiazepines are not recommended for the primary treatment of psychotic illness.

Benzodiazepines should not be used alone to treat depression or anxiety associated with depression (suicide may be precipitated in such patients).

Benzodiazepines should be used with extreme caution in patients with a history of alcohol or drug abuse.

Myorelaxant Effect:
Because of the myorelaxant effect there is a danger of falls, particularly for elderly patients on getting up at night.

4.5 Interaction with other medicinal products and other forms of interaction

Not recommended:
Concomitant intake with alcohol. The sedative effect may be enhanced when the product is used in combination with alcohol. This affects the ability to drive or use machines.

Take into account:
Combination with CNS depressants. Enhancement of the central depressive effect may occur in cases of concomitant use with antipsychotics (neuroleptics), hypnotics, anxiolytics/sedatives, antidepressant agents, narcotic analgesics, anti-epileptic drugs, anaesthetics and sedative antihistamines.

In the case of narcotic analgesics, enhancement of the euphoria may also occur with benzodiazepines leading to an increase in psychic dependence.

Compounds which inhibit certain hepatic enzymes (particularly cytochrome P450) may enhance the activity of benzodiazepines. To a lesser degree this also applies to benzodiazepines that are metabolised only by conjugation.

4.6 Pregnancy and lactation

As a precaution, Noctamid should not be used during pregnancy, delivery and lactation.

Animal studies with benzodiazepines have shown minor effects on the foetus while a few studies have reported late behavioural disturbances in offspring exposed in utero.

If Noctamid 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, Noctamid is administered during the late phase of pregnancy, or during labour, effects on the neonate, such as hypothermia, hypotonia, hypotension, moderate respiratory depression and sucking

difficulties (“floppy infant syndrome”) 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 dependence and may be at some risk of developing withdrawal symptoms in the post-natal period.

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

4.7 Effects on ability to drive and use machines

Sedation, amnesia, impaired concentration and impaired muscular function may adversely affect the ability to drive or to use machines or to perform tasks requiring alertness. If insufficient sleep duration occurs, the likelihood of impaired alertness may be increased. Reactions can be impaired depending on the time of ingestion, the individual sensitivity and dosage. This applies to an increased extent in association with alcohol.

4.8 Undesirable effects

Drowsiness during the day, numbed emotions, reduced alertness, confusion, fatigue, headache, dizziness, muscle weakness, ataxia or double vision. These phenomena occur predominantly at the start of therapy and usually disappear with repeated administration. Other side effects like gastrointestinal disturbances, changes in libido or skin reactions have been reported occasionally.

Amnesia:
Anterograde amnesia may occur using therapeutic dosages, the risk increasing at higher dosages (cf. “4.4 Special warnings and special precautions for use”). Amnestic effects may be associated with inappropriate behaviour.

*Depression**:***
Pre-existing depression may be unmasked during benzodiazepine use. Suicide may be precipitated in such patients (cf. “4.4 Special warnings and special precautions for use”).

Psychiatric and paradoxical reactions:
Reactions like restlessness, agitation, irritability, aggressiveness, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour and other adverse behavioural effects are known to occur when using benzodiazepines or benzodiazepine-like agents. Paradoxical reactions are more likely to occur in children and in elderly patients (cf. “4.4 Special warnings and special precautions for use”).

Dependence:
Use (even at therapeutic doses) may lead to the development of physical dependence; discontinuation of the therapy may result in withdrawal or rebound phenomena (cf. “4.4 Special warnings and special precautions for use”). Psychic dependence may occur.

Abuse of benzodiazepines has been reported.

4.9 Overdose

As with other benzodiazepines, overdose should not present a threat to life unless combined with other CNS depressants (including alcohol).

In the management of overdose with any medicinal product, it should be borne in mind that multiple agents may have been taken.

Following overdose with oral benzodiazepines, vomiting should be induced (within one hour) if the patient is conscious or gastric lavage undertaken with the airway protected if the patient is unconscious. If there is no advantage in emptying the stomach, activated charcoal should be given to reduce absorption. Special attention should be paid to respiratory and cardiovascular functions in intensive care.

Overdose of benzodiazepines is usually manifested by degrees of central nervous system depression ranging from drowsiness to coma. In mild cases, symptoms include drowsiness, mental confusion and lethargy, in more serious cases, symptoms may include ataxia, hypotonia, hypotension, respiratory depression, rarely coma and vary rarely death.

Flumazenil may be useful as an antidote.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A benzodiazepine with sedative characteristics.

5.2 Pharmacokinetic properties

Lormetazepam is rapidly absorbed from the gastrointestinal tract and is metabolised by a simple one step process to a pharmacologically inactive glucuronide. There are no major metabolites. Peak plasma levels are reached after 2 hours. Lormetazepam has a terminal phase half-life of about 11 hours. Clinical studies have shown minimal effects on REM sleep and on psychomotor performance on the day after treatment with lormetazepam.

5.3 Preclinical safety data

No remarks.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Maize starch
Povidone
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

5 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

PVC/AI blister strips, 10 tablets/strip, in a cardboard carton.

Pack size: 30 tablets.

6.6 Instructions for use and handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

HE Clissmann T/A Schering
Dublin

8 MARKETING AUTHORISATION NUMBER

PA 12/51/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st November 1982

Date of last renewal: 1st November 2002

10 DATE OF REVISION OF THE TEXT

February 2006