SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Bendroflumethiazide Tablets 5.0 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Bendroflumethiazide 5.0 mg per tablet.

For the full list of excipients, see section 6.1.

Each tablet contains 55.50 mg of lactose.

3. PHARMACEUTICAL FORM

Tablet.

White flat bevelled edge tablets engraved with the company logo on one side and C218 with breakline on the other.

4.1 Therapeutic indications

Oedema: Bendroflumethiazide is indicated in the treatment of oedema associated with conditions such as congestive heart failure, nephrotic syndrome, cirrhosis of the liver and pre-menstrual oedema.

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In non-oedematous patients, there may be little noticeable diuretic effect.

Essential hypertension: Bendroflumethiazide produces a moderate but fully prolonged fall of blood pressure in hypersensitive patients.Bendroflumethiazide may be used as the sole antihypertensive agent or used concurrently with other drugs whose action it potentiates. Bendroflumethiazide may also be used to suppress lactation

Cases where the reduction of fluid retention by dieresis is required; oedema of cardiac, renal or hepatic origin and iatrogenic oedema

4.2 Posology and method of administration

Route of administration: Oral
It is recommended that the tablets should be taken in the morning to avoid nocturia

ADULTS:

Oedema:

Initially: 5 - 10mg in the morning, once daily or on alternative days.

Maintenance: - 5mg-10mg two one to or three times a week.

Essential hypertension: 2.5 mg in the morning Higher doses are rarely necessary. alone or in conjunction with other antihypertensive agents in more severe hypertension. the dosage of such agents should be reduced and then adjusted as necessary

The dosage should be reduced in the elderly with impaired renal function.
Suppression of lactation: 5mg in the morning and 5mg at midday for about five days
Pre-menstrual oedema: 2.5mg each morning for seven days before the period is due

CHILDREN under 12 years of age:

Initial: 0.4 mg per kg of body-weight per day.

Maintenance: 0.05 to 0.1 mg per kg of body-weight per day. A more appropriate dosage form may be required.

: 0.05 to 0.4 mg/kg body-weight per day as a single dose or in two divided daily doses, adjusted according to response.

ELDERLY:

The dosage of thiazide diuretics may need to be reduced in the elderly, particularly when renal function is impaired, because of the possibility of electrolyte imbalance.

4.3 Contraindications

Hypersensitivity to Bendroflumethiazide or any of the excipients and other sulphonamide-derived drugs and other excipients listed in section 6.1.

Bendroflumethiazide is contra-indicated in patients with:

- severe renal insufficiency or anuria
- Addison's disease
- refractory hypokalaemia
- hyponatraemia
- hypercalcaemia
- serious hepatic disorders (risk of precipitation of encephalopathy)
- symptomatic hyperuricaemia

4.4 Special warnings and precautions for use

Hypokalaemia
Electrolytes should be monitored during treatment as continued or intensive use of bendroflumethiazide may result in hypokalaemia. This effect may be enhanced with concomitant use of medicines that can also cause hypokalaemia such as other diuretics or beta-2 agonists. Hypokalaemia can increase the risk of cardiac arrhythmia particularly when the patient is also taking an anti arrhythmic, anti-histamine, anti-malarial, anti-psychotic or digoxin (see section 4.5).
Potassium replacement or conservation may be necessary in patients at risk from the cardiac effects of hypokalaemia, such as those with prolonged QT intervals, severe heart disease, those taking digitalis preparations or high doses of diuretics and in patients with severe liver disease. If hypokalaemia (< 3.4 mmol potassium) is detected, it must be corrected and it should be prevented in at-risk patients.
Potassium supplements should not be given in renal insufficiency complicated by hyperkalaemia.
Potassium supplementation alone may not be sufficient to correct hypokalaemia in patients who are also deficient in magnesium.

Hyponatraemia
Some patients may be particularly susceptible to hyponatraemia, including the elderly and those with severe heart failure who are very oedematous, particularly with large doses of thiazides in conjunction with restricted salt in the diet. The onset of hyponatraemia can be sudden and life-threatening.
All patients, including the elderly who may be particularly susceptible, should be carefully observed for signs of fluid and electrolyte imbalance, especially in the presence of vomiting or during parenteral fluid therapy.
Regular serum electrolyte determinations should be performed in the elderly and in patients receiving long-term therapy.

Hypomagnesaemia
There is an increased risk of hypomagnesaemia in patients with alcoholic cirrhosis taking bendroflumethiazide. Hypomagnesaemia has been implicated as a risk factor for arrhythmias. Electrolyte levels including magnesium should be monitored during treatment of patients with alcoholic cirrhosis.
HypercalcaemiaThiazides may decrease urinary calcium excretion and may cause intermittent and slight elevation of serum calcium. Marked hypercalcaemia may be evidence of hidden hyperparathyroidism. Thiazides should be discontinued before carrying out tests for parathyroid function.

Choroidal effusion, acute myopia and secondary angle-closure glaucoma:

Sulfonamide or sulfonamide derivative drugs can cause an idiosyncratic reaction resulting in choroidal effusion with visual field defect, transient myopia and acute angle-closure glaucoma. Symptoms include acute onset of decreased visual acuity or ocular pain and typically occur within hours to weeks of drug initiation. Untreated acute angle-closure glaucoma can lead to permanent vision loss. The primary treatment is to discontinue drug intake as rapidly as possible. Prompt medical or surgical treatments may need to be

considered if the intraocular pressure remains uncontrolled. Risk factors for developing acute angle-closure glaucoma may include a history of sulfonamide or penicillin allergy.

Regular ongoing monitoring and blood tests are to be performed in elderly patients and patients who are on long term treatment with bendroflumethiazide.

Mild or moderate hepatic or renal impairment

Use with caution in renal impairment (severe renal insufficiency is a contraindication to use, see 4.3). Renal function should be monitored during bendroflumethiazide therapy. Thiazides can cause electrolyte balance which is more severe in patients with hepatic and renal impairment and in those receiving higher or prolonged doses.

Use with caution in hepatic impairment (severe hepatic impairment is a contraindication to use, see 4.3). In case of hepatic impairment, thiazide diuretics may precipitate hepatic encephalopathy, particularly in case of electrolyte imbalance. Administration of the diuretic must be stopped immediately if this occurs.

Concomitant use with lithium

Bendroflumethiazide inhibits the tubular elimination of lithium resulting in an elevated plasma lithium concentration and risk of toxicity. Both lithium and thiazide and related diuretics can cause hypokalaemia, increasing the risk of torsade de pointes. Avoid concurrent use unless lithium levels and potassium concentrations can be closely monitored and the lithium dose adjusted as necessary. Advise patients to report lithium adverse effects (tremor, dysarthria, ataxia, confusion) (see section 4.5).

Concomitant use with pimozide, sertindole or thioridazine

Diuretic-induced hypokalaemia increases the risk of ventricular arrhythmias with pimozide, sertindole and thioridazine therefore concomitant use should be avoided (see section 4.5).

Photosensitivity

Cases of photosensitivity reactions have been reported with thiazides andthiazide-related diuretics (see section 4.8). If photosensitivity reaction occurs during treatment, it is recommended to stop the treatment. If re-administration of the diuretic is deemed necessary, it is recommended to protect exposed
areas to the sun or to artificial UVA

Systemic lupus erythematosus

Thiazide diuretics can induce a cutaneous lupus-like adverse reaction. Thiazide diuretics may also exacerbate or activate systemic lupus erythematosus (SLE) in susceptible patients.

Pancreatitis

Pancreatitis has been reported during thiazide therapy. Thiazide therapy is associated with hypercalcaemia and hyperlipidaemia both of which are risk factors for pancreatitis.

Gout

Thiazide use may aggravate gout. Serum uric acid levels may be raised with or without gout in some patients.

Diabetes mellitus

Bendroflumethiazide may precipitate diabetes mellitus and may impair

glycaemic control in patients with diabetes.

Hyperlipidaemia

Caution should be exercised when used in patients with hyperlipidaemia.

Lactose

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

4.5 Interaction with other medicinal products and other forms of Interaction

Pharmacodynamic and Pharmacokinetic interactions

Analgesics: Diuretics such as bendroflumethiazide increase the risk of nephrotoxicity associated with non-steroidal anti-inflammatory analgesics (NSAIDs). NSAIDs, particularly indometacin and ketorolac may antagonise the natriuresis and increase in plasma renin activity caused by thiazide diuretics. It may also reduce the antihypertensive effect and increase in urine volume caused by thiazide diuretics, possibly by inhibiting renal prostaglandin synthesis and/or by causing sodium and fluid retention. This occurs to lesser extent with ibuprofen, piroxicam and naproxen. Concomitant use with opiates leads to an increased risk of postural hypotension. The effects of concurrent use should be monitored and the dose of bendroflumethiazide modified if necessary.

Alcohol
Co-administration of alcohol may potentiate orthostatic hypotension.

Aldesleukin
Enhanced hypotensive effect may occur when aldesleukin and thiazide diuretics are used concomitantly.

Anaesthetics, general
Enhanced hypotensive effect may occur when general anaesthetics and thiazide diuretics are used concomitantly.

Antibacterials
Severe hyponatraemia may occur with concomitant administration of bendroflumethiazide and trimethoprim.

Anti-depressants
Co-administration of tricyclic antidepressants may increase the risk of postural hypotension. Enhanced hypotensive effect with monoamine oxidase inhibitors (MAOIs). Possibly increased risk of hypokalaemia if thiazides given with reboxetine.

Anion-exchange resins: colestyramine and colestipol lead to decreased absorption of thiazides. It has been recommended that administration is at least 2 hours, prior to, or after the ingestion of bendroflumethiazide.

Antidiabetics:
Bendroflumethiazide may antagonise the hypoglycaemic effects of antidiabetic drugs including insulin possibly necessitating adjustment of the dose of the antidiabetic agent.
Chlorpropamide increases the risk of hyponatraemia associated with taking thiazides

Antiepileptics: There is an increased risk of hyponatraemia occurring when thiazide diuretics, such as bendroflumethiazide, are used concomitantly with carbamazepine.

Antifungals: There is an increased risk of hypokalaemia if thiazides are given with amphotericin.

Antihistamines (see section 4.4): Patients with hypokalaemia or other electrolyte imbalance have an increased risk of ventricular arrhythmias with arrhythmias with drugs that prolong the QT interval, such as astemizole and terfenadine.

Antihypertensives: Concurrent use of bendroflumethiazide with antihypertensives enhances the hypotensive effect including angiotensin-converting enzyme (ACE) inhibitors
(potential for enhanced first-dose hypotension), angiotensin-II antagonists, calcium channel blockers, beta-blockers, hydralazine and diazoxide. The dosage of concomitantly administered antihypertensive drugs may need to be reduced when bendroflumethiazide is added to the regimen. There is an increased risk of first-dose hypotensive effect of post- synaptic alpha-blockers such as prazosin. Concurrent administration of thiazides with beta-blockers or diazoxide has the potential to produce hyperglycaemia which may necessitate adjustment of the dose of antidiabetic medication including insulin. Intravascular immune haemolysis may occur in patients taking bendroflumethiazide and methyldopa.

Antipsychotics: Patients with hypokalaemia have an increased risk of ventricular arrhythmias with pimozide. Concomitant use should be avoided.

Alprostadil: Concomitant use with alprostadil enhances the hypotensive effect.

Anti-arrhythmics: The cardiac toxicity associated with amiodarone, disopyramide, flecainide, and quinidine is increased if hypokalaemia occurs. The action of lidocaine and mexiletine is antagonised by hypokalaemia. Hypokalaemia increases risk of ventricular arrhythmias with sotalol, a beta-blocker.

Antidepressants: There is a possible increased risk of postural hypotension with tricyclic antidepressants and of hypokalaemia if thiazides are given with reboxetine.

Antimalarials (see section 4.4)
Bendroflumethiazide -induced hypokalaemia may increase the risk of arrhythmias with drugs that prolong the QT interval, such as halofantrine.

Antipsychotics (see section 4.4)
Diuretic-induced hypokalaemia increases the risk of ventricular arrhythmias with pimozide, sertindole and thioridazine therefore concomitant use should be avoided. Enhanced hypotensive effect may occur when phenothiazines and
thiazide diuretics are used concomitantly.

Antigout agents
Potential for increased toxicity and hypersensitivity/allergic reactions with concomitant use of allopurinol and thiazide diuretics.

Barbiturates
Postural hypotension associated with therapy may be enhanced by concomitant ingestion of barbiturates.

Calcium salts & Vitamins: There is an increased risk of hypercalcaemia with thiazides such as bendroflumethiazide. There is an increased risk of developing milk-

alkali syndrome in patients given large amounts of calcium or vitamin D in combination with thiazides

Calcium-channel blockers and peripheral vasodilators: Concomitant use with bendroflumethiazide enhances the hypotensive effect and moxisylyte may be enhanced when co-administered with bendroflumethiazide.

Cardiac glycosides: The concurrent use of cardiac glycosides with thiazide diuretics may enhance the possibility of cardiac toxicity associated with hypokalaemia, resulting in cardiac arrhythmias.

Corticosteroids, Xanthines, beta-agonists, ACTH: There is an increased risk of thiazide-induced hypokalaemia, mainly with the naturally occurring corticosteroids such as cortisone and hydrocortisone. The diuretic effect is antagonised mainly with the naturally occurring corticosteroids such as cortisone and hydrocortisone. Adrenocorticotropic hormone (ACTH) can also exacerbate hypokalaemia associated with bendroflumethiazide use.

Cytotoxics: Concurrent use of diuretics such as bendroflumethiazide with cisplatin increases the risk of nephrotoxicity and ototoxicity.

Ciclosporin
Increased risk of nephrotoxicity and/or hypermagnesaemia with concomitant use of ciclosporin and thiazide diuretics, such as Bendroflumethiazide

Digoxin (see section 4.4)
Sensitivity to digitalis glycosides may be increased by the hypokalaemic effect of concurrent bendroflumethiazide. Patients should be observed for signs of digitalis intoxication, in particular arrhythmias, and if these appear, treatment with cardiac glycosides may have to be temporarily suspended and a potassium supplement given to restore stability.

Diuretics
Increased risk of hypokalaemia with concurrent administration of other thiazides and other diuretics including acetazolamide and loop diuretics.

Dopaminergics
Enhanced hypotensive effect may occur when levodopa and thiazide diuretics are used concomitantly.

General
Some electrolyte disturbances (e.g. hypokalaemia, hypomagnesaemia) may increase the toxicity of certain other drugs (e.g. digitalis preparations and drugs inducing QT interval prolongation syndrome).

Nitrates
Enhanced hypotensive effect may occur when nitrates and thiazide diuretics are used concomitantly.

Hormone Antagonists: There is an increased risk of hypercalcaemia when thiazides are used concomitantly with toremifene. There is an increased risk of hyponatraemia when thiazides are used concomitantly with aminoglutethimide.

Thiazides such as bendroflumethiazide increase the risk of hypercalcaemia with toremifene.

Moxisylyte: Concomitant use with bendroflumethiazide enhances the hypotensive effect.

Muscle relaxants: An enhanced hypotensive effect is associated with concomitant use with baclofen and tizanidine. Bendroflumethiazide interacts with nondepolarising neuromuscular blocking drugs leading to prolonged neuromuscular blockade e.g. tubocurarine.

Oestrogens and Progestogens: The diuretic effect is antagonised with Oestrogens and combined oral contraceptives.

Opioids
Postural hypotension associated with therapy may be enhanced by concomitant ingestion of opioids.

Prostaglandins
Hypotensive effect may be potentiated by alprostadil.

Other diuretics: There is an increased risk of hypokalaemia if thiazides such as bendroflumethiazide, loop diuretics or acetazolamide are taken together.

Sympathomimetics: There is an increased risk of hypokalaemia if thiazides are given with high doses of bambuterol, fenoterol, formoterol, reproterol, ritodrine, salbutamol, salmeterol, terbutaline and tulobuterol. Potentially serious hypokalaemia may result from $beta_2$ agonist therapy.

Theophylline: There is an increased risk of hypokalaemia with thiazides such as Bendroflumethiazide and Concomitant administration of xanthines such as theophylline.

Ulcer-healing Drugs: There is an increased risk of hypokalaemia if thiazides are given with carbenoxolone. Carbenoxolone also antagonises the diuretic effect. Patients should be
monitored and given potassium supplements when required.

Other interactions: vitamin D preparations (leading to increased risk of hypercalcaemia), alcohol and barbiturates (leading to increased risk of postural hypotension) have also been reported.

Lithium (see section 4.4)
Bendroflumethiazide inhibits the tubular elimination of lithium resulting in an elevated plasma lithium concentration and risk of toxicity. Both lithium and thiazide and related diuretics can cause hypokalaemia, increasing the risk of torsade de pointes. Avoid concurrent use unless lithium levels and potassium concentrations can be closely monitored and the lithium dose adjusted as necessary. Advise patients to report lithium adverse effects (tremor, dysarthria, ataxia, confusion).

Muscle relaxants
Diuretic-induced hypokalaemia may enhance the neuromuscular blocking activity of non-depolarising muscle relaxants, such as tubocurarine, gallamine, alcuronium and pancuronium. An enhanced hypotensive effect may occur with tizanidine.

Interference with tests for parathyroid function
Because thiazides may affect calcium metabolism, bendroflumethiazide may interfere with tests for parathyroid function. Bendroflumethiazide should be stopped before parathyroid function is tested.

4.6 Fertility, pregnancy and lactation

Diuretics are best avoided for the management of oedema of pregnancy or hypertension in pregnancy as it crosses the placenta and their use may be associated with hypokalaemia, hypovolaemia, and reduced placental perfusion and increased risk of acute haemorrhagic pancreatitis.

There is inadequate evidence of safety in human pregnancy. Foetal bone marrow depression,

Neonatal jaundice, thrombocytopenia, and severe electrolyte imbalances, including hypokalaemia and hyponatraemia have been reported in newborn infants.

As diuretics pass into breast milk and bendroflumethiazide can suppress lactation, its use should be avoided in mothers who wish to breast-feed.

4.7 Effects on ability to drive and use machines

Dizziness, drowsiness, postural hypotension, and mental confusion may occur. This may impair ability to drive or operate machinery

4.8 Undesirable effects

Serious adverse reactions include pancreatitis, hypersensitivity reactions, serious skin reactions and blood dyscrasias.

Adverse reactions listed below are based on available data for bendroflumethiazide and classified according to frequency and system organ class (SOC). Frequency categories are defined according to the following convention: 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), and not known (cannot be estimated from the available data). All thiazide diuretics can produce a degree of electrolyte imbalance, e.g. hypokalaemia.

Thiazide diuretics may raise the serum uric acid levels with subsequent exacerbation of gout in susceptible subjects.

Thiazide diuretics sometimes lower carbohydrate tolerance and the insulin dosage of the diabetic patient may require adjustment. Care is necessary when bendroflumethiazide is administered to those with a known predisposition to diabetes.

Immune system disorders: Hypersensitivity reactions are not known.

Mild gastro-intestinal effects

Investigations: Increased triglyceride, total cholesterol, low-density and very-low density lipoprotein cholesterol concentrations, hypokalaemia, hypomagnesaemia, hyponatraemia hypercalcaemia, hypochloraemic alkalosis, hyperuricaemia with/without gout, hyperglycaemia, and altered plasma lipid concentration are not known.

Nervous system disorders: Headache, Dizziness, Paraesthesia, Drowsiness are not known.

Eye disorders: choroidal effusion* is not known.

Vascular disorders like Postural hypotension and Vasculitis are not known.

Gastrointestinal disorders like Nausea, vomiting, diarrhoea, constipation, dry mouth, thirst and gastric irritation are not known. Pancreatitis is rare.

Musculoskeletal and connective tissue disorders: Systemic lupus erythematosus are not known.

Renal and urinary disorders: Acute interstitial nephritis; non-opaque urate calculi and Oliguria are not known.

Skin and subcutaneous tissue disorders: Rashes (including exfoliative dermatitis), photosensitivity; Skin eruptions resembling lichen planus and subacute cutaneous lupus erthyematosus; Erythema multiforme and Pseudoporphyria are not known.

Blood and lymphatic system disorders: Blood dyscrasias, including agranulocytosis, including neutropenia, aplastic anaemia, thrombocytopenia and leucopenia are rare.

Respiratory thoracic and mediastinal disorders: Pneumonitis and pulmonary oedema (as part of hypersensitivity reaction) are not known.

Endocrine disorders: Thiazides may cause hyperglycaemia and aggregate or unmask diabetes mellitus are not known.

Hepatobiliary disorders: Cholestasis and Cholecystitis are not known.

Reproductive system and breast disorders: Impotence (reversible on discontinuing the drug) are not known.

*see subsection below for additional information

Description of selected adverse reactions
Choroidal effusion: Cases of choroidal effusion with visual field defect have been reported after the use of thiazide and thiazide-like diuretics.

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

4.9 Overdose

Symptoms of overdosage include anorexia, nausea, vomiting, diarrhoea, diuresis, dehydration, hypotension, dizziness, weakness, muscle cramps, paraesthesia, tetany, convulsions, increased frequency of micturition with polyuria and thirst, hyponatraemia, hypo- or hyperglycaemia, hypomagnesaemia, hypercalcaemia,, hypokalaemia can occur and is especially important in patients with preexisting cardiac disease and metabolic alkalosis. Initial treatment consists of either emesis or gastric lavage, if appropriate. Otherwise treatment should be symptomatic and supportive including the correction of fluid and electrolyte imbalance can lead to arrhythmias.

Extreme cases may show depletion of intravascular volume, hypotension and peripheral circulatory failure.

CNS depression (e.g. drowsiness, lethargy and coma) may occur without cardiovascular or respiratory depression

Management of overdose
Treatment should be supportive and directed at fluid and electrolyte replacement which should be monitored together with blood pressure, blood glucose, ECGs and renal function. Cathartics should be avoided.

There is no specific antidote.

5.1 Pharmacodynamic properties

Pharmacotherapeutic classification: Low-Ceiling Diuretics Thiazides - Bendroflumethiazide
ATC code: CO3A A01

Bendroflumethiazide is a thiazide diuretic which reduces the reabsorption of electrolytes from the renal tubules, thereby increasing the excretion of sodium and chloride ions, and consequently of water. The excretion of other electrolytes, notably potassium and magnesium, is also increased. Because potassium excretion is promoted, metabolic alkalosis may occur secondary to hypokalaemia. There is no important effect upon carbonic anhydrase. Bendroflumethiazide exerts its diuretic effect in about 2 hours and this lasts for 12 to 18 hours or longer. The excretion of other electrolytes, notably potassium and magnesium, is also increased. The excretion of calcium is reduced. Thiazides also reduce the carbonic anhydrase activity so that bicarbonate excretion is increased but this effect is generally small and does not appreciably alter the acid base balance or the pH of the urine. Thiazides also have a hypotensive effect, due to a reduction in peripheral resistance and enhance the effects of other antihypertensive agents.

5.2 Pharmacokinetic properties

Absorption: Bendroflumethiazide is completely absorbed from the gastrointestinal tract

and it is fairly extensively metabolised. The onset of diuretic action of the thiazides following oral administration occurs within two hours and the peak effect between three and
six hours after administration. The duration of the diuretic action of bendroflumethiazide is initiated in about 2 hours and last between 12-18 and 24 hours. The onset of the hypotensive action is generally three or four days.

Distribution: Bendroflumethiazide is more than 90% bound to plasma proteins.

Metabolism: There is indication that it is fairly extensively metabolised. Peak plasma levels are reached in 2 hours and a plasma half-life of between 3 and 8.5 hours on average.

*Elimination:*About 30% is excreted unchanged in
the urine with the remainder excreted as uncharacterized metabolites.

5.3 Preclinical safety data

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose
Maize starch
Pregelatinised starch
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

As packaged for sale:

3 years for opaque plastic containers.
2 years for blister packaging.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

1. Opaque plastic containers composed of polypropylene tubes and polyethylene tamper-evident closures for pack sizes of 28, 30, 42, 50, 56, 60, 84, 90, 100, 112, 250, 500 and 1000 tablets.

2. Opaque plastic containers composed of either high density polypropylene or high density polyethylene with a tamper evident or child resistant tamper evident closure composed of high density polyethylene with a packing inclusion of polyether foam or polyethylene or polypropylene filler in pack sizes of 28, 30, 42, 50, 56, 60, 84, 90, 100, 112, 250, 500 and 1000 tablets.

3. Blister packs of aluminium/opaque PVC subsequently packed in printed cartons in pack sizes of 28, 30, 42, 56, 60, 84, 90 and 112 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special instructions for use/handling.

7 MARKETING AUTHORISATION HOLDER

Crescent Pharma Limited,
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8 MARKETING AUTHORISATION NUMBER(S)

PL 20416/0218

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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