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 the 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

It is indicated in the treatment of glaucoma.

4.2 Posology and method of administration

Posology
Adults
250mg – 1,000 mg daily; One to four 250mg tablets a day in divided doses.

Paediatric population
This product is not intended for administration to children.

Elderly
Diamox should be used with particular caution in older people or those with potential obstruction in the urinary tract or with disorders rendering their electrolyte balance precarious or with liver dysfunction.

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.

Method of administration
For oral use only.
Tablets should be swallowed whole. Do not chew or crush.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Acetazolamide therapy is contra-indicated in cases of marked kidney 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 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 should not be used in patients hypersensitive to sulphonamides or other sulphonamide derivatives.

4.4 Special warnings and precautions for use

Risk of suicide
Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic agents in several indications. A meta-analysis of randomized placebo-controlled trials of anti-epileptic drugs has also shown a small increased risk of suicidal ideation and behaviour. The mechanism of this risk is not known, and the available data do not exclude the possibility of an increased risk for Acetazolamide.

Therefore, patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour emerge.

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

Long term therapy
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
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.

Electrolyte disorder
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.

Glycaemic disorders
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.

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

The occurrence at the treatment initiation of a feverish generalized erythema associated with pustula may be a symptom of acute generalised exanthematous pustulosis (AGEP) (See section 4.8). In case of AGEP diagnosis, acetazolamide should be discontinued, and any subsequent administration of acetazolamide contraindicated.

Cases of choroidal effusion/detachment have been reported after the use of acetazolamide. Symptoms include acute onset of decreased visual acuity or ocular pain and can occur within hours after initiation of acetazolamide treatment. If choroidal effusion/detachment is suspected, acetazolamide should be discontinued as rapidly as possible.

Information on Sodium Content:

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free.

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 administrating 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 Fertility, pregnancy and lactation

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.

Breast-feeding
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.

Fertility
No data available

4.7 Effects on ability to drive and use machines

Diamox has major influence on the 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

The following undesirable effects have been reported in treatment with acetazolamide.
Undesirable effects are listed by MedDRA System Organ Class.

Adverse reactions are ranked by frequency of occurrence, using the following convention:
Rare: (³1/10,000 to <1/1,000)>
Not known (cannot be estimated from available information).

System organ Class	**Frequency**	• **Adverse effects**
Blood and lymphatic system disorders	Not known	• - agranulocytosis • thrombocytopenia • thrombocytopenic purpura • leukopenia • aplastic anaemiabone marrow depression pancytopenia
Endocrine disorders	Not Known	• hyperglycaemia* • hypoglycaemia*
Metabolism and nutrition disorders	Not Known	• metabolic acidosis* • electrolyte imbalance* • hypokalaemia*, ** • hyponatraemia*-decreased appetite
Psychiatric disorders	Not known	- depression - loss of libido
Nervous system disorders	Not Known	• paraesthesia • peripheral coldness • headache • dizziness- agitation • ataxia • somnolence • confusional state • paralysis flaccid • convulsion
Eye disorders	Not known	- myopia*** - choroidal effusion - choroidal detachment
Ear and labyrinth disorders	Not known	• hearing impaired • tinnitus
Gastrointestinal disorders	Not known	• dysgeusia • nausea • vomiting • diarrhoea • melaena • hematochezia
Hepatobiliary disorders	Rare	• hepatitis • jaundice cholestatic • hepatic necrosis****
Skin and subcutaneous tissue disorders	Not known	• urticaria • rash • erythema multiforme • Stevens-Johnson Syndrome • toxic epidermal necrolysis • acute generalised exanthematous pustulosis (AGEP)

	Rare	- photosensitivity reaction
Musculoskeletal and connective tissue disorders	Not known	- arthralgia
Renal and urinary disorders	Not known	-polyuria -haematuria -glycosuria -crystalluria -calculus formation -renal colic -renal injury -renal failure -nephrolithiasis*****
General disorders and administration site conditions	Not known	-anaphylactic reaction -pyrexia -flushing -fatigue -thirst - irritability
Investigations	Not known	- liver function test abnormal

***** May occasionally occur during long term therapy.
** Generally transient and rarely clinically significant.
******* Transient myopia. This condition invariably subsides upon diminution or withdrawal of the medication.
**** Fulminant.
*****Long - term therapy with acetazolamide increases the risk of nephrolithiasis.

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
Electrolyte imbalance, development of an acidotic state and central nervous effects might be expected to occur.

Management
No specific antidote.
Treatment should be symptomatic and supportive.
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

Pharmacotherapeutic group: Carbonic anhydrase inhibitors, ATC code: S01EC01

Mechanism of action
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

Absorption
Acetazolamide is fairly rapidly absorbed from the gastro-intestinal tract with peak plasma concentrations occurring about 2 hours after administration by mouth.

Distribution
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.

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

7 MARKETING AUTHORISATION HOLDER

Amdipharm Limited
Temple Chambers
3 Burlington Road
Dublin 4
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8 MARKETING AUTHORISATION NUMBER

PA1142/020/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 April 1978

Date of last renewal: 01 April 2008

10 DATE OF REVISION OF THE TEXT

January 2024