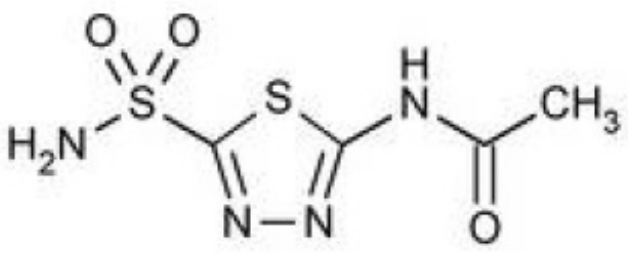
ACETAZOLAMIDE- acetazolamide tablet
Northwind Health Company, LLC

Acetazolamide Tablets USP

Rx only

DESCRIPTION

Acetazolamide, an inhibitor of the enzyme carbonic anhydrase is a white to faintly yellowish white crystalline, odorless powder, weakly acidic, very slightly soluble in water and slightly soluble in alcohol. The chemical name for acetazolamide is *N*-(5-Sulfamoyl-1,3,4-thiadiazol-2-yl) acetamide and has the following chemical structure:



Molecular Weight: 222.25

Molecular Formula: $C_4H_6N_4O_3S_2$

Acetazolamide Tablets, USP are available for oral administration each containing 125 mg and 250 mg of acetazolamide respectively. Additionally, they contain the following inactive ingredients: lactose monohydrate, magnesium stearate, microcrystalline cellulose, povidone, pregelatinized starch, sodium lauryl sulfate, and sodium starch glycolate.

CLINICAL PHARMACOLOGY

Acetazolamide is a potent carbonic anhydrase inhibitor, effective in the control of fluid secretion (eg, some types of glaucoma), in the treatment of certain convulsive disorders (eg, epilepsy), and in the promotion of diuresis in instances of abnormal fluid retention (eg, cardiac edema).

Acetazolamide is not a mercurial diuretic. Rather, it is a nonbacteriostatic sulfonamide possessing a chemical structure and pharmacological activity distinctly different from the bacteriostatic sulfonamides.

Acetazolamide is an enzyme inhibitor that acts specifically on carbonic anhydrase, the enzyme that catalyzes the reversible reaction involving the hydration of carbon dioxide and the dehydration of carbonic acid. In the eye, this inhibitory action of acetazolamide decreases the secretion of aqueous humor and results in a drop in intraocular pressure, a reaction considered desirable in cases of glaucoma and even in certain

nonglaucomatous conditions. Evidence seems to indicate that acetazolamide has utility as an adjuvant in the treatment of certain dysfunctions of the central nervous system (eg, epilepsy). Inhibition of carbonic anhydrase in this area appears to retard abnormal, paroxysmal, excessive discharge from central nervous system neurons. The diuretic effect of acetazolamide is due to its action in the kidney on the reversible reaction involving hydration of carbon dioxide and dehydration of carbonic acid. The result is renal loss of HCO_3 ion, which carries out sodium, water, and potassium. Alkalinization of the urine and promotion of diuresis are thus affected. Alteration in ammonia metabolism occurs due to increased reabsorption of ammonia by the renal tubules as a result of urinary alkalinization.

Placebo-controlled clinical trials have shown that prophylactic administration of acetazolamide at a dose of 250 mg every eight to 12 hours (or a 500 mg controlled-release capsule once daily) before and during rapid ascent to altitude results in fewer and/or less severe symptoms (such as headache, nausea, shortness of breath, dizziness, drowsiness, and fatigue) of acute mountain sickness (AMS). Pulmonary function (eg, minute ventilation, expired vital capacity, and peak flow) is greater in the acetazolamide treated group, both in subjects with AMS and asymptomatic subjects. The acetazolamide treated climbers also had less difficulty in sleeping.

INDICATIONS AND USAGE

For adjunctive treatment of: edema due to congestive heart failure; drug-induced edema; centrencephalic epilepsies (petit mal, unlocalized seizures); chronic simple (open-angle) glaucoma, secondary glaucoma, and preoperatively in acute angle-closure glaucoma where delay of surgery is desired in order to lower intraocular pressure. Acetazolamide Tablets are also indicated for the prevention or amelioration of symptoms associated with acute mountain sickness in climbers attempting rapid ascent and in those who are very susceptible to acute mountain sickness despite gradual ascent.

CONTRAINDICATIONS

Hypersensitivity to acetazolamide or any excipients in the formulation. Since acetazolamide is a sulfonamide derivative, cross sensitivity between acetazolamide, sulfonamides and other sulfonamide derivatives is possible.

Acetazolamide therapy is contraindicated in situations in which sodium and/or potassium blood serum levels are depressed, in cases of marked kidney and liver disease or dysfunction, in suprarenal gland failure, and in hyperchloremic acidosis. It is contraindicated in patients with cirrhosis because of the risk of development of hepatic encephalopathy.

Long-term administration of acetazolamide is contraindicated 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.

WARNINGS

Fatalities have occurred, although rarely, due to severe reactions to sulfonamides including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic

necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias, and anaphylaxis. Sensitizations may recur when a sulfonamide is readministered irrespective of the route of administration. If signs of hypersensitivity or other serious reactions occur, discontinue use of this drug.

Caution is advised for patients receiving concomitant high-dose aspirin and acetazolamide, as anorexia, tachypnea, lethargy, metabolic acidosis, coma, and death have been reported.

PRECAUTIONS

General

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

Information for Patients

Adverse reactions common to all sulfonamide derivatives may occur: anaphylaxis, fever, rash (including erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis), crystalluria, renal calculus, bone marrow depression, thrombocytopenic purpura, hemolytic anemia, leukopenia, pancytopenia, and agranulocytosis. Caution is advised for early detection of such reactions and the drug should be discontinued and appropriate therapy instituted.

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

Gradual ascent is desirable to try to avoid acute mountain sickness. If rapid ascent is undertaken and acetazolamide tablets are used, it should be noted that such use does not obviate the need for prompt descent if severe forms of high altitude sickness occur, ie, high altitude pulmonary edema (HAPE) or high altitude cerebral edema.

Caution is advised for patients receiving concomitant high-dose aspirin and acetazolamide, as anorexia, tachypnea, lethargy, metabolic acidosis, coma, and death have been reported (see **WARNINGS**).

Both increases 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.

Acetazolamide treatment may cause electrolyte imbalances, including hyponatremia and hypokalemia, 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 a patient to, electrolyte and acid/base imbalances, such as patients with impaired renal function (including elderly patients; see **PRECAUTIONS, Geriatric Use**), patients with diabetes mellitus, and patients with impaired alveolar ventilation.

Some adverse reactions to acetazolamide, such as drowsiness, fatigue, and myopia,

may impair the ability to drive and operate machinery.

Laboratory Tests

To monitor for hematologic reactions common to all sulfonamides, it is recommended that a baseline CBC and platelet count be obtained on patients prior to initiating acetazolamide tablet therapy and at regular intervals during therapy. If significant changes occur, early discontinuance and institution of appropriate therapy are important. Periodic monitoring of serum electrolytes is recommended.

Drug Interactions

Aspirin - See **WARNINGS**.

Acetazolamide modifies phenytoin metabolism with increased serum levels of phenytoin. This may increase or enhance the occurrence of osteomalacia in some patients receiving chronic phenytoin therapy. Caution is advised in patients receiving chronic concomitant therapy.

By decreasing the gastrointestinal absorption of primidone, acetazolamide may decrease serum concentrations of primidone and its metabolites, with a consequent possible decrease in anticonvulsant effect. Caution is advised when beginning, discontinuing, or changing the dose of acetazolamide in patients receiving primidone.

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

Acetazolamide may increase the effects of other folic acid antagonists.

Acetazolamide may increase or decrease blood glucose levels. Consideration should be taken in patients being treated with antidiabetic agents.

Acetazolamide decreases urinary excretion of amphetamine and may enhance the magnitude and duration of their effect.

Acetazolamide reduces urinary excretion of quinidine and may enhance its effect.

Acetazolamide may prevent the urinary antiseptic effect of methenamine.

Acetazolamide increases lithium excretion and the lithium may be decreased.

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

Acetazolamide may elevate cyclosporine levels.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate the carcinogenic potential of acetazolamide have not been conducted. In a bacterial mutagenicity assay, acetazolamide was not mutagenic when evaluated with and without metabolic activation.

The drug had no effect on fertility when administered in the diet to male and female rats at a daily intake of up to 4 times the recommended human dose of 1,000 mg in a 50 kg individual.

Pregnancy: Teratogenic effects

Acetazolamide, administered orally or parenterally, has been shown to be teratogenic (defects of the limbs) in mice, rats, hamsters, and rabbits. There are no adequate and well-controlled studies in pregnant women. Acetazolamide should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

Because of the potential for serious adverse reactions in nursing infants from acetazolamide, a decision should be made whether to discontinue nursing or to discontinue the drug taking into account the importance of the drug to the mother. Acetazolamide should only be used by nursing women if the potential benefit justifies the potential risk to the child.

Pediatric Use

The safety and effectiveness of acetazolamide in pediatric patients have not been established.

Growth retardation has been reported in children receiving long-term therapy, believed secondary to chronic acidosis.

Geriatric Use

Metabolic acidosis, which can be severe, may occur in the elderly with reduced renal function.

Clinical studies of acetazolamide did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS

Body as a whole: Headache, malaise, fatigue, fever, pain at injection site, flushing, growth retardation in children, flaccid paralysis, anaphylaxis

Digestive: Gastrointestinal disturbances such as nausea, vomiting, diarrhea

Hematological/Lymphatic: Blood dyscrasias such as aplastic anemia, agranulocytosis, leukopenia, thrombocytopenia, thrombocytopenic purpura, melena

Hepato-biliary disorders: Abnormal liver function, cholestatic jaundice, hepatic insufficiency, fulminant hepatic necrosis

Metabolic/Nutritional: Metabolic acidosis, electrolyte imbalance, including hypokalemia, hyponatremia, osteomalacia with long-term phenytoin therapy, loss of appetite, taste alteration, hyper/hypoglycemia

Nervous: Drowsiness, paraesthesia (including numbness and tingling of extremities and face), depression, excitement, ataxia, confusion, convulsions, dizziness

Skin: Allergic skin reactions including urticaria, photosensitivity, Stevens-Johnson

syndrome, toxic epidermal necrolysis

Special senses: Hearing disturbances, tinnitus, transient myopia. Transient myopia is the result of forward movement of the ciliary body leading to a narrowing of the angle.

Urogenital: Crystalluria, increased risk of nephrolithiasis with long-term therapy, hematuria, glycosuria, renal failure, polyuria

To report SUSPECTED ADVERSE REACTIONS, contact Avet Pharmaceuticals Inc. at 1-866-901-DRUG (3784) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

OVERDOSAGE

No specific antidote is known. 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 levels 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 intraerythrocytic 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.

DOSAGE AND ADMINISTRATION

Glaucoma: Acetazolamide should be used as an adjunct to the usual therapy. The dosage employed in the treatment of *chronic simple (open-angle) glaucoma* ranges from 250 mg to 1 g of acetazolamide per 24 hours, usually in divided doses for amounts over 250 mg. It has usually been found that a dosage in excess of 1 g per 24 hours does not produce an increased effect. In all cases, the dosage should be adjusted with careful individual attention both to symptomatology and ocular tension. Continuous supervision by a physician is advisable.

In treatment of secondary glaucoma and in the preoperative treatment of some cases of *acute congestive (closed-angle) glaucoma*, the preferred dosage is 250 mg every four hours, although some cases have responded to 250 mg twice daily on short-term therapy. In some acute cases, it may be more satisfactory to administer an initial dose of 500 mg followed by 125 or 250 mg every four hours depending on the individual case. Intravenous therapy may be used for rapid relief of ocular tension in acute cases. A complementary effect has been noted when acetazolamide has been used in conjunction with miotics or mydriatics as the case demanded.

Epilepsy: It is not clearly known whether the beneficial effects observed in epilepsy are due to direct inhibition of carbonic anhydrase in the central nervous system or whether they are due to the slight degree of acidosis produced by the divided dosage. The best results to date have been seen in petit mal in pediatric patients. Good results, however, have been seen in patients, both pediatric patients and adult, in other types of seizures such as grand mal, mixed seizure patterns, myoclonic jerk patterns, etc. The suggested total daily dose is 8 to 30 mg per kg in divided doses. Although some patients respond

to a low dose, the optimum range appears to be from 375 to 1,000 mg daily. However, some investigators feel that daily doses in excess of 1 g do not produce any better results than a 1 g dose. When acetazolamide tablets are given in combination with other anticonvulsants, it is suggested that the starting dose should be 250 mg once daily in addition to the existing medications. This can be increased to levels as indicated above.

The change from other medications to acetazolamide should be gradual and in accordance with usual practice in epilepsy therapy.

Congestive Heart Failure: For diuresis in congestive heart failure, the starting dose is usually 250 to 375 mg once daily in the morning (5 mg/kg). If, after an initial response, the patient fails to continue to lose edema fluid, do not increase the dose but allow for kidney recovery by skipping medication for a day. Acetazolamide tablets yields best diuretic results when given on alternate days, or for two days alternating with a day of rest.

Failures in therapy may be due to overdosage or too frequent dosage. The use of acetazolamide does not eliminate the need for other therapy such as digitalis, bed rest, and salt restriction.

Drug-Induced Edema: Recommended dosage is 250 to 375 mg of acetazolamide once a day for one or two days, alternating with a day of rest.

Acute Mountain Sickness: Dosage is 500 mg to 1,000 mg daily, in divided doses using tablets or sustained-release capsules as appropriate. In circumstances of rapid ascent, such as in rescue or military operations, the higher dose level of 1,000 mg is recommended. It is preferable to initiate dosing 24 to 48 hours before ascent and to continue for 48 hours while at high altitude, or longer as necessary to control symptoms.

Note: The dosage recommendations for glaucoma and epilepsy differ considerably from those for congestive heart failure, since the first two conditions are not dependent upon carbonic anhydrase inhibition in the kidney which requires intermittent dosage if it is to recover from the inhibitory effect of the therapeutic agent.

Interference with Laboratory Tests

Sulfonamides may give false negative or decreased values for urinary phenolsulfonphthalein and phenol red elimination values for urinary protein, serum non-protein and for serum uric acid. 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.

HOW SUPPLIED

Acetazolamide Tablets USP, 125 mg are available for oral administration as white to off white, round tablet, debossed **HP 287** on one side and scored on other side. They are supplied as follows:

Bottles of 30 Tablets NDC 51655-331-52

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to

30°C (59° to 86°F). [See USP Controlled Room Temperature].

Dispense in a tight, light-resistant container as defined in the USP using a child-resistant closure.

Keep container tightly closed.

KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.

Distributed by:

Avet Pharmaceuticals Inc.

East Brunswick, NJ 08816

1.866.901.DRUG (3784)

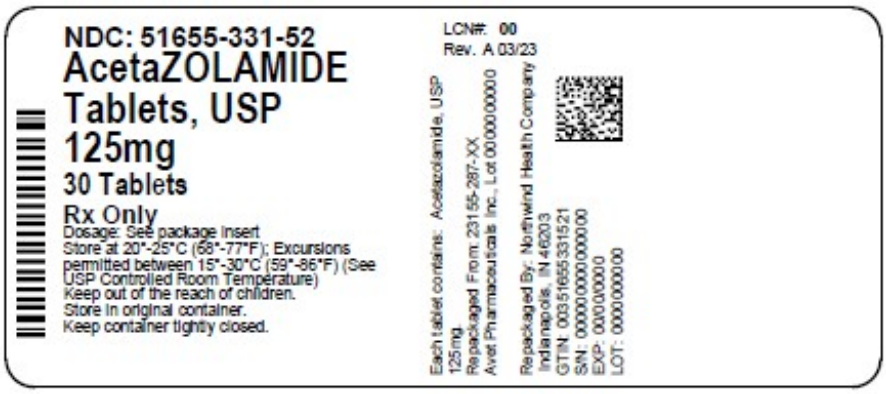
Avet Pharma®

51U000000129US06

Revised: 06/2022

PRINCIPAL DISPLAY PANEL

NDC: 51655-331-52



ACETAZOLAMIDE

acetazolamide tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:51655-331(NDC:23155-287)
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ACETAZOLAMIDE (UNII: O3FX965V0I) (ACETAZOLAMIDE - UNII:O3FX965V0I)	ACETAZOLAMIDE	125 mg

Inactive Ingredients

Ingredient Name	Strength
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
POVIDONE (UNII: FZ989GH94E)	
STARCH, CORN (UNII: O8232NY3SJ)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	

Product Characteristics

Color	white	**Score**	2 pieces
Shape	ROUND	**Size**	9mm
Flavor		**Imprint Code**	HP;287
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:51655-331-52	30 in 1 BOTTLE, PLASTIC; Type 0: Not a Combination Product	03/28/2023	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA205530	03/28/2023	

Labeler - Northwind Health Company, LLC (036986393)

Registrant - Northwind Health Company, LLC (036986393)

Establishment

Name	Address	ID/FEI	Business Operations
Northwind Health Company, LLC		036986393	repack(51655-331)

Revised: 1/2026 Northwind Health Company, LLC