

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Diamox 250 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Acetazolamide 250 mg.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

White circular, biconvex tablet engraved with 'FW' and '147' on one side and scored in quarters on the other.

The tablet can be divided in equal halves.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Glaucoma

4.2 Posology and method of administration

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

Adults: One or two 250mg tablets a day.

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

Use in Elderly Patients: DIAMOX 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 not exceed 250mg per day or the dosage interval should be increased to every 12 hours. lithium in the proximal tubule.

4.3 Contraindications

Acetazolamide 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, adrenal gland failure, and hyper-chloraemic 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 hypokalemia and hyponatraemia.

Long-term administration of DIAMOX is contra-indicated in patients with chronic noncongestive 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 should not be used in patients hypersensitive to sulphonamides 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 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 Steven-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 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 transient 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. Severe metabolic acidosis has been reported in patients with normal renal function during treatment with acetazolamide and salicylates. 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 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 aspirin may result in severe acidosis and increase central nervous system toxicity. Adjustment of dose may be required when DIAMOX is given with cardiac glycosides or hypertensive agents.

When given concomitantly, acetazolamide 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 antidiabetic 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 formation 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:

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 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 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 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 and hyponatraemia, may occasionally occur. Hypokalaemia is generally transient and is rarely clinically significant. Osteomalacia with long-term phenytoin therapy, hyperglycaemia and hypoglycaemia, may occasionally occur during long term therapy. The acidosis can usually be corrected by the administration of bicarbonate. Transient myopia has been reported. This condition invariably subsides upon diminution or withdrawal 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 have been reported. 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.

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 an inhibitor of carbonic anhydrase. By inhibiting the reaction catalysed by this enzyme in the renal tubules, acetazolamide increases the excretion of bicarbonate and of cations, chiefly sodium and potassium, and so promotes alkaline diuresis.

Continuous administration of acetazolamide is associated with metabolic acidosis and resultant loss of diuretic activity. Therefore, the effectiveness of Diamox in diuresis diminishes with continuous use.

By inhibiting carbonic anhydrase in the eye, acetazolamide decreases intra-ocular pressure and is therefore useful in the treatment of glaucoma.

5.2 Pharmacokinetic properties

Acetazolamide is fairly rapidly absorbed from the gastro-intestinal tract with peak plasma concentrations occurring about 2 hours after administration by mouth. It has been estimated to have a plasma half-life of about 4 hours. It is tightly bound to carbonic anhydrase and accumulates in tissues containing this enzyme, particularly red blood cells and the renal cortex. It is also bound to plasma proteins. It is excreted unchanged in the urine; renal clearance being enhanced in alkaline urine.

5.3 Preclinical safety data

Nothing of note to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium hydrogen phosphate dihydrate
Maize starch
Magnesium stearate
Sodium starch glycolate type A
Povidone

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

5 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original container with the lid tightly closed in order to protect from light and moisture.

6.5 Nature and contents of container

Polypropylene bottles with plastic screw-on caps.

The product is supplied in bottles of 112 and 1000 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.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Goldshield Pharmaceuticals Limited
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8 MARKETING AUTHORISATION NUMBER

PA 899/21/3

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