SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Cetamoks 250mg Tablets

Acetazolamide 250mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 250mg acetazolamide.

For the full list of excipients see 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White to off-white, round tablets with “250” debossed on one side and cross scored on the other. The tablet can be divided into equal halves, but should not be divided into quarters.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Acetazolamide is an enzyme inhibitor which acts specifically on carbonic anhydrase.

Acetazolamide is indicated in adults and children.

It is indicated in the treatment of:

i) *Glaucoma:* Acetazolamide 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:* Acetazolamide 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 can be used in conjunction with other diuretics when effects on several segments of the nepbron are desirable in the treatment of fluid retaining states.

iii) *Epilepsy:* In conjunction with other anticonvulsants best results with acetazolamide 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

i) 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.

ii) 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 250mg tablets every other day. The use of Acetazolamide 250mg 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.

iii) 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 should be gradual.

Elderly: Acetazolamide 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

For oral administration

4.3 Contraindications

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 250mg tablets should not be used in patients with hepatic cirrhosis as this may increase the risk of hepatic encephalopathy.

Long-term administration of 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 lowered intraocular pressure.

Acetazolamide 250mg tablets should not be used in patients hypersensitive to the active substance, sulphonamides or to any of the excipients listed in section 6.1.

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 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 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 therapy.

In patients with pulmonary obstruction or emphysema where alveolar ventilation may be impaired, acetazolamide 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.

Non-cardiogenic pulmonary oedema
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**.**

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 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 this medicine 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 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: there is no human or animal data available on the effect of acetazolamide on fertility

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

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

	Acetazolamide effects	**Sulphonamide class effects**
Blood & lymphatic system disorders		
Occasional		Agranulocytosis; thrombocytopenia; thrombocytic purpura; leukopenia; aplastic anaemia; bone marrow depression; pancytopenia
Immune system disorders		
Occasional		Anaphylaxis
Metabolism & nutrition disorders		
Common	Loss of appetite; thirst;	
Occasional	metabolic acidosis; electrolyte imbalance	
Psychiatric disorders		
Common	Irritability;	
Uncommon	depression; confusion	
Nervous system disorders		
Common	Paraesthesia; headache; dizziness;	
Uncommon	drowsiness	
Rare	Flaccid paralysis; convulsions	
Eye disorders		
Uncommon	Transient myopia	
Not known	Choroidal effusion, choroidal detachment	
Ear & labyrinth disorders		
Uncommon	Impaired hearing; tinnitus	
Vascular disorders		

Common	Flushing	
Gastrointestinal disorders		
Common	Taste disturbance; nausea; vomiting; diarrhoea	
Very rare	Melaena	
Hepatobiliary disorders		
Occasional	Abnormal liver function	
Rare	hepatitis; cholestatic jaundice;	Fulminant hepatic necrosis;
Skin & subcutaneous tissue disorders		
Rare	Photosensitivity; rash	
Occasional	urticaria	Rash including erythema multiforme; Stevens-Johnson syndrome; toxic epidermal necrolysis;
Not known	Acute generalised exanthematous pustulosis (AGEP)	
Renal & Urinary disorders		
Common	Polyuria	
Occasional	glycosuria; renal failure	Crystalluria; calculus formation; renal colic; ureteral colic; renal lesions;
Very rare	haematuria;	
Reproductive system & breast disorders		
Uncommon	Reduced libido	
General disorders & Administration Site conditions		
Common	Fatigue	
Occasional		Fever
Respiratory, thoracic and mediastinal disorders		
Not known	Non-cardiogenic pulmonary oedema	

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 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

Not applicable

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Crospovidone,

Maize starch,

Povidone,

Anyhydrous Calcium Hydrogen Phosphate,

Magnesium Stearate,

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Bottle pack: 36 months.

Blister pack: 36 months.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions but should be stored in the original packaging in order to protect from light and moisture.

6.5 Nature and contents of container

Aluminium- OPA/Aluminium/PVC foil blister pack containing 10 tablets

Aluminium- OPA/Aluminium/PVC foil blister pack containing 12 tablets

and

HDPE white opaque container with PP closure containing 112 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Blumont Pharma Ltd

23 Moortown Close

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NG31 9GG

UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 31103/0024

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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04/02/2025