

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Diamox SR 250mg Modified Release Hard Capsules.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains Acetazolamide 250 mg.

Excipients: Contains FD + C Yellow no.6 (E110)

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Modified-release capsule.

Hard shell capsule with clear body and orange cap, containing orange spherical pellets.
Capsules are printed GS 250 in black.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

DIAMOX SR Capsules are for oral administration.

Glaucoma.

4.2 Posology and method of administration

Capsules should be swallowed whole. Do not chew or crush.

Adults: One or two 250mg capsules a day.

Children: This product is not intended for administration to children.

Use in Elderly Patients: DIAMOX SR should be used with particular caution in elderly patients or those with potential obstruction in the urinary tract or with disorders rendering their electrolyte balance precarious or with liver dysfunction.

Use in Patients with Renal Impairment: In patients with moderate to severe renal impairment, the dose should be reduced by half or the dosage interval should be increased to every 12 hours.

4.3 Contraindications

DIAMOX SR therapy is contra-indicated in situations in which sodium and / or potassium blood serum levels are depressed, in cases of marked kidney and liver disease or dysfunction, suprarenal gland failure, and hyperchloraemic acidosis. Diamox should not be used in patients with liver disease or impairment of liver function including cirrhosis as this may increase the risk of hepatic encephalopathy. DIAMOX is contra-indicated in patients with hypokalaemia and hyponatraemia.

Long term administration of DIAMOX SR is contra-indicated in patients with chronic non-congestive angle-closure glaucoma since it may permit organic closure of the angle to occur while the worsening glaucoma is masked by lowered intraocular pressure.

DIAMOX SR should not be used in patients hypersensitive to sulphonamide or other sulphonamide derivatives including acetazolamide or any excipients in the formulation.

4.4 Special warnings and precautions for use

Increasing the dose does not increase the diuresis and may increase the incidence of drowsiness and / or paraesthesia.

When DIAMOX SR is prescribed for long-term therapy, special precautions are advisable. The patient should be cautioned to report any unusual skin rash. Prior to initiating therapy and at regular intervals during therapy monitoring of blood cell counts and electrolyte levels are recommended. Fatalities have occurred, although rarely, due to severe reactions to sulphonamides including acetazolamide, such as Stevens-Johnson syndrome and toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anaemia and other blood dyscrasias and anaphylaxis. A precipitous drop in formed blood cell elements or the appearance of toxic skin manifestations should call for immediate cessation of DIAMOX SR therapy.

Hypersensitivity reactions may recur if a sulphonamide or sulphonamide derivative is re-administered, irrespective of the route of administration. If signs of hypersensitivity reactions or other serious reactions occur, acetazolamide must be discontinued.

Acetazolamide treatment may cause electrolyte imbalances, including hyponatraemia and hypokalaemia, as well as metabolic acidosis. Therefore, periodic monitoring of serum electrolytes is recommended. Particular caution is recommended in patients with conditions that are associated with, or predispose to, electrolyte and acid/base imbalances, such as patients with impaired renal function (including elderly patients), pulmonary obstruction, emphysema, patients with diabetes mellitus and patients with impaired alveolar ventilation.

Both increased and decreases in blood glucose levels have been described in patients treated with acetazolamide. This should be taken into consideration in patients with impaired glucose tolerance or diabetes mellitus.

In patients with a past history of renal calculi, benefit should be balanced against the risks of precipitating further calculi.

4.5 Interaction with other medicinal products and other forms of interaction

Diamox SR is a sulphonamide derivative. Sulphonamides may potentiate the effects of folic acid antagonists. Possible potentiation of the effects of folic acid antagonists, hypoglycaemics and oral anti-coagulants may occur. Concurrent administration of acetazolamide and acetylsalicylic acid may result in severe toxicity and increase central nervous system toxicity. Adjustments of dose may be required when DIAMOX SR is given with cardiac glycosides or hypertensive agents.

When given concomitantly DIAMOX SR modifies the metabolism of phenytoin leading to increased serum levels of phenytoin. Severe osteomalacia has been noted in a few patients taking acetazolamide in combination with other anticonvulsants. There have been isolated reports of reduced primidone and increased carbamazepine serum levels with concurrent administration of acetazolamide.

Concomitant use with other carbonic anhydrase inhibitors is not advisable because of possible additive effects.

Both increases and decreases in blood glucose levels have been described in patients with acetazolamide. This should be taken into consideration in patients treated with anti-diabetic agents.

By increasing the pH of renal tubular urine, acetazolamide reduces the urinary excretion of amphetamine and quinidine and so may enhance the magnitude and duration of the effect of amphetamines and enhance the effect of quinidine.

By increasing the pH of urine, acetazolamide may prevent the urinary excretion of methenamine compounds.

Acetazolamide increases lithium excretion due to impaired re-absorption of lithium in the proximal tubule. The effect of lithium carbonate may be decreased.

The use of concurrent sodium bicarbonate therapy enhances the risk of renal calculus formulation in patients taking acetazolamide.

When given concomitantly, acetazolamide may elevate cyclosporine blood levels. Caution is advised when administering acetazolamide in patients receiving cyclosporine.

Interference with Laboratory and other Diagnostic Tests: Sulphonamides may give false negative or decreased values for urinary phenolsulphonphthalein and phenol red elimination values for urinary protein, serum non-protein and for serum uric acid. Acetazolamide may produce an increased level of crystals in the urine.

Acetazolamide interferes with the HPLC method of assay for theophylline. Interference with the theophylline assay by acetazolamide depends on the solvent used in the extraction; acetazolamide may not interfere with other assay methods for theophylline.

4.6 Pregnancy and lactation

Use in pregnancy:

Acetazolamide has been reported to be teratogenic (defects of the limbs) and embryotoxic in rats, mice, hamsters and rabbits at oral or parenteral doses in excess of ten times those recommended in human beings. Although there is no evidence of these effects in human beings, there are no adequate and well-controlled studies in pregnant women. Therefore, DIAMOX SR should not be used in pregnancy, especially during the first trimester.

Use in lactation:

DIAMOX has been detected in low levels in the milk of lactating women who have taken DIAMOX. Although it is unlikely that this will lead to any harmful effects in the infant, extreme caution should be exercised when DIAMOX SR is administered to lactating women.

4.7 Effects on ability to drive and use machines

Some adverse reactions to acetazolamide, such as drowsiness, fatigue and myopia, may impair the ability to drive and operate machinery.

4.8 Undesirable effects

Adverse reactions during short-term therapy are usually non-serious. Those effects which have been noted include: paraesthesia, particularly a "tingling" feeling in the extremities; some loss of appetite, taste disturbance, polyuria, flushing, thirst, headache, dizziness, fatigue, irritability, excitement, ataxia, depression, reduced libido, and occasional instances of drowsiness and confusion. Rarely, photosensitivity has been reported.

During long-term therapy, metabolic acidosis and electrolyte imbalance, including hypokalaemia, hyponatraemia, osteomalacia with long-term phenytoin therapy, hyperglycaemia and hypoglycaemia, may occasionally occur. This can usually be corrected by the administration of bicarbonate.

Transient myopia has been reported. This condition invariably subsides upon diminution or discontinuation of the medication.

Gastro-intestinal disturbances such as nausea, vomiting and diarrhoea.

DIAMOX is a sulphide derivative and therefore some side-effects similar to those caused by sulphonamides have occasionally been reported. These include fever, agranulocytosis, thrombocytopenia, thrombocytic purpura, leukopenia, and aplastic anaemia, bone marrow depression, pancytopenia, rash (including erythema multiforme, Stevens-Johnson Syndrome, toxic epidermal necrolysis), anaphylaxis, crystalluria, calculus formation, renal and ureteral colic, and renal lesions. Rarely, fulminant hepatic necrosis has been reported.

Other occasional adverse reactions include: urticaria, melaena, haematuria, glycosuria, impaired hearing and tinnitus, abnormal liver function, renal failure, and rarely; hepatitis or cholestatic jaundice, flaccid paralysis, and convulsions.

Growth retardation has been reported in children receiving long-term therapy owing to chronic acidosis.

Long-term therapy with acetazolamide increases the risk of nephrolithiasis.

4.9 Overdose

No specific antidote.

Treatment should be symptomatic and supportive.

Electrolyte imbalance, development of an acidotic state and central nervous effects might be expected to occur. Serum electrolyte levels, (particularly potassium) and blood pH should be monitored.

Supportive measures are required to restore electrolyte and pH balance. The acidotic state can usually be corrected by the administration of bicarbonate.

Despite its high intra-erythrocytic distribution and plasma protein binding properties, acetazolamide is dialyzable. This may be particularly important in the management of acetazolamide overdosage when complicated by the presence of renal failure.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Acetazolamide is a potent inhibitor of the enzyme carbonic anhydrase; the enzyme that catalyses the reversible reaction involving the hydration of carbon dioxide and the dehydration of carbonic acid. In the eye, this inhibitory action of acetazolamide decreases the secretion of the aqueous humor and results in a drop of intraocular pressure and is thus used to treat glaucoma.

5.2 Pharmacokinetic properties

Acetazolamide is readily absorbed after oral administration and binds tightly to plasma proteins as well as to the enzyme carbonic anhydrase. The drug begins to accumulate in tissues in which this enzyme is present notably red blood cells and the renal cortex. It is eliminated unchanged in the urine with a half-life of about 4 hours.

5.3 Preclinical safety data

Nothing of note to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Film coated pellets:

Microcrystalline cellulose

Sodium laurilsulfate

Ethylcellulose

Hydroxypropylmethyl cellulose

Paraffin, light liquid

Opaspray K-IR-2506 orange:

[hydroxypropyl cellulose, titanium dioxide (E171) and FD&C Yellow No. 6 (E110)].

Capsule shells:

Gelatin

Titanium dioxide (E171)

Yellow iron oxide (E172)

Erythrosine (E127).

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 30°C.

Store in the original package. Keep the blisters in the outer carton.

6.5 Nature and contents of container

Blister Packs: 28 or 30 capsules/pack.

Opaque UPVC/PVDC blister pack.

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

Goldshield Pharmaceuticals Limited
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CRO 0XT,
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8 MARKETING AUTHORISATION NUMBER

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