

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

DIAMOX® Sodium 500mg Powder for Solution for Injection
Acetazolamide 500mg Powder for solution for Injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Acetazolamide 500mg / vial

For excipients see 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for injection.

4 CLINICAL PARTICULARS

4.1. Therapeutic Indications

Diamox is an enzyme inhibitor which acts specifically on carbonic anhydrase. It is indicated in the treatment of :

i) Glaucoma: DIAMOX is useful in glaucoma (chronic simple (open angle) glaucoma, secondary glaucoma and perioperatively in acute angle closure glaucoma where delay of surgery is desired in order to lower intraocular pressure) because it acts on inflow, decreasing the amount of aqueous secretion.

ii) Abnormal retention of fluids: DIAMOX is a diuretic whose effect is due to the effect on the reversible hydration of carbon dioxide and dehydration of carbonic acid reaction in the kidney. The result is a renal loss of HCO_3^- ion which carries out sodium, water and potassium.

DIAMOX can be used in conjunction with other diuretics when effects on several segments of the nephron are desirable in the treatment of fluid retaining states.

iii) Epilepsy: In conjunction with other anticonvulsants best results with DIAMOX have been seen in petit mal in children. Good results, however, have been seen in patients, both children and adults, with other types of seizures such as grand mal, mixed seizure patterns, myoclonic jerk patterns, etc.

4.2. Posology and Method of Administration

Routes of Administration: Intravenous or intramuscular injection. The direct intravenous route is preferred as intramuscular use is limited by the alkaline pH of the solution.

i) Glaucoma (simple acute congestive and secondary):

Adults: 250 - 1000mg per 24 hours, usually in divided doses for amounts over 250mg daily.

ii) Abnormal retention of fluid: Congestive heart-failure, drug-induced oedema.

Adults: For diuresis, the starting dose is usually 250 - 375mg once daily in the morning. If, after an initial response, the patient fails to continue to lose oedema fluid, do not increase the dose but allow for kidney recovery by omitting a day. Best results are often obtained on a regime of 250 - 375mg daily for two days, rest a day, and repeat or merely giving DIAMOX every other day. The use of DIAMOX does not eliminate the need for other therapy, e.g. digitalis, bed rest and salt restriction in congestive heart failure and proper supplementation with elements such as potassium in drug-induced oedema.

For cases of fluid retention associated with pre-menstrual tension, a daily dose (single) of 125 - 375mg is suggested.

iii) Epilepsy

Adults: 250 - 1000mg daily in divided doses.

Children: 8 - 30mg/kg in daily divided doses and not to exceed 750mg/day.

The change from other medication to DIAMOX should be gradual.

Elderly: DIAMOX should only 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.

4.3. Contra-Indications

Acetazolamide is contraindicated in situations in which sodium and/or potassium blood levels are depressed, in cases of marked kidney and liver dysfunction, suprarenal gland failure and hyper-chloremic acidosis. Diamox should not be used in patients with hepatic cirrhosis as this may increase the risk of hepatic encephalopathy.

Long-term administration of DIAMOX acetazolamide 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 lower intraocular pressure.

DIAMOX should not be used in patients hypersensitive to sulphonamides.

4.4 Special warnings and precautions for use

Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic agents in several indications. A meta-analysis of randomised 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 DIAMOX.

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.

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

Increasing the dose often results in a decrease in diuresis. Under certain circumstances, however, very large doses have been given in conjunction with other diuretics in order to secure diuresis in complete refractory failure.

When DIAMOX is prescribed for long-term therapy, special precautions are advisable. The patient should be cautioned to report any unusual skin rash. Periodic blood cell counts and electrolyte levels are recommended. Fatalities have occurred, although rarely, due to severe reactions to sulphonamides. A precipitous drop in formed blood cell elements or the appearance of toxic skin manifestations should call for immediate cessation of DIAMOX therapy.

In patients with pulmonary obstruction or emphysema where alveolar ventilation may be impaired, DIAMOX acetazolamide which may aggravate acidosis, should be used with caution.

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

The pH of parenteral acetazolamide is 9.1. Care should be taken during intravenous administration of alkaline preparations to avoid extravasation and possible development of skin necrosis.

4.5. Interactions 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. Concurrent administration of acetazolamide and aspirin may result in severe acidosis and increase central nervous system toxicity. Adjustments of dose may be required when DIAMOX is given with cardiac glycosides or hypertensive agents.

When given concomitantly DIAMOX 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.

Because of possible additive effects with other carbonic anhydrase inhibitors, concomitant use is not advisable.

4.6. Pregnancy and Lactation

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 acetazolamide should not be used in pregnancy, especially during the first trimester.

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

Increasing the dose does not increase the diuresis and may increase the incidence of drowsiness and/or paraesthesia. Less commonly, fatigue, dizziness and ataxia have been reported. Disorientation has been observed in a few patients with oedema due to hepatic cirrhosis. Such cases should be under close supervision. Transient myopia has been reported.

These conditions invariably subside upon diminution or discontinuance of the medication.

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, depression, reduced libido and occasional instances of drowsiness and confusion. Rarely, photosensitivity has been reported.

During long-term therapy, metabolic acidosis and electrolyte imbalance 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 sulphonamide 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.

4.9. Overdose

No specific antidote. Supportive measures with correction of electrolyte and fluid balance. Force fluids.

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 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 the alkaline urine.

5.3 Preclinical Safety Data

Nothing of note to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Water for injection
Sodium hydroxide
Hydrochloric acid

6.2 Incompatibilities

None.

6.3 Shelf Life

24 months.

6.4 Special Precautions for Storage

Do not store above 25°C.

6.5 Nature and Contents of Container

Glass vial with butyl rubber plug and aluminium ring seal.

Pack size 500mg vial.

6.6 Instruction for Use, Handling and Disposal

Reconstitute each vial of DIAMOX Parenteral with at least 5ml of water for injection prior to use. The reconstituted injection does not contain an

antimicrobial preservative. Any unused solution can be stored in a refrigerator for up to 24 hours but any solution not used within this period must be discarded.

The direct intravenous route of administration is preferred. Intramuscular injection may be employed but is painful due to the alkaline pH of the solution.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 12762/0146

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

11th February 1988 / 16th February 2004

10 DATE OF REVISION OF THE TEXT

06/04/2009