Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Lioresal 10 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 10 mg baclofen.

Excipient with known effect: wheat starch 61mg/tablet

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablet.
Circular, flat, bevelled edged white to faintly yellowish tablet with the letters 'CG' on one surface and 'KJ' on the other side with a single scoreline to facilitate breaking of the tablet for ease of swallowing. The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Lioresal is indicated for the relief of spasticity of voluntary muscle resulting from such disorders as: multiple sclerosis, other spinal lesions, e.g. syringomyelia, motor neurone disease, transverse myelitis.

Lioresal is also indicated in adults for the relief of spasticity of voluntary muscle arising from e.g. cerebrovascular accidents, cerebral palsy, meningitis, traumatic head injury.

Patient selection is important when initiating Lioresal therapy; it is likely to be of most benefit in patients whose spasticity constitutes a handicap to activities and/or physiotherapy. Treatment should not be commenced until the spastic state has become stabilised.

Paediatric population
Baclofen is indicated in patients below 18 years for the symptomatic treatment of spasticity of cerebral origin, especially where due to infantile cerebral palsy, as well as following cerebrovascular accidents or in the presence of neoplastic or degenerative brain disease.
Baclofen is also indicated for the symptomatic treatment of muscle spasms occurring in spinal cord diseases of infectious, degenerative, traumatic, neoplastic, or unknown origin such as multiple sclerosis, spastic spinal paralysis, amyotrophic lateral sclerosis, syringomyelia, transverse myelitis, traumatic paraplegia or paraparesis, and compression of the spinal cord.

4.2 Posology and method of administration

Lioresal is given orally in either tablet or liquid form. These two formulations are bioequivalent. The liquid may be particularly suitable for children or those adults who are unable to take tablets. Dosage titration can be more precisely managed with the liquid formulation.

Titration of dosage is necessary to meet the individual patients requirements while avoiding adverse effects or interference with function depending on the activity of voluntary muscles e.g. bladder, central posture support. The lowest dose compatible with an optimal response is recommended.

If no benefit is apparent within 6 to 8 weeks of achieving the maximum dosage, a decision should be taken whether to continue with Lioresal.

Treatment should always, (unless serious adverse effects occur), be gradually discontinued by successively reducing the dosage over a period of about 1-2 weeks.

Discontinuation of the treatment should always be gradual by successively reducing the dosage over a period of approximately 1 to 2 weeks, except in overdose-related emergencies, or where serious adverse effects have occurred (see Section 4.4 Special warnings and precautions for use).

Adults: Treatment should be started with a dosage of 15 mg daily, preferably in 2 to 4 divided doses. Dose should be titrated upwards cautiously by 15 mg/day increments at 3-day intervals until the requisite daily dosage has been attained. In certain patients reacting sensitively to drugs, it may be advisable to begin with a lower daily dosage (5 or 10 mg) and to raise this dosage more gradually (*see Section 4.4 Special warnings and precautions for use*). The optimum dosage generally ranges from 30 to 80 mg daily.

Satisfactory control of symptoms is usually obtained with doses of up to 60mg daily, but a careful adjustment is often necessary to meet the requirements of each individual patient. The dose may be increased slowly if required, but a maximum daily dose of more than 100mg is not advised unless the patient is in hospital under careful medical supervision. In such cases, 100mg-120mg may occasionally be necessary. Small frequent dosage may prove better in some cases than larger spaced doses. Also some patients benefit from the use of Lioresal only at night to counteract painful flexor spasm. Similarly a single dose given approximately 1 hour prior to performance of specific tasks such as washing, dressing, shaving, physiotherapy, will often improve mobility.

Once the maximum recommended dose has been reached, if the therapeutic effect is not apparent within 6 weeks a decision whether to continue with Lioresal should be taken.

Elderly: Elderly patients may be more susceptible to side effects, particularly in the early stages of introducing Lioresal. Small doses should therefore be used at the start of treatment, the dose being titrated gradually against the response, under careful supervision. There is no evidence that the eventual average maximum dose differs from that in younger patients.

Paediatric patients (below 18 years): Treatment should usually be started with a very low dose (corresponding to approximately 0.3 mg/kg a day), in 2-4 divided doses (preferably in 4 divided doses). Therefore, Lioresal tablets are not suitable for use in children with a body weight below 33 kg. Lioresal syrup may be used in this population. For children above 33kg body weight, the most suitable formulation should be considered.

The dosage should be raised cautiously, at about 1 to 2 week intervals, until it becomes sufficient for the child's individual requirements.

The usual daily dosage for maintenance therapy ranges between 0.75 and 2 mg/kg body weight. Lioresal tablets are not suitable for use in children below 33kg body weight.

Renal Impairment
In patients with impaired renal function or undergoing chronic haemodialysis, a particularly low dosage of Lioresal should be selected ie. approx. 5mg daily.

Lioresal should be administered to end stage renal failure patients only if the expected benefit outweighs the potential risk. These patients should be closely monitored for prompt diagnosis of early signs and/or symptoms of toxicity (e.g. somnolence, lethargy) (see *section 4.4 Special warnings and precautions for use* and *section 4.9 Overdose*).

Hepatic impairment
No studies have been performed in patients with hepatic impairment under Lioresal therapy. Liver does not play a significant role in the metabolism of baclofen after oral administration of Lioresal (see *section 5.2 Clinical Pharmacology*). However, Lioresal has the potential of elevating liver enzymes, Lioresal should be prescribed with caution in patients with hepatic impairment (see *section 4.4 special warnings and precautions for use*).

Geriatric patients (aged 65 years or above)
Since unwanted effects are more likely to occur in elderly patients, it is therefore recommended that a cautious dosage schedule be adopted and that the patient be kept under appropriate surveillance.

Patients with spastic states of cerebral origin
Since unwanted effects are more likely to occur in patients with spastic states of cerebral origin, it is recommended that a cautious dosage schedule be adopted in such cases and that the patient be kept under appropriate surveillance.

Method of administration
Lioresal should be taken during meals with a little liquid.

4.3 Contraindications

Hypersensitivity to baclofen or to any of the excipients.

4.4 Special warnings and precautions for use

Psychiatric and nervous system disorders

Porphyria, history of alcoholism, hypertension, psychotic disorders, schizophrenia depressive or manic disorders, confusional states or Parkinson's disease may be exacerbated by treatment with Lioresal. Patients suffering from these conditions should therefore be treated cautiously and kept under close surveillance.

Suicide and suicide-related events have been reported in patients treated with baclofen. In most cases, the patients had additional risk factors associated with an increased risk of suicide including alcohol use disorder, depression and/or a history of previous suicide attempts. Close supervision of patients with additional risk factors for suicide should accompany drug therapy. Patients (and caregivers of patients) should be alerted about the need to monitor for clinical worsening, suicidal behaviour or thoughts or unusual changes in behaviour and to seek medical advice immediately if these symptoms present.
Cases of misuse, abuse and dependence have been reported with baclofen. Caution should be exercised in patients with a history of substance abuse and the patient should be monitored for symptoms of baclofen misuse, abuse or dependence e.g. dose escalation, drug-seeking behaviour, development of tolerance.

Epilepsy
Lioresal should only be used with great caution in patients with a history of convulsions since exacerbation of such condition may occur and seizures have occasionally been reported in connection with the discontinuation of Lioresal or with overdosage. Adequate anticonvulsive therapy should be continued and the patient carefully monitored.
Lioresal should be used with extreme care in patients already receiving antihypertensive therapy, (see Interactions).

Others
Lioresal should be used with caution in patients with a history of peptic ulcers, cerebrovascular disease or from respiratory or hepatic impairment. Since unwanted effects are more likely to occur, a cautious dosage schedule should beadopted in elderly and patients with spasticity of cerebral origin (see *section 4.2 posology and method of administration*).

Paediatric population

There is very limited clinical data on the use of Lioresal in children under the age of one year. Use in this patient population should be based on the physician's consideration of individual benefit and risk therapy.

Renal impairment
Lioresal should be used with caution in patients with renal impairment and should be administered to end stage renal failure patients only if the expected benefit outweighs the potential risk (See *section 4.2 Posology and method of administration*).
Neurological signs and symptoms of overdose including clinical manifestations of toxic encephalopathy (e.g. confusion, somnolence, hallucination) have been observed in patients with renal impairment taking Lioresal at doses of more than 5mg per day and at doses of 5mg per day in patients with end-stage renal failure being treated with chronic haemodialysis. Patients with renal impairment should be closely monitored for prompt diagnosis of early signs and symptoms of toxicity(*See section 4.9 Overdose*)
Particular caution is required when combining Lioresal to drugs or medicinal products that can significantly impact renal function. Renal function shall be closely monitored and Lioresal daily dosage adjusted accordingly to prevent baclofen toxicity. Besides discontinuing treatment, unscheduled haemodialysis might be considered as a treatment alternative in patients with severe baclofen toxicity. Haemodialysis effectively removes baclofen from the body, alleviates clinical symptoms of overdose and shortens the recovery time in these patients.

Urinary disorders

Under treatment with Lioresal, neurogenic disturbances affecting the emptying of the bladder may show an improvement. In patients with pre-existing sphincter hypertonia acute retention of urine may occur; the drug should be used with caution in such cases.

Laboratory tests

In rare instances elevated aspartate aminotransferase, blood alkaline phosphatase and blood glucose levels in serum have been recorded. Appropriate laboratory tests should therefore be performed in patients with liver diseases or diabetes mellitus in order to ensure that no drug induced changes in these underlying diseases have occurred.
Patients with rare hereditary problems of fructose intolerance should not take this medicine.

Abrupt discontinuation
Treatment should always, (unless serious adverse effects occur), be gradually discontinued by successively reducing the dosage over a period of about 1-2 weeks. Anxiety and confusional state, delirium, hallucinations, psychotic disorder, mania or paranoia, convulsion (status epilepticus), dyskinesia, tachycardia, hyperthermia, **rhabdomyolysis** and temporary aggravation of spasticity as a rebound phenomenon have been reported with abrupt withdrawal of Lioresal, especially after long term medication.

Drug withdrawal reactions including postnatal convulsions in neonates have been reported after intrauterine exposure to oral Lioresal. As a precautionary measure, Lioresal administration to neonates with gradual tapering can help in controlling and preventing the withdrawal reactions. This recommendation is based on a limited number of case reports in the literature.

For the intrathecal formulation of Lioresal, it has been reported that clinical characteristics of withdrawal may resemble autonomic dysreflexia, malignant hyperthermia,neuroleptic-malignant syndrome, or other conditions associated with a hypermetabolic state or widespread rhabdomyolysis.

Except in overdose-related emergencies or where serious adverse effects have occurred, the treatment should always be gradually discontinued by successively reducing the dosage (over a period of approximately 1 to 2 weeks).

Excipients

This medicine contains only very low levels of gluten (from wheat starch) and is very unlikely to cause problems if you have coeliac disease.

One tablet of Lioresal 10 mg contains no more than 6.1 micrograms of gluten.
If you have wheat allergy (different from coeliac disease) you should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interactions

Observered Interactions to be considered
Levodopa/Dopa Decarboxylase (DDC) inhibitor (Carbidopa)
In patients with Parkinson's disease receiving treatment with Lioresal and levodopa (alone or in combinations with DDC inhibitor, carbidopa), there have been reports of mental confusion, hallucinations, headaches, nausea and agitation. Worsening of the symptoms of Parkinsonism has also been reported. Hence, caution should be exercised during concomitant administration of Lioresal and levodopa/carbidopa.

Drugs causing Central Nervous System (CNS) depression
Increased sedation may occur whenLioresal is taken concomitantly with other drugs causing CNS depression including other muscle relaxants (such as tizanidine) with synthetic opiates or with alcohol (*see driving and using machines under Section 4.4 special warnings and precautions for use*).

The risk of respiratory depression is also increased. In addition, hypotension has been reported with comcomitant use of morphine and intrathecal baclofen. Careful monitoring of respiratory and cardiovascular functions is essential especially in patients with cardiopulmonary disease and respiratory muscle weakness.

Concurrent use of baclofen with MAO inhibitors may result in increased CNS-depressant and hypotensive effects; caution is recommended and dosage of one or both agents may require reduction.

Antidepressants
During concomitant treatment with tricyclic antidepressants, the effect of Lioresal may be potentiated, resulting in pronounced muscular hypotonia.

Lithium
Concomitant use of oral Lioresal and lithium resulted in aggravated hyperkinetic symptoms. Thus, caution should be exercised when Lioresal is used concomitantly with lithium.

Antihypertensives
Since concomitant treatment with Lioresal and anti-hypertensives is likely to increase the fall in blood pressure, the dosage of antihypertensive medication should be adjusted accordingly**.**

Agents reducing renal function
Drugs which may produce renal insufficiency eg. ibuprofen may reduce baclofen excretion leading to toxic effects (see *section 4.4 special warnings and precautions for use*). Since balcofen may increase blood glucose concentrations, dosage adjustments of insulin and/or oral hypoglycemic agents may be necessary during and after concurrent therapy.

4.6 Fertility, pregnancy and lactation

Pregnancy
Baclofen given orally has been shown to increase the incidence of omphaloceles (ventral hernias) in foetuses of rats given approximately 13 times the maximum oral dose (on a mg/kg basis) recommended for human use. This abnormality was not seen in mice or rabbits (see section 5.3 Preclinical Safety data).

There are no adequate and well-controlled studies in pregnant women. Baclofen crosses the placental barrier and should be used during pregnancy only if the expected benefit outweighs the potential risk to the foetus.

Drug withdrawal reactions including postnatal convulsions in neonates have been reported after intra-uterine exposure to oral Lioresal.

Breast-feeding
In mothers taking Lioresal at therapeutic doses, the active substance passes into the breast milk, but in quantities so small that no undesirable effects are to be expected in the infant.

Fertility
There are no data available on the effect of baclofen on fertility in humans. Baclofen did not impair male or female fertility in rats at dose levels not toxic to them.

Women of child-bearing potential
There are no data supporting any special recommendations in women of child-bearing potential.

4.7 Effects on ability to drive and use machines

Lioresal may be associated with adverse effects such as dizziness, sedation, somnolence and visual impairment (see *section 4.8 Undesirable effects*) which may impair the patient's reaction. Patients experiencing these adverse reactions should be advised to refrain from driving or using machines.

Posture and balance
Lioresal should be used with caution when spasticity is needed to sustain upright posture and balance in locomotion (see *section 4.2 posology and method of administration*).

4.8 Undesirable effects

Side-effects: Unwanted effects occur mainly at the start of treatment, if the dosage is raised too rapidly, if large doses are employed, or in elderly patients. They are often transitory and can be attenuated or eliminated by reducing the dosage; they are seldom severe enough to necessitate withdrawal of the medication.

Should nausea persist following a reduction in dosage, it is recommended that Lioresal be ingested with food or a milk beverage.

Lowering of the convulsion threshold and convulsions may occur, particularly in epileptic patients.

Certain patients have shown increased muscle spasticity as a paradoxical reaction to the medication.

In patients with a case history of psychiatric illness or with cerebrovascular disorders (e.g. stroke) as well as in elderly patients, adverse reactions may assume a more serious form.

Adverse reactions are ranked under heading of frequency, the most frequent first, using the following convention: very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000) very rare (< 1/10,000), including isolated reports.

Nervous System Disorders:
Very common: Sedation, somnolence.
Common: Respiratory depression, fatigue, confusional state, dizziness, headache, insomnia, euphoria mood, depression, muscular weakness, ataxia, tremor, hallucination, nightmare, myalgia, nystagmus, dry mouth.
Rare: Paraesthesia, dysarthria, dysgeusia. Lowering of the convulsion threshold and convulsions may occur, particularly in epileptic patients.
Unknown: Sleep Apnoea syndrome*

Eyes disorders:
Common: Accommodation disorder, visual impairment.

Gastro-intestinal disorders:
Very common: Nausea.
Common: Gastro-intestinal disorder, constipation, diarrhoea, retching, vomiting.
Rare: Abdominal pain

Cardiac Disorders:
Common: Cardiac output decreased.
Not known: Bradycardia

Vascular disorders:
Common: Hypotension

Renal and urinary disorders:
Common: Pollakiuria, enuresis, dysuria.
Rare: Urinary retention

Reproductive system and breast disorders:
Rare: Erectile dysfunction

Hepatobiliary disorders:
Rare: Hepatic function abnormal.

Skin and subcutaneous tissue disorders:
Common: Hyperhidrosis, skin rash.
Not known: Urticaria

General disorders and administration site conditions
Very rare: Hypothermia

Not known: Drug withdrawal syndrome (see *section 4.4 special warnings and preacautions for use*).

Investigations
Not known: Blood glucose increased

* Cases of central sleep apnoea syndrome have been observed with baclofen at high doses (≥ 100 mg) in patients who are alcohol dependent".

Certain patients have shown increased spasticity as a paradoxical reaction to the medication.

An undesirable degree of muscular hypotonia - making it more difficult for patients to walk or fend for themselves - may occur and can usually be relieved by re-adjusting the dosage (ie. by reducing the doses given during the day and possibly increasing the evening dose).

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, Website: www.hpra.ie

4.9 Overdose

Symptoms: Prominent features are signs of central nervous depression: somnolence, depressed level of consciousness, respiratory depression, coma, tinnitus. .

Also liable to occur are: confusion, hallucinations, agitation, convulsion, abnormal electroencephalogram (burst suppression pattern and triphasic waves), accommodation disorder, impaired pupillary reflex; generalised muscular hypotonia, myoclonia, hyporeflexia or areflexia; convulsions; peripheral vasodilatation, hypotension or hypertension, bradycardia or tachycardia, or cardiac arrhythmia; hypothermia; nausea, vomiting, diarrhoea, salivary hypersecretion; increased hepatic enzymes, sleep apnea, rhabdomyolysis.

A deterioration in the condition may occur if various substances or drugs acting on the central nervous system (eg. alcohol, diazepam, tricyclic antidepressants) have been taken at the same time.

Treatment: No specific antidote is known.
Supportive measures and symptomatic treatment should be given for complications such as hypotension, hypertension, convulsions, gastrointestinal disturbances, and respiratory or cardiovascular depression.

Since the drug is excreted chiefly via the kidneys, generous quantities of fluid should be given, possibly together with a diuretic. Haemodialysis (sometimes unscheduled) may be useful in severe poisoning associated with renal failure (see section 4.4 Special warnings and precautions for use).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antispastic with spinal site of action, ATC Code: M03B X01.
Mechanism of action (MOA)
Lioresal is a highly effective antispastic agent acting at the spinal level. A gamma-aminobutyric acid (GABA) derivative, Lioresal is chemically unrelated to other antispastic agents.

Lioresal depresses monosynaptic and polysynaptic reflex transmission, probably by stimulating the GABAB-receptors, this stimulation in turn inhibiting the release of the excitatory amino acids glutamate and aspartate. Neuromuscular transmission is unaffected by Lioresal.

Lioresal also exerts an antinociceptive effect. General well being is often improved and sedation is less often a problem than with centrally acting drugs.

In neurological diseases associated with spasm of the skeletal muscles, the clinical effects of Lioresal take the form of a beneficial action on reflex muscle contractions and marked relief from painful spasm, automatism, and clonus. Lioresal improves the patient's mobility, facilitating management of daily activities (including catheterisation) and physiotherapy. Prevention and healing of decubitus ulcers, and improvement in sleep patterns (due to elimination of painful muscle spasms) and in bladder and sphincter function, have also been observed as indirect effects of treatment with Lioresal.

Baclofen stimulates gastric acid secretion.

5.2 Pharmacokinetic properties

Absorption: Lioresal (baclofen) is rapidly and completely absorbed from the gastro-intestinal tract. No significant difference between the liquid and tablet formulations is observed in respect of Tmax, Cmax and bioavailability. Following oral administration of single doses (10-30 mg) peak plasma concentrations are recorded after 0.5 to 1.5 hours and areas under the serum concentration curves are proportional to the dose.

Distribution: The volume of distribution of baclofen is 0.7 l/kg. The protein binding is approximately 30% and is constant in the concentration range of 10 nanogram/mL to 300 microgram/mL. In cerebrospinal fluid active substance concentrations are approximately 8.5 times lower than in the plasma.

Biotransformation: Baclofen is metabolised to only a minor extent. Deamination yields the main metabolite, β-(p-chlorophenyl)-4-hydroxybutyric acid, which is pharmacologically inactive.

Elimination/excretion: The plasma elimination half-life of baclofen averages 3 to 4 hours. The serum protein binding rate is approximately 30%.

Baclofen is eliminated largely in unchanged form. Within 72 hours, about 75% of the dose is excreted via the kidneys with about 5% of this amount as metabolites.

Special populations

Elderly patients (aged 65 years or above)
The pharmacokinetics of baclofen in elderly patients are virtually the same as in patients below 65 years of age. The pharmacokinetics of baclofen in elderly patients are virtually the same as in patients below 65 years of age. Following a single oral dose, elderly patients have slower elimination but a similar systemic exposure of baclofen compared to adults below 65 years of age. Extrapolation of these results to multi-dose treatment suggests no significant pharmacokinetic difference between patients below 65 years of age and elderly patients.

Pediatric patients
Following oral administration of 2.5 mg Lioresal tablet in children (aged 2 to 12 years), Cmax of 62.8±28.7 nanogram/mL, and T_{max} in the range of 0.95 to 2 hours have been reported. Mean plasma clearance (Cl) of 315.9 mL/h/kg; volume of distribution (Vd) of 2.58 L/kg; and half-life ($T_{1/2}$) of 5.10 h have been reported.

Hepatic impairment
No pharmacokinetic data is available in patients with hepatic impairment after administration of Lioresal. However, as liver does not play a significant role in the disposition of baclofen, it is unlikely that baclofen pharmacokinetics would be altered to a clinically significant level in patients with hepatic impairment.

Renal impairment
No controlled clinical pharmacokinetic study is available in patients with renal impairment after administration of Lioresal. Baclofen is predominantly eliminated unchanged in urine. Sparse plasma concentration data collected only in female patients under chronic hemodialysis or compensated renal failure indicate significantly decreased clearance and increased half-life of baclofen in these patients. Dosage adjustment of baclofen based on its systemic levels should be considered in renal impairment patients, and prompt hemodialysis is an effective means of reversing excess baclofen in systemic circulation.

5.3 Preclinical safety data

Reproductive toxicity
Oral baclofen was shown to not have adverse effects on fertility or postnatal development at non-maternally toxic dose levels in rats. Baclofen is not teratogenic in mice, rats, and rabbits at doses at least 2.1-times the maximum oral mg/kg dose in adults. Lioresal given orally has been shown to increase the incidence of omphaloceles (ventral hernias) in fetuses of rats given approximately 8.3-times the maximum oral adult dose expressed as a mg/kg dose. This abnormality was not seen in mice or rabbits. Lioresal dosed orally has been shown to cause delayed fetal growth (ossification of bones) at doses that also caused maternal toxicity in rats and rabbits.

Mutagenitiicy and Carcinogenicity
Baclofen was negative for mutagenic and genotoxic potential in tests in bacteria, mammalian cells, yeast, and Chinese hamsters. The evidence suggests that baclofen is unlikely to have mutagenic potential.

Baclofen showed no carcinogenic potential in a 2-year study in rats. An apparently dose related increase in the incidence of ovarian cysts, and a less marked increase in enlarged and/or haemorrhagic adrenals have been observed in female rats treated for 2 years. The clinical relevance of these findings is not known.
Experimental evidence to date suggests that baclofen does not possess either carcinogenic or mutagenic properties.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal anhydrous silica
Microcrystalline cellulose
Magnesium stearate
Povidone
Wheat starch

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 25°C.

Blister packs - Store in the original package in order to protect from moisture.
Tablet containers – Keep the container tightly closed in order to protect from moisture.

6.5 Nature and contents of container

PVC/PE/PVDC blister packs in cardboard outers of 84 or 100 and/or high density polyethylene tablet containers of 84, 100 and 200 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.

7 MARKETING AUTHORISATION HOLDER

Novartis Ireland Limited
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8 MARKETING AUTHORISATION NUMBER

PA0896/017/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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