Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Clobazam Brown & Burk 10mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10 mg Clobazam.

Excipient(s) with known effect
Each 10 mg tablet contains 68.80 mg of lactose (as lactose monohydrate) and 18.04 mg of lactose.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

White to off white, oval tablet with a functional score line on one face and "1" and "0" debossed on the other face, having approximate size 8.70 mm length x 5.05 mm width.

The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Anxiety

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

- As adjunctive therapy in epilepsy, when the patient cannot be sufficiently stabilized with other antiepileptic drugs alone.

4.2 Posology and method of administration

Anxiety

Treatment should be as short as possible. The patient must be re-assessed after a period not exceeding 4 weeks and regularly thereafter in order to evaluate the need for continued treatment, especially where the patient is free of symptoms. Generally the overall duration of treatment (i.e. including tapering-off process) must not exceed 8 to 12 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 with special expertise. It is strongly recommended that prolonged periods of uninterrupted treatment be avoided, since they may lead to dependance.

Adults: The usual anxiolytic dose for adults is 20-30 mg daily in divided doses or as a single dose given at night. Doses of up to 60 mg daily have been used in the treatment of adult in-patients with severe anxiety.

The lowest dose that can control symptoms should be used. After improvement of symptoms the dose may be reduced. It should not be used for longer than 4 weeks.

Due regard must be paid to the possibility of interference with alertness and reaction time.

Long term chronic use as an anxiolytic is not recommended. Treatment should always be withdrawn gradually. Patients who have taken Clobazam for a long time may require a longer period during which doses are reduced.

Elderly: Doses of 10-20 mg daily in anxiety may be used in the elderly and debilitated who are usually more sensitive to the effects of psychoactive agents. Treatment requires low initial doses and gradual dose increments under careful observation.

Treatment of Epilepsy in association with one or more other anticonvulsants
Adults: In epilepsy a starting dose of 5-15 mg daily with increases of 10mg increments, as necessary up to a maximum of 80 mg daily.

Children aged 6 years and above: When prescribed for treatment requires low initial doses and gradual dose increments under careful observation. It is recommended that normally treatment should be started at 5 mg daily. A maintenance dose of 0.3 to 1 mg/kg body weight daily is usually sufficient. As there is no age appropriate formulation to enable safe and accurate dosing, no dosage recommendations can be made in children under 6 years of age.

The patient must be re-assessed after a period not exceeding 4 weeks and regularly thereafter in order to evaluate the need for continued treatment. A break in therapy may be beneficial if drug exhaustion develops, recommencing therapy at a low dose. At the end of treatment (including in poor-responding patients), since the risk of withdrawal phenomena/rebound phenomena is greater after abrupt discontinuation of treatment, it is recommended to gradually decrease the dosage.

The tablets can be administered whole, or crushed and mixed in applesauce and used immediately (please refer to section 5.2). The 10mg tablets can be divided into equal halves of 5mg. Clobazam can be given with or without food.

Patients with impairment of renal or hepatic function: Increased responsiveness and higher susceptibility to adverse effects may be present in these patients and require low initial doses and gradual dose increments under careful observation. The maximum dose should not be exceeded.

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.

Dosage Treatment should be started with the lowest possible dose. Due to the long half-life, it is possible that accumulation may occur with daily use of Clobazam Brown & Burk.It should also be borne in mind that the effect of the substance may still be noticeable for a few days after discontinuing the use of Clobazam Brown & Burk.

4.3 Contraindications

Hypersensitivity to clobazam, benzodiazepines or any of the excipients listed in section 6.1.
Myasthenia gravis
Severe respiratory insufficiency
Sleep apnoea syndrome
Severe hepatic insufficiency
In breast-feeding women.

4.4 Special warnings and precautions for use

- **Alcohol**

It is recommended that patients abstain from drinking alcohol during treatment with clobazam (increased risk of sedation and other adverse effects (please refer to section 4.5 Interactions with other Medicinal Products and other forms of Interaction)).

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

- **Risks from concomitant use of opioids and benzodiazepines**

Concomitant use of clobazam 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 clobazam with opioids should be reserved for patients for whom alternative treatment options are not possible.

If a decision is made to prescribe clobazam 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 environment 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.

In the treatment of epilepsy with benzodiazepines – including clobazam – consideration must be given to the possibility of a decrease in anticonvulsant efficacy (development of tolerance) in the course of treatment.

- **Dependence**

Use of benzodiazepines may lead to the development of physical and psychic dependence upon these products. The risk of dependence increases with increasing dose and duration of treatment. However, this risk is present even with daily use of clobazam for several weeks at therapeutic doses and not only with possible abuse with particularly high doses. The risk is greater for patients with a history of alcohol or drug abuse. Therefore the duration of treatment should be as short as possible (see Posology).

Once physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms (or rebound phenomena). These may consist of headaches, muscle pain, extreme anxiety, tension, restlessness, confusion and irritability. 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.

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 Posology). Extension beyond these periods should not take place without revaluation 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.

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 (for example Clobazam Brown & Burk) 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 drug should be discontinued.
They are more likely to occur in children and the elderly.

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

- **Specific patient groups**

Benzodiazepines must not be given to children without careful assessment of the need for their use. Clobazam Brown & Burk must not be used in children between the ages of 6 months and 3 years, other than in exceptional cases for anticonvulsants treatment where there is a compelling indication.

The duration of treatment must be kept to a minimum.

- **Elderly patients**

After prolonged use of benzodiazepines, especially in elderly patients, in very rare cases a depression of consciousness may occur, sometimes accompanied by respiratory disorders; these effects may persist for a considerable period. In the elderly, due to the increased sensitivity to adverse reactions such as drowsiness, dizziness, muscle weakness, there is an increased risk of fall that may result in serious injury. A dose reduction is recommended.

- **Serious Skin Reactions**

Serious skin reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported with clobazam in both children and adults during the post-marketing experience. A majority of the reported cases involved the concomitant use of other drugs, including antiepileptic drugs, that are associated with serious skin reactions.

SJS/TEN could be associated with a fatal outcome. Patients should be closely monitored for signs or symptoms of SJS/TEN, especially during the first 8 weeks of treatment. Clobazam should be immediately discontinued when SJS/TEN is suspected. If signs or symptoms suggest SJS/TEN, use of this drug should not be resumed and alternative therapy should be considered (see Section 4.8)

- **Respiratory Depression**

A lower dose is also recommended for patients with chronic or acute respiratory insufficiency due to the risk of respiratory depression (respiratory functions must be monitored and a dose reduction may be necessary). Clobazam is contraindicated in patients with severe respiratory insufficiency (please refer to section 4.3 Contraindications).

- **Renal and hepatic impairment**

In patients with impairment of renal or hepatic function, responsiveness to clobazam and susceptibility to adverse effects are increased, and a dose reduction may be necessary. In long term treatment renal and hepatic function must be checked regularly. Benzodiazepines are not indicated to treat patients with severe hepatic insufficiency as they may precipitate encephalopathy.

- **Muscle weakness**

Clobazam may cause muscle weakness, therefore, in patients with pre-existing muscle weakness or spinal or cerebellar ataxia, special observation is required and a dose reduction may be necessary. Clobazam is contraindicated in patients with myasthenia gravis.

- **Suicidal ideation/suicide attempt/ suicide and depression**

Some epidemiological studies suggest an increased incidence of suicidal ideation, suicide attempt and suicide in patients with or without depression, and treated with benzodiazepines and other hypnotics, including clobazam. However, a causal relationship has not been established (see section 4.8).

- **CYP2C19 poor metabolizers**

In patients who are CYP2C19 poor metabolisers, levels of the active metabolite N-desmethyl clobazam are expected to be increased as compared to extensive metabolizers. Dosage adjustment of clobazam may be necessary (e.g. low starting dose with care dose titration (please refer to section 5.2)).

- **Concomitant use of cannabidiol**

The concomitant use of clobazam with cannabidiol-containing medicinal and nonmedicinal products may result in increased exposure to N-desmethyl clobazam, leading to increased incidence of somnolence and sedation. Dosage adjustment of clobazam may be necessary. Nonmedicinal products containing cannabidiol must not be taken in combination with clobazam as they contain unknown quantities of cannabidiol and are of variable quality (see Section 4.5, and 5.2)

- **Anxiety**

In patients with depression or anxiety associated with depression, Clobazam Brown & Burk must be used only in conjunction with adequate concomitant treatment.

Before treatment of anxiety states associated with emotional instability, it must first be determined whether the patient suffers from a depressive disorder requiring adjunctive or different treatment.

In patients with schizophrenic or other psychotic illnesses, use of benzodiazipines is recommended only for adjunctive, i.e. not for primary treatment.

Clobazam Brown & Burk tablets contains lactose
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose- galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

- **Alcohol**

Concomitant consumption of alcohol can increase the bioavailability of clobazam by 50% (please refer to Section 5.2) and therefore increase the effects of Clobazam e.g. sedation. This affects the ability to drive or use machines.

- **Central nervous system depressant drugs**

Enhancement of the central depressive effect may occur in cases of concomitant use with antipsychotics, hypnotics, anxiolytics/sedatives, antidepressant agents, narcotic analgesics, anti-epileptic drugs, anaesthetics and sedative antihistamines. Special caution is also necessary when clobazam is administered in cases of intoxication with such substances or with lithium.

- **Opioids**

The concomitant use of sedative medicines such as benzodiazepines or related drugs such as clobazam 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).

- **Anticonvulsants**

Addition of clobazam to established anticonvulsant medication (e.g phenytoin, valproic acid) might cause a change in plasma levels of these drugs. If used as an adjuvant in epilepsy the dose of Clobazam Brown & Burk should be determined by monitoring the EEG and the plasma levels of the other drugs checked.

Phenytoin and carbamazepine may cause an increase in the metabolic conversion of clobazam to the active metabolite N–desmethyl clobazam which may result in adverse reactions.

Stiripentol increases plasma levels of clobazam and its active metabolite N-desmethyl clobazam, through inhibition of CYP3A and CYP2C19. Monitoring of blood levels is recommended, prior to initiation of stiripentol, and then once new steady-state concentration has been reached, i.e. after 2 weeks approximately.

- **Narcotic analgesics**

If clobazam is used concomitantly with narcotic analgesics, possible euphoria may be enhanced; this may lead to increased psychological dependence.

- **Muscle relaxants**

The effects of muscle relaxants, analgesics and nitrous oxide may be enhanced.

- **CYP 2C19 inhibitors**

Strong and moderate inhibitors of CYP2C19 may result in increased exposure to N-desmethylclobazam (N-CLB), the active metabolite of clobazam. Dosage adjustment of clobazam may be necessary when co-administered with strong (e.g. fluconazole, fluvoxamine, ticlopidine) or moderate (e.g. omeprazole) CYP2C19 inhibitors (please refer to Section 5.2).

- **Cannabidiol**

When cannabidiol and clobazam are co-administered, bi-directional PK interactions occur. Based on a healthy volunteer study, elevated levels (3-to 4-fold) of N-desmethyl clobazam (an active metabolite of clobazam) can occur when combined with cannabidiol, likely mediated by CYP2C19 inhibition. Increased systemic levels of these active substances may lead to enhanced

pharmacological effects and to an increase in adverse drug reactions. Concomitant use of cannabidiol and clobazam increases the incidence of somnolence and sedation. Reduction in dose of clobazam should be considered if somnolence or sedation are experienced when clobazam is co-administered with cannabidiol.

- **CYP 2D6 substrates**

Clobazam is a weak CYP2D6 inhibitor. Dose adjustment of drugs metabolized by CYP2D6 (e.g. dextromethorphan, pimozide, paroxetine, nebivolol may be necessary.

- **Hepatic inhibitors such as cimetidine and hormonal contraceptives**

The effects of clobazam, which is dependent on certain liver enzymes for metabolism, may be enhanced by drugs that inhibit these enzymes, such as cimetidine and hormonal contraceptives.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are limited amount of data from the use of clobazam in pregnant women. Nevertheless, a large amount of data collected from cohort studies has not demonstrated evidence of the occurrence of major malformations following exposure to benzodiazepines during the first trimester of pregnancy, although incidences of cleft lip and palate were reported in certain case-control studies.

Clobazam is not recommended during pregnancy and in women of childbearing potential not using contraception. Clobazam crosses the placenta. Animal studies have demonstrated reproductive toxicity (see section 5.3).

Women of childbearing potential should be informed of the risks and benefits of the use of clobazam during pregnancy.

Women of childbearing potential should be informed to contact her physician regarding discontinuation of the product if they are pregnant or intend to become pregnant. If clobazam treatment is continued, it should be used at the lowest effective dose.

Cases of reduced fetal movement and fetal heart rate variability have been described after administration of benzodiazepines during the second and/or third trimester of pregnancy.

If clobazam is administered during the late phase of pregnancy or during childbirth, effects on the neonate, such as respiratory depression (including respiratory distress and apnea), sedation signs, hypothermia, hypotonia, and feeding difficulties in the newborn (so-called "floppy infant syndrome") are to be expected.

Moreover, infants born to mothers who have taken benzodiazepines over longer periods during the later stages of pregnancy may have developed physical dependence and may be at risk of developing a withdrawal syndrome in the postnatal period. Appropriate monitoring of the newborn in the postnatal period is recommended.

Breast-feeding
Since benzodizepines are found in the breast milk, clobazam must not be used in breast-feeding women.

Fertility
There is insufficient information to assess effects of clobazam on fertility in humans

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. If insufficient sleep duration occurs, the likelihood of impaired alertness may be increased (see also Interactions).

4.8 Undesirable effects

Metabolism and nutrition disorders
Common: **decreased appetite**

Psychiatric disorders
Common: **irritability, aggression, restlessness, depression (pre-existing depression may be unmasked), drug tolerance (**especially during prolonged use)**, agitation**

Uncommon: **abnormal behaviour, confusional state, anxiety, delusion, nightmare, loss of libido (**particularly with high doses or in long-term treatment and is reversible)

Not known: **dependence** (especially during prolonged use)**, initial insomnia, anger, hallucination, psychotic disorder, poor quality sleep, suicidal ideation**

Nervous system disorders
Very common: **somnolence,** especially at the beginning of treatment and when higher doses are used
Common: **sedation, dizziness, disturbance in attention, slow speech/dysarthria/ speech disorder (**particularly with high doses or in long-term treatment, and are reversible)**, headache, tremor, ataxia**

Uncommon: **emotional poverty, amnesia (may be associated with abnormal behaviour), memory impairment, anterograde amnesia (**in the normal dose range, but especially at higher dose levels)

Not known: **cognitive disorder, altered state of consciousness** (particularly in elderly patients, may be combined with respiratory disorders)**, nystagmus (**particularly with high doses or in long-term treatment)**, gait disturbance** (particularly with high doses or in long-term treatment and is reversible)

Eye Disorders
Uncommon: **diplopia (**particularly with high doses or in long-term treatment and is reversible)

Respiratory, thoracic and mediastinal disorders
Not known: **respiratory depression respiratory failure** (**particularly in patients with pre-existing compromised respiratory function** e.g. in patients with bronchial asthma or brain damage) (see Sections 4.3 Contraindications and 4.4Warnings and Precautions)

Gastrointestinal disorders
Common: **dry mouth, nausea, constipation**

Skin and subcutaneous tissue disorders
Uncommon: **rash**

Not known: **urticaria; Steven-Johnson syndrome, toxic epidermal necrolysis (including some cases with fatal outcome);**

Musculoskeletal and connective tissue disorders
Not known: **muscle spasms, muscle weakness**

General disorders and administration site conditions
Very common: **fatigue**, especially at the beginning of treatment and when higher doses are used

Not known: **slow response to stimuli, hypothermia**

Investigations
Uncommon: **weight increased** (particularly with high doses or in long-term treatment)

Injury poisoning and procedural complications
Uncommon: **fall**

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 HPRA Pharmacovigilance Website: www.hpra.ie.

4.9 Overdose

As with other benzodiazepines, overdose should not present a threat to life unless combined with other CNS depressants. The risk of a fatal outcome is increased in cases of combined poisoning with other CNS depressants, including alcohol.

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

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.

Secondary elimination of clobazam (by forced diuresis or haemodialysis) is ineffective.

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 very rarely death.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Benzodiazepine derivatives
ATC code: N05BA09.

Clobazam is a 1,5-benzodiazepine. In single doses up to 20mg or in divided doses up to 30mg, clobazam does not affect psychomotor function, skilled performance, memory or higher mental functions.

5.2 Pharmacokinetic properties

- *Absorption*

After oral administration, clobazam is rapidly and extensively absorbed

Time to peak plasma concentrations (T_{max}) is achieved from 0.5 – 4.0 hrs.
The administration of clobazam tablets with food or crushed in applesauce slows the rate of absorption by approximately 1 hour, but it does not affect the overall extent of absorption. Clobazam can be given without regard to meals.

Concomitant intake of alcohol can increase the bioavailability of clobazam by 50%.

- *Distribution*

After a single dose of 20 mg clobazam, marked inter-individual variability in maximum plasma concentrations (222 to 709 ng/ml) was observed after 0.25 to 4 hours. Clobazam is lipophilic and distributes rapidly throughout the body. Based on a population pharmacokinetic analysis, the apparent volume of distribution at steady-state was approximately 102 L, and is concentration independent over the therapeutic range. Approximately 80-90% of clobazam is bound to plasma protein.

Clobazam accumulates approximately 2-3 fold to steady-state while the active metabolite N-desmethylclobazam (N-CLB) accumulates approximately 20-fold following clobazam twice daily administration. Steady state concentrations are reached within approximately 2 weeks.

- *Metabolism*

Clobazam is rapidly and extensively metabolized in the liver. Clobazam metabolism occurs primarily by hepatic demethylation to N-desmethylclobazam (N-CLB), mediated by CYP3A4 and to a lesser extent by CYP2C19. N-CLB is an active metabolite and the main circulating metabolite found in human plasma.

N-CLB undergoes further biotransformation in the liver to form 4-hydroxy-N-desmethylclobazam, primarily mediated by CYP2C19.

CYP2C19 poor metabolizers exhibit a 5-fold higher plasma concentration of N-CLB compared to extensive metabolizers.

Clobazam is a weak CYP2D6 inhibitor. Co-administration with dextromethorphan led to increases of 90% in AUC and 59% in C_{max} values for dextromethorphan.

- *Elimination*

Based on a population pharmacokinetic analysis, plasma elimination half-lives of clobazam and N-CLB were estimated to be 36 hours and 79 hours respectively.

Clobazam is cleared mainly by hepatic metabolism with subsequent renal elimination. In a mass balance study, approximately 80% of the administered dose was recovered in urine and about 11% in the faeces. Less than 1 % of unchanged clobazam and less than 10% of unchanged N-CLB are excreted through the kidneys.

5.3 Preclinical safety data

A study in which clobazam (150, 450, or 750 mg/kg/day) was orally administered to pregnant rats throughout the period of organogenesis, embryo-fetal mortality and incidences of fetal skeletal variations were increased at all doses. The low effect dose for developmental toxicity in rats (150 mg/kg/day) was associated with plasma exposures (AUC) for clobazam and desmethyl clobazam less than those in humans at the maximum recommended human dose of 60 mg/day.
Oral administration of clobazam (10, 30, or 75 mg/kg/day) to pregnant rabbits throughout the period of organogenesis resulted in decreased fetal body weights, and increased incidences of fetal malformations (visceral and skeletal) at the mid and high doses, and an increase in embryo-fetal mortality at the high dose. Incidences of fetal variations were increased at all doses. The highest dose tested was associated with severe maternal toxicity (mortality). The low effect dose for embryo-fetal toxicity in rabbits (10 mg/kg/day) was associated with plasma exposures for clobazam and N-desmethyl clobazam less than those in humans at the maximum recommended human dose of 60 mg/day.
Additionally, oral administration of clobazam (50, 350, or 750 mg/kg/day) to rats throughout pregnancy and lactation resulted in increased embryo-fetal mortality at the high dose, decreased pup survival at the mid and high doses and alterations in offspring behaviour (locomotor activity) at all doses.
The low effect dose for pre- and postnatal development in rats (50 mg/kg/day) was associated with plasma exposures for clobazam and N-desmethylclobazam less than those in humans at the maximum recommended human dose of 60 mg/day.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

lactose monohydrate
lactose
pregelatinized starch
maize starch
colloidal anhydrous silica
talc
magnesium stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

4 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

OPA/Alu/PVC-Aluminium blister pack of 30 tablets

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

Brown & Burk IR Limited
22 Northumberland Road
Ballsbridge
Dublin 4
Ireland

8 MARKETING AUTHORISATION NUMBER

PA23148/009/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 17th of April 2026

10 DATE OF REVISION OF THE TEXT