Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Mogadon 5 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Mogadon tablet contains 5 mg of Nitrazepam.
Excipients: also includes lactose monohydrate 301mg per tablet.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.
Round, white tablets with "V" over "MOG5" marked on one side and with a single break-line on the other. The tablet can be divided into equal halves.

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
Adults:

The usual total daily dosage is 5 to 10 mg before retiring. In hospitalised patients a single dose of 20mg may be given.

Elderly or debilitated patients:
The elderly or patients with impaired renal and/or hepatic function will be particularly susceptible to adverse effects of Mogadon. Doses should not exceed half those normally recommended.
If organic brain changes are present, the dosage of Mogadon should not exceed 5mg in these patients.

Children:
Not recommended.

Other populations:
In patients with chronic pulmonary insufficiency and in patients with chronic renal or hepatic disease, dosage may need to be reduced.

Treatment should be as short as possible and should be started with the lowest possible dose. The maximum dose should not be exceeded. Generally the duration of treatment varies from a few days to two weeks with a maximum of four weeks; including the tapering off process. Patients who have taken benzodiazepines for a prolonged time may require a longer period during which doses are reduced. Specialist help may be appropriate. Little is known regarding the efficacy or safety of benzodiazepines in long-term use.
In certain cases, extension beyond the maximum treatment period may be necessary; if so, it should not take place without a re-evaluation of the patient's status. Long-term chronic use is not recommended. Mogadon therapy should not be stopped abruptly, but the dose tapered off.

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

Myasthenia Gravis
Hypersensitivity to benzodiazepines or to any of the excipients
Severe respiratory insufficiency
Sleep apnoea syndrome
Severe hepatic insufficiency
Acute pulmonary insufficiency
Phobic or obsessional states
Chronic psychosis
Short-term treatment of insomnia in children

4.4 Special warnings and precautions for use

Risk from concomitant use of opioids:
Concomitant use of Mogadon 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 Mogadon with opioids should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe Mogadon 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).

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

Lactose intolerance
Mogadon tablets contain lactose. 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 when high doses are used, especially when given over long periods. This is particularly so 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.

Once physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms.

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

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 or epileptic seizures.

In rare instances, withdrawal following excessive dosages may produce confusional states and psychotic manifestations and convulsions. Abuse of the benzodiazepines has been reported.

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

Rebound insomnia and anxiety: 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 section 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 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.

Amnesia
Benzodiazepines may induce anterograde amnesia. The condition usually occurs 1 to 2 hours after ingesting the product and may last up to several hours. 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).

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 drug should be discontinued.

They are most likely to occur in children and the elderly.

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 section 4.2, Posology and method of administration). Due to myorelaxant effect there is a risk of falls and consequently of hip fractures particularly for elderly 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.

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).

4.5 Interaction with other medicinal products and other forms of interactions

Opioids:
The concomitant use of sedative medicines such as benzodiazepines or related drugs such as Mogadon 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).

Enhancement of the central depressive effect may occur in cases of concomitant use with centrally-acting drugs such as neuroleptics, tranquillisers, 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 leading to an increase in psychic dependence. The elderly require special supervision.

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

Known inhibitors of hepatic enzymes (particularly cytochrome P450) have been shown to reduce the clearance of benzodiazepines and may potentiate their action and known inducers of hepatic enzymes, e.g. rifampicin, may increase the clearance of benzodiazepines .

Concomitant intake with alcohol should be avoided. The sedative effect may be enhanced when the product is used in combination with alcohol. This adversely affects the ability to drive or to use machines.

4.6 Fertility, pregnancy and lactation

Fertility
Animal studies with benzodiazepines have shown minor effects on the foetus while a few studies have reported late behavioural disturbance in offspring exposed *inutero*.

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.

Pregnancy
Administration 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, 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 some risk for developing withdrawal symptoms in the postnatal period.

Lactation
Since benzodiazepines are found in the breastmilk, the use of Mogadon 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, Mogadon may 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. If insufficient sleep duration occurs, the likelihood of impaired alertness may be increased, Patients should further be advised that alcohol may intensify any impairment, and should, therefore, be avoided during treatment, (see also section 4. 5, Interaction with other medicinal products and other forms of interaction).

4.8 Undesirable effects

Within the system organ classes, adverse reactions are listed under headings of the 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 (< 10,000)
Not known (cannot be estimated from the available data)

Blood and lymphatic system disorders
Rare: Blood disorder
Immune system disorder
Rare: Allergic skin reaction
Very rare: Anaphylactic reaction, angioedema

Psychiatric disorders
Common: Emotional disorder, confusional state, depression (pre-existing depression may be unmasked)
Uncommon: Delirium, insomnia, cognitive impairment
Rare: Libido disorder, dependence, withdrawal syndrome, mood altered, anxiety, restlessness, drug abuse, agitation, aggression, delusion,
anger, nightmare, hallucination, psychotic disorder.
Since the risk of withdrawal phenomena/rebound phenomena is greater abrupt discontinuation of treatment, it is recommended that the dosage be decreased gradually.

Nervous system disorders
The elderly are particularly sensitive to the effects of centrally-depressant durgs.

Common: Drowsiness, headache, dizziness, anterograde amnesia
Uncommon: Balance disorder, hypokinesia, tremor
Rare: Epilepsy, vertigo

Eye disorders
Common: Diplopia
Rare: Visual impairment

Vascular disorders
Rare: Hypotension

Respiratory, thoracic and mediastinal disorders
Common: Respiratory depression, increased bronchial secretion

Gastrointestinal disorders
Rare: Abdominal discomfort

Hepatobiliary disorders
Rare: Jaundice

Skin and subcutaneous tissue disorders
Rare: Rash, urticaria, pruritus, dermatitis, erythema multiforme, Stevens-Johnsons syndrome

Musculoskeletal and connective tissues disorders
Due to the myorelaxant effect there is a risk of falls and consequently fractures in the elderly.

Common: Muscular weakness
Rare: Muscle spasm

Renal and urinary disorders
Common: Urinary retention

General disorders and administration site conditions
Common: Fatigue
Uncommon: Ataxia
Rare: Irritability, rebound affect
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 in overdosage, Mogadon presents f ew problems in management and should not present a threat to life unless combined with other CNS depressant (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. Overdosage 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, dysarthria and lethargy; in more serious cases, symptoms may include ataxia, hypotonia, hypotension, respiratory depression, rarely coma and very rarely death.

The value of dialysi s has not been determined. –Flumazenil is a specific IV antidote for use in emergency situations. Patients r equiring such interventions should be monitored closely in hospital (see separate prescribing information). The benzodiazepine antagonist flumazenil is not indicated in patients with epilepsy who have been treated with benzodiazepines. Antagonism of the benzodiazepine effect in such patients may trigger seizures.

If excitation occurs, barbiturates should not be used.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: N05CD02

Mogadon is a benzodiazepine compound with sedative properties. It acts in 30 to 60 minutes to produce sleep lasting 6 to 8 hours.

5.2 Pharmacokinetic properties

The drug is well absorbed from the GI tract with peak blood levels being achieved within 2 hours of administration. Two hours after administration, the concentration of nitrazepam in the cerebrospinal fluid is about 8% and after 36 hours approximately 16% of the concentration in the plasma. The cerebrospinal fluid concentration thus corresponds to the non-protein-bound fraction of active ingredient in the plasma. The half-life is, on average, 24 hours. Steady-state levels are achieved within 5 days. Nitrazepam undergoes biotransformation to a number of metabolites, none of which possess significant clinical activity.

About 5% is excreted unchanged in the urine together with less than 10% each of the 7-amino-and-acetylamino metabolites in the first 48 hours. In younger persons the volume of distribution is 2L/kg, in elderly patients the volume of distribution is greater and the mean elimination half-life rises to 40 hours.

No clear correlation has been demonstrated between the blood levels of Mogadon and its clinical effects.

5.3 Preclinical safety data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Maize starch
Magnesium stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

5 years

6.4 Special precautions for storage

Bottles: Do not store above 25°C. Store in the original container.
Blisters: Do not store above 25°C. Keep blisters in the outer carton.

6.5 Nature and contents of container

Outer cardboard box containing a HDPE bottle with snap-lid cap.
Each HDPE bottle contains 30 tablets.
PVC/A1 blister packs containing 30 tablets.

Not all pack sizes may be marketed.

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.

6.6 Special precautions for disposal

6.6 Special precautions for disposal and other handling

7 MARKETING AUTHORISATION HOLDER

Mylan IRE Healthcare Limited
Unit 35/36

Grange Parade
Baldoyle Industrial Estate
Dublin 13
Ireland

8 MARKETING AUTHORISATION NUMBER

PA2010/024/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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