SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Acetazolamide DAWA 250mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Acetazolamide Ph. Eur 250 mg
Excipient with known effect:
Each tablet contains 115 mg of lactose (as monohydrate).

For the full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White coloured, round shaped tablet with break line on one side & plain on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Acetazolamide Tablets are for oral administration.

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

- Glaucoma: Acetazolamide Tablets 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.
- Abnormal retention of fluids: Acetazolamide Tablets 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 renal loss of HC03- ion which carries out sodium, water and potassium. Acetazolamide Tablets 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.

- Epilepsy: In conjunction with other anticonvulsants best results with Acetazolamide Tablets 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

Posology

- Glaucoma (simple acute congestive and secondary):

Adults: 250 - 1,000mg (1-4 tablets) per 24 hours, usually in divided doses for amounts over 250mg daily.

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

Adults: For diuresis, the starting dose is usually 250 - 375mg (1-1½ tablets) 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 (1-1½ tablets) daily for two days, rest a day, and repeat, or merely giving the Acetazolamide tablets every other day. The use of Acetazolamide tablets 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.

- Epilepsy:

Adults: 250 - 1,000mg daily in divided doses.

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

The change from other medication to Acetazolamide tablets should be gradual.

Elderly: Acetazolamide tablets 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.

Method of administration
Oral

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Acetazolamide is contra-indicated in situations in which sodium and/or potassium blood levels are depressed, in cases of marked kidney and liver disease or dysfunction, suprarenal gland failure, and hyperchloremic acidosis.

Acetazolamide tablets should not be used in patients with hepatic cirrhosis as this may increase the risk of hepatic encephalopathy.

Long-term administration of Acetazolamide tablets 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.

Acetazolamide tablets 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 does 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.

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 Acetazolamide tablets 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 Acetazolamide tablets therapy.

<u>Non-cardiogenic pulmonary oedema</u>

Severe cases of non-cardiogenic pulmonary oedema have been reported after taking acetazolamide, also after a single dose (see section 4.8). Non-cardiogenic pulmonary oedema typically developed within minutes to hours after acetazolamide intake. Symptoms included dyspnoea, hypoxia, and respiratory insufficiency. If non-cardiogenic pulmonary oedema is suspected, acetazolamide should be withdrawn, and supportive treatment should be given. Acetazolamide should not be administered to patients who previously

experienced non-cardiogenic pulmonary oedema following acetazolamide intake**.**

In patients with pulmonary obstruction or emphysema where alveolar ventilation may be impaired, Acetazolamide tablets may aggravate acidosis and 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 occurrence at the treatment initiation of a feverish generalised 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.

Lactose
Acetazolamide tablets contain Lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Sodium
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

Acetazolamide 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 anticoagulants 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 Acetazolamide tablets 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.

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

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

Ciclosporin: Acetazolamide may elevate ciclosporin levels.

Methenamine: Acetazolamide may prevent the urinary antiseptic effect of methenamine.

Lithium: Acetazolamide increases lithium excretion and the blood lithium levels may be decreased.

Sodium bicarbonate: Acetazolamide and sodium bicarbonate used concurrently increases the risk of renal calculus formation.

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

Breast-feeding

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

Fertility

The effect of acetazolamide on human fertility has not been established.

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

The following adverse reactions are classified by system organ class and ranked under heading of frequency using the following convention:

Not known: frequency cannot be estimated from the available data

System organ class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Not known	Thrombocytopaenia, Leukopenia, Aplastic anaemia, Bone marrow depression, Pancytopenia, Agranulocytosis****
Ear and labyrinth disorders	Not known	Impaired hearing and tinnitus
Eye disorders	Not known	Choroidal effusion, choroidal detachment, Transient myopia***
Gastrointestinal disorders	Not known	Melaena, Taste disturbance, Nausea, Vomiting, Diarrhoea
General disorders and administration site conditions	Not known	Fever****, Fatigue, Anaphylaxis****, Flushing
Hepatobiliary disorders	Not known	Fulminant hepatic necrosis****, Hepatitis or cholestatic jaundice
Investigations	Not known	Abnormal liver function
Metabolism and nutrition disorder	Not known	Metabolic acidosis, electrolyte imbalance* and thirst**
Nervous system disorders	Not known	Paraesthesia, particularly a “tingling” feeling in the extremities, Dizziness, Headache, Occasional instances of drowsiness, Convulsions, Flaccid paralysis
Psychiatric disorders	Not known	Depression, Irritability, Reduced libido, Occasional instances of confusion
Renal and urinary disorders	Not known	Haematuria, Crystalluria****, Renal

		and ureteral colic****, Renal lesions, Renal failure, Calculus formation****, Glycosuria, Polyuria
Respiratory, thoracic and mediastinal disorders	Not known	Non-cardiogenic pulmonary oedema
Skin and subcutaneous tissue disorders	Not known	Urticaria, Rash (including Erythema multiforme, Stevens-Johnson syndrome, Toxic epidermal necrolysis)****, Thrombocytic purpura, Photosensitivity, Acute generalised exanthematous pustulosis (AGEP)

*During long-term therapy, metabolic acidosis and electrolyte imbalance may occasionally occur. This can usually be corrected by the administration of bicarbonate.

**Adverse reactions during short-term therapy are usually non-serious.

***This condition invariably subsides upon diminution or withdrawal of the medication.

****Acetazolamide is a sulphonamide derivative and therefore some side effects similar to those caused by sulphonamides have occasionally been reported.

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**. By reporting side effects, you can help provide more information on the safety of this medicine.

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Carbonic anhydrase inhibitors.

ATC Code: S01EC01

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 Acetazolamide tablets 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

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium starch glycolate,

Maize Starch,

Lactose monohydrate,

Povidone K30,

Purified water,

Anhydrous calcium hydrogen phosphate,

Magnesium Stearate

6.2 Incompatibilities

None

6.3 Shelf life

48 months
Bottle Pack: Once opened: Use within 3 months.

6.4 Special precautions for storage

Store in the original pack in order to protect from light.

6.5 Nature and contents of container

Blister Pack: 100 or 112 tablets packed in a blister made of Aluminium lidding foil 25micron/ PVC-PEPVDC triplex white opaque (250/25/90) foil.

Bottle Pack: 100 or 112 tablets packed in a white opaque high density polyethylene bottle (150cc) with Polypropylene screw cap with liner (38mm).

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

DAWA Limited
5 Sandridge Close
Harrow, Middlesex
HA1 1XD, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 30684/0285

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

20/03/2025

10 DATE OF REVISION OF THE TEXT

29/10/2025