Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dalmapam 15mg Hard Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Flurazepam (as flurazepam monohydrochloride) 15 mg

Each capsule also contains 159.1mg of lactose monohydrate.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Capsule, hard

Size 3, ivory / light grey hard gelatin capsules, marked ‘Flu 15’

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

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

4.2 Posology and method of administration

Insomnia
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 process of four weeks.

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

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

Adults:
The usual dosage is 15-30mg before retiring. 15mg is optimal for most patients. Patients with severe insomnia may require 30mg but residual effects on awakening, associated with an anxiolytic effects, are more frequent at this dose.

Older or debilitated patients:
Older patients will be particularly susceptible to the adverse effects of Dalmapam. The initial dose should not exceed 15mg. If organic brain changes are present, the dosage of Dalmapam should be reduced (see section 4.4).

Use in patients with hepatic and renal impairment:
The dosage should be reduced in patients with renal or hepatic impairment. Dalmapam is contraindicated in patients with severe hepatic failure (see sections 4.3 and 4.4).

Use in patients with chronic pulmonary insufficiency:
In patients with chronic pulmonary insufficiency the dosage may need to be reduced.

Children:
Not recommended.

Method of administration
Oral use.

The product should be taken just before going to bed. The patient should be checked regularly at the start of the treatment in order to decrease if necessary, the dose or frequency of administration to prevent overdose due to accumulation.

4.3 Contraindications

- Patients with hypersensitivity to flurazepam, other benzodiazepines, or to any of the excipients listed in section 6.1;
- Myasthenia gravis
- Severe pulmonary insufficiency
- Severe respiratory insufficiency
- Sleep apnoea syndrome
- Severe hepatic insufficiency
- Phobic or obsessional states
- Chronic psychosis

4.4 Special warnings and precautions for use

Dalmapam should not be used alone to treat depression or anxiety associated with depression since suicide may be precipitated in such patients. Benzodiazepines should be used with extreme caution in patients with a history of alcohol or drug abuse.

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

In cases of loss or bereavement, psychological adjustment may be inhibited by benzodiazepines.

Dalmapam is not indicated in patients with spinal and cerebellar ataxia.

Dalmapam should not be given in acute intoxication with alcohol, sedative agents, hypnotic agents, analgesics or psychotropic agents (neuroleptic agents, antidepressants, lithium).

Dalmapam is not indicated for children. If necessary for compelling reasons, benzodiazepines should be prescribed for children and adolescents after careful appraisal of the risk-benefit ratio.

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

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

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 or in patients with marked personality disorders. Regular monitoring in such patients is essential, routine repeat prescriptions should be avoided and treatment should be withdrawn gradually.

Symptoms such as depression, nervousness, extreme anxiety, tension, restlessness, confusion, mood changes, rebound insomnia, irritability, sweating, diarrhea, headaches and muscle pain has been reported following abrupt cessation of treatment in patients receiving even normal therapeutic doses for short periods of time.

In severe cases the following symptoms may occur: derealization, depersonalization, hyperacusis, numbness and tingling of the extremities, hypersensitivity to light, noise and physical contact, hallucinations or epileptic seizures. In rare instances, withdrawal following excessive dosages may produce confusional states, psychotic manifestations and convulsions. Abuse of benzodiazepines has been reported.

Rebound insomnia and anxiety
This is a transient syndrome whereby the symptoms that led to treatment with a benzodiazepine recur in an 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.

Duration of treatment
The duration of treatment should be as short as possible (see 4.2, Posology and method of Administration), depending on the indication,but should not exceed 4 weeks including tapering off process. Extension beyond these periods should not take place without reevaluation 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 minimizing anxiety over such symptoms should that occur while the medicinal product is being discontinued.

There are indications that, in the case of benzodiazepines with a short duration of action, withdrawal phenomena can become manifest within the dosage interval, especially when the dosage is high. 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 section 4.8, Undesirable Effects).

If the patient is awoken during the period of maximum drug activity, recall may be impaired.

Psychiatric and 'paradoxical' reactions
Abnormal psychological reactions to benzodiazepines have been reported. Rare behavioural effects included paradoxical aggressive outbursts, excitement, confusion, restlessness, agitation, irritability, delusion, rages, nightmares, hallucinations, psychoses, inappropriate behaviour and the uncovering of depression with suicidal tendencies. If any of these reactions occur, use of the drug should be discontinued. These reactions may be quite severe and more likely to occur in children and older patients.

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.

Older patients should be given reduced dose (see section 4.2, Posology and Method of Administration). Due to myorelaxant effect of Dalmapam there is a risk of falls and consequently of hip fractures particularly for older patients when they get up at night.

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 and reduced doses should be given to patients with renal or hepatic disease.

The dosage should be reduced in patients with organic brain changes. 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.

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 adversely affects the ability to drive or use machines.

Take into account Combination with CNS depressants
Benzodiazepines, including flurazepam, produce additive CNS depressant effects when coadministered with other drugs such as barbiturates, antipsychotics (neuroleptics), sedatives/hypnotics, anxiolytics antidepressant,narcotic analgesics, sedative antihistamines, anticonvulsants, anesthetics, antihypertensives and beta (receptor) blockers. Administration of theophylline or aminophylline may reduce the sedative effects of benzodiazepines. In the case of narcotic analgesics enhancement of the euphoria may also occur leading to an increase in psychological dependence. Older patients require special supervision.

Known inhibitors of hepatic enzymes particularly, e.g. cimetidine, omeprazole and disulfuram have been shown to reduce the clearance of benzodiazepines and may potentiate their actions and known inducers of hepatic enzymes, e.g. rifampicin, may increase the clearance of benzodiazepines.

When Dalmapam is used in conjunction with anti-epileptic drugs, side-effects and toxicity may be more evident, particularly with hydantoins or barbiturates or combinations including them. This requires extra care in adjusting dosage in the initial stages of treatment.

Concomitant intake with muscle relaxants may increase the relaxant effect of flurazepam.

In the case of narcotic analgesics enhancement of the euphoria may also occur 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 metabolized only by conjugation.

4.6 Fertility, pregnancy and lactation

Pregnancy

Benzodiazepines should only be used during pregnancy or lactation if considered essential by the physician. Animal studies with benzodiazepines have shown minor effects on the foetus while a few studies have reported late behavioural disturbance in offspring exposed in utero. There is no evidence as to drug safety in human pregnancy or evidence from animal work that it is free from hazard. Therefore, Dalmapam should not be used during pregnancy, especially during the first and last trimesters, unless there are compelling reasons.

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, effects on the neonate, such as hypothermia, hypotonia, and moderate respiratory depression in the neonate, can be expected, due to the pharmacological action of the compound.

Administration of high doses of benzodiazepines in the last trimester of pregnancy or during labour has been reported to produce irregularities in the foetal heart rate, and hypotonia, poor sucking and hypothermia and moderate respiratory depression in the neonate.

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

Breast -feeding
No data regarding the passage of flurazepam into the breast milk are available. However, in common with other benzodiazepines, its passage into breast milk might be expected. If possible, the use of Dalmapam in mothers who are breast- feeding should be avoided.

4.7 Effects on ability to drive and use machines

Patients should be advised that, like all medicaments of this type, Dalmapam might modify patients' performance at skilled tasks. Sedation, amnesia, impaired concentration and impaired muscular function may adversely affect the ability to drive or to use machinery to a varying degree depending upon dosage. This applies in particular following insufficient duration of sleep. Patients should further be advised that alcohol may intensify any impairment, and should, therefore, be avoided during treatment.

4.8 Undesirable effects

Common adverse effects include drowsiness (when the product is used as a hypnotic it should be stated explicitly: drowsiness during the day), emotional poverty, reduced alertness, confusion, fatigue, headache, dizziness, muscle weakness, ataxia and diplopia. These phenomena are dose-related and are likely to be uncommon with the recommended dosage; they occur predominantly at the start of therapy and usually disappear with repeated administration. Older patients are particularly sensitive to the effects of centrally-depressant drugs. Other side effects like gastrointestinal disturbances, changes in libido or skin reactions have been reported occasionally.

Within the system organ classes, adverse reactions are listed under headings of frequency (number of patients expected to experience the reaction), using the following categories:
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)
Frequency not known (cannot be estimated from the available data)

Blood and lymphatic system disorder
Frequency not known: Blood disorders (e.g. thrombocytopenia, leucopenia, agranulocytosis, pancytopenia)

Immune system
Rare: Hypersensitivity (e.g. angioedema)

Psychiatric disorders
Common: Emotional poverty
Frequency not known: Confusional state, hallucinations, dependence, withdrawal syndrome, rebound effect, depression, paradoxical drug reactions (e.g. anxiety, sleep disorders, insomnia, nightmares, restlessness, agitation, irritability, aggression, delusion, psychotic disorder, abnormal behaviour, emotional disturbances, suicide attempt, suicide ideation

Nervous system disorders
Common: Somnolence, decreased alertness, ataxia, dizziness, headache, dysgeusia, amnesia
Frequency not known: Extrapyramidal disorder, anterograde amnesia

Eye disorders
Rare: Visual impairment (e.g. diplopia)

Ear and labyrinth disorders
Rare: Vertigo

Vascular disorders
Rare: Hypotension

Respiratory, thoracic and mediastinal disorders
Rare: Respiratory depression (particularly at night)

Gastrointestinal disorders
Rare: Abdominal discomfort, nausea

Hepatobiliary disorders
Very rare: Jaundice, hepatic enzyme increased

Skin and subcutaneous tissue disorders
Rare: Skin reactions (e.g. rash)

Musculoskeletal and connective tissue disorders
Common: Muscle weakness. Due to the myorelaxant effect there is a risk of falls and consequently fractures in the elderly.

Renal and urinary disorders
Rare: Urinary retention

Reproductive system and breast disorders
Rare: Libido disorder

General disorders and administration site conditions
Common: Fatigue

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

Depression
Pre-existing depression may be unmasked during benzodiazepine 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. They may be quite severe with this product. They are more likely to occur in children and the elderly.

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 (See section 4.4, Special warnings and precautions for use). Psychic dependence may occur. Abuse of benzodiazepines has been reported.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

4.9 Overdose

When taken alone, Dalmapam presents few problems in management and should not present a threat to life unless combined with other CNS depressants (including alcohol).

Signs and symptoms
Depending on the dose ingested, intoxication with benzodiazepines is usually manifested by various degrees of central nervous system depression ranging from somnolence, mental confusion, dysarthria and lethargy, impaired vision and dystonia to ataxia, unconsciousness, central respiratory and/or circulatory depression and rarely coma and very rarely death.

Management:

In the management of overdose with any medicinal product, it should be borne in mind that multiple agents have been taken.
Following overdose with 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. General supportive and symptomatic measures are recommended.

Special attention should be paid to respiratory and cardiovascular functions in intensive care.

The value of dialysis has not been determined and is expected to be low for Dalmapam. Flumazenil is a specific IV antidote for use in emergency situations. Patients requiring such intervention should be monitored closely in hospital (see separate prescribing information).

The physician should be aware of a risk of seizure in association with flumazenil treatment, particularly in long-term benzodiazepine users and cyclic antidepressant overdose.

If excitation occurs, barbiturates should not be used.
When taken with centrally-acting drugs, especially alcohol, the effects of over- dosage are likely to be more severe and, in the absence of supportive measures, may prove fatal.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: N05C D01
A benzodiazepine with sedative and hypnotic properties.

5.2 Pharmacokinetic properties

A benzodiazepine hypnotic well absorbed, rapidly metabolised to an active desalkyl derivative and hydroxy metabolite, widely distributed and excreted in urine with a T½ of 40-100 hours.

5.3 Preclinical safety data

None

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose Monohydrate
Microcrystalline Cellulose
Colloidal Anhydrous Silica
Talc
Magnesium Stearate

Capsule Shell
Black Iron Oxide (E172)
Titanium Dioxide (E171)
Yellow Iron Oxide (E172)
Gelatin

Capsule Ink
Shellac Glaze
Iron Oxide Red (E127)
Propylene Glycol (E1520)
Potassium Hydroxide
Strong Ammonia Solution

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Al/PVC/PvdC blisters

Pack size: 30 capsules

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements

7 MARKETING AUTHORISATION HOLDER

Pinewood Laboratories Limited
Ballymacarbry
Clonmel
Co. Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0281/073/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 14 April 1993

Date of last renewal: 14 April 2008

10 DATE OF REVISION OF THE TEXT

May 2017