SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Tapclob 5mg/5ml Oral Suspension

Clobazam Martindale Pharma 5mg/5ml Oral Suspension

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml of suspension contains 5mg of Clobazam

Excipients with known effect

Each 5ml of suspension contains 1250mg of Sorbitol, 10.3mg of Sodium Methyl Hydroxybenzoate and 1.12mg of Sodium Propyl Hydroxybenzoate

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Oral Suspension

An off white viscous suspension with an odour of raspberry

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Clobazam is a 1,5-benzodiazepine indicated for the short-term relief (2-4 weeks) only of anxiety that is severe, disabling or subjecting the individual to unacceptable distress, occurring alone or in association with insomnia or short term psychosomatic, organic or psychotic illness. The use of clobazam to treat short-term “mild” anxiety is inappropriate and unsuitable.

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. Indeed, in patients with anxiety associated with depression, clobazam must be used only in conjunction with adequate concomitant treatment. Use of benzodiazepine (such as clobazam) alone, can precipitate suicide in such patients.

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

Clobazam may be used as adjunctive therapy in epilepsy in adults or children over 2 years of age, if standard treatment with one or more anticonvulsants has failed.

Clobazam oral suspension should only be used in children from 6 months to 2 years old, under exceptional situations, where there is a clear epilepsy indication.

4.2 Posology and method of administration

Posology

If low doses are required, the 5mg/5ml strength product is the most suitable presentation. If high doses are required, the 10mg/5ml strength product is the most suitable presentation.

For patients who require only small doses of less than 1ml, the 150ml pack size of the 5mg/5ml strength should be used, which is provided with a 1ml oral syringe.

Treatment of anxiety

Adults

The usual anxiolytic dose for adults is 20-30 mg daily in divided doses or as a single dose given at night. Doses up to 60mg 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 the symptoms, the dose may be reduced.

It should not be used for longer than 4 weeks. Long term chronic use as an anxiolytic is not recommended. In certain cases, extension beyond the maximum treatment period may be necessary; treatment must not be extended without re-evaluation of the patient's status using special expertise. It is strongly recommended that prolonged periods of uninterrupted treatment be avoided, since they may lead to dependence. 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, who are 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

The oral suspension is suitable for any epilepsy patient in whom the clinician feels an oral suspension is preferable to clobazam tablets.

In all cases, treatment should be initiated at the lowest effective dose with gradual dose increments under careful observation.

Adults

In epilepsy a starting dose of 20-30 mg/day is recommended, increasing as necessary up to a maximum of 60 mg daily.

Elderly

Treatment requires low initial doses and gradual dose increments under careful observation.

Paediatric population aged 6 years and above:

When prescribed for children treatment requires low initial doses and gradual dose increments under careful observation. It is recommended that normally treatment should be started at 5mg daily. A maintenance dose of 0.3 to 1mg/kg body weight daily is usually sufficient.

Paediatric population aged 2 and above:

Initial: 5 mg/day (aged 6 years and above) or 0.1 mg/kg/day for younger patients. The dose may be increased slowly by steps of 0.1 to 0.2 mg/kg/day at 7 days intervals, until the required clinical effect is achieved or side effects occur.

Maintenance dose: usually 0.3 to 1 mg/kg/day . The daily dose can be taken in divided doses or as single dose at night.

Paediatric population aged 6 month-2 years:

Clobazam oral suspension should only be used in children from 6 months to 2 years old, under exceptional situations, when there is a clear epilepsy indication. Use 0.1mg/kg/day and titrate upwards very slowly (increasing not more often than every 5 days) to achieve required clinical effect, in divided doses twice daily.

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.

Method of administration

For oral use only

Once titrated to an effective dose of clobazam, patients should remain on their treatment and care should be exercised when changing between different formulations.

4.3 Contraindications

Clobazam must not be used:

− In patients with hypersensitivity to the active substance, benzodiazepines or to any of the excipients listed in section 6.1

− In patients with any history of drug or alcohol dependence (increased risk of development of dependence).

− In patients with myasthenia gravis (risk of aggravation of muscle weakness).

− In patients with severe respiratory insufficiency (risk of deterioration).

− In patients with sleep apnoea syndrome (risk of deterioration).

− In patients with severe hepatic insufficiencies (risk of precipitating encephalopathy).

− In breast-feeding women.

− During the first trimester of pregnancy (for use during second and third trimester, see section 4.6).

Benzodiazepines must not be given to children without careful assessment of the need for their use. Clobazam must not be used in children between the ages of 6 month to 2 years old, other than in exceptional cases for anticonvulsant treatment where there is a compelling indication.

4.4 Special warnings and precautions for use

Amnesia

Amnesia may occur with benzodiazepines. In case of loss or bereavement psychological adjustment may be inhibited by benzodiazepines.

Muscle weakness

Clobazam can cause muscle weakness.Special caution is necessary if clobazam is used in patients with pre-existing muscle weakness, spinal or cerebellar ataxia or sleep apnoea. 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).

Personality disorders

Disinhibiting effects may be manifested in various ways. Suicide may be precipitated in patients who are depressed and aggressive behaviour towards self and others may

be precipitated. Extreme caution should therefore be used in prescribing benzodiazepines in patients with personality disorders.

Dependence

Use of benzodiazepines - including clobazam - may lead to the development of physical and psychological 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. Therefore the duration of treatment should be as short as possible (see section 4.2 Posology).;

Once physical dependence has developed, abrupt termination of treatment will be accompanied by withdrawal symptoms (or rebound phenomena). Rebound phenomena are characterised by a recurrence in enhanced form of the symptoms which originally led to clobazam treatment. This may be accompanied by other reactions including mood changes, anxiety or sleep disturbances and restlessness.

A withdrawal syndrome may also occur when abruptly changing over from a benzodiazepine with a long duration of action (for example, clobazam) to one with a short duration of action.

Respiratory depression

Respiratory function should be monitored in patients with chronic or acute severe respiratory insufficiency and a dose reduction of clobazam may be necessary.

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.

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 period. A majority of the reported cases involved the concomitant use of other drugs, including anti-epileptic 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).

Elderly patients
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.

Tolerance in epilepsy

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

CYP2C19 poor metabolisers
In patients who are CYP2C19 poor metabolisers, levels of the active metabolite N-desmethylclobazam are expected to be increased as compared to extensive metabolisers. As this may lead to increased side effects, dosage adjustment of clobazam may be necessary (e.g. low starting dose with careful dose titration (see section 5.2).

Alcohol
It is recommended that patients abstain from drinking alcohol during treatment with clobazam (increased risk of sedation and other adverse effects) (see section 4.5).

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 benzodiazepines 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 caregivers (where applicable) to be aware of these symptoms (see section 4.5).

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.

Concomitant use of cannabidiol

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

Excipients in the formulation

Tapclob Oral Suspension contains sorbitol. Patients with a rare hereditary problems of fructose intolerance should not take this medicine.

The medicine also contains sodium methyl and propyl hydroxybenzoates which may cause allergic reactions. The signs may include a rash, swallowing or breathing problems and swelling of the lips, face, throat or tongue.

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% (see section 5.2) and therefore increase the effects of clobazam e.g. sedation (see section 4.5).

Central nervous system depressant drugs

Especially when clobazam is administered at higher doses, an enhancement of the central depressive effect may occur in cases of concomitant use with antipsychotics, hypnotics, anxiolytics/sedatives, antidepressant agents, narcotic analgesics, anti-convulsant 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 benzodiazepines 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).

Anti-convulsants

Addition of clobazam to established anti-convulsant medication (e.g. phenytoin, valproic acid) may cause a change in plasma levels of these drugs. If used as an adjuvant in epilepsy the dosage of Tapclob 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.

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

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 (see section 5.2).

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.

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-desmethylclobazam (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.

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

Fertility
No clinical data on fertility are available.In a fertility study in male and female rats no effect on fertility was observed (see section 5.3).

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).

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

The following CIOMS frequency rating is used, when applicable: 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); not known (cannot be estimated from the available data).
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) (see section 4.4), 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) (see section 4.4), initial insomnia, anger, hallucination, psychotic disorder, poor sleep quality, 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 is 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 injury***)) (see section 4.3 and 4.4)

Gastrointestinal disorders
Common: dry mouth, nausea, constipation

Skin and subcutaneous tissue disorders
Uncommon: rash

Not known: photosensitivity reaction, urticaria, Stevens-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

Uncommon: weight increased (particularly with high doses or in long-term treatment, and is reversible)

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 Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

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. 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, it is recommended that the possible involvement of multiple agents be taken into consideration.

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.

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

Consideration should be given to the use of flumazenil as a benzodiazepine antagonist.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Absorption of clobazam is virtually complete after oral administration.
Approximately 85% is protein bound in man. It is metabolised by demethylation and hydroxylation. It is excreted unchanged and as metabolites in the urine (87%) and faeces.
The peak plasma level of clobazam after oral administration of Tapclob oral suspension 2 mg/ml was higher than that observed after administration of a reference 10 mg tablet in a single dose, randomised, crossover bioequivalence study (mean Cmax 267.5 ± 64.5 ng/ml and 220.4 ± 49.9 ng/ml, respectively).
Concomitant intake of alcohol can increase the bioavailability of clobazam by 50%.

Distribution

After a single dose of 20 mg clobazam, marked interindividual 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) accumulatesapproximately 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 Cmax values for dextromethorphan.
Concomitant administration of 400 mg ketoconazole (CYP3A4 inhibitor) increased Clobazam AUC by 54% with no effect on Cmax.

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

Teratogenicity

Oral administration of clobazam to pregnant rats and rabbits throughout the period of organogenesis resulted in increased embryofetal mortality and increased incidences of fetal skeletal variations. In rabbits clobazam also decreased fetal body weights and increased the incidence of fetal malformations (visceral and skeletal). Additionally, oral administration of clobazam to rats throughout pregnancy and lactation resulted in decreased pup survival and alterations in offspring behaviour (locomotor activity). The observed embryo-fetal effects were associated with plasma exposures for clobazam and its major active metabolite N-desmethylclobazam less than those in humans at the maximum recommended dose.

Impairment of fertility

A study in rats in which clobazam was orally administered to male and female rats prior to and during mating and continuing in females to gestation day 6 had no effect on fertility and early embryonic development. The study was limited as the highest dose was associated with plasma exposures for clobazam and N-desmethylclobazam less than those in humans at the maximum recommended dose.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitol (E420)

Xanthan Gum (E415)

Acesulfame Potassium (E950)

Raspberry Flavour

Sodium Propyl Hydroxybenzoate (E217)

Sodium Methyl Hydroxybenzoate (E219)

Disodium Hydrogen Phosphate Dihydrate (for pH-adjustment)

Sodium Dihydrogen Phosphate Dihydrate (for pH-adjustment)

Purified Water

6.2 Incompatibilities

None

6.3 Shelf life

2 years

28 days after first opening

6.4 Special precautions for storage

Do not store above 25ºC

6.5 Nature and contents of container

Amber glass bottles sealed with tamper evident, child-proof plastic screw caps. The bottle is packed in a cardboard carton containing a 5ml syringe with an adaptor and a 30ml measuring cup along with the patient information leaflet.

Pack sizes: 100 ml, 150 ml and 250 ml.

Not all pack sizes may be marketed

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
This product may settle during storage. Please shake the bottle thoroughly before use.

7 MARKETING AUTHORISATION HOLDER

Martindale Pharmaceuticals Ltd

Trading As Martindale Pharma

Bampton Road

Harold Hill

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RM3 8UG

8 MARKETING AUTHORISATION NUMBER(S)

PL00156/0322

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11/02/2013/ 09/08/2018

10 DATE OF REVISION OF THE TEXT

12/10/2021