

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Amiloride Tablets BP 5mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Amiloride Hydrochloride BP 5.70mg
(equivalent to 5.0mg
anhydrous Amiloride Hydrochloride)

3 PHARMACEUTICAL FORM

Tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Potassium conserving diuretic.

While Amiloride may be used independently, its main indication is for concurrent therapy with either thiazides or more potent diuretics in order to conserve potassium during episodes of vigorous diuresis and during long-term maintenance therapy.

- (i) Congestive heart failure, primarily for concurrent use in patients receiving thiazides or more potent diuretic agents.
- (ii) Hypertension, as an adjunctive agent.
- (iii) Hepatic cirrhosis with ascites and oedema.

4.2 Posology and method of administration

Adults:

The initial dosage should be 10mg either as a single dose or 5mg twice a day. This may be increased if necessary, but must not exceed 20mg (4 tablets) per day. After diuresis has been achieved, the dosage may be reduced to the least amount required (by 5mg increments).

Congestive heart failure:

Amiloride may be started at a dosage of 5mg or 10mg (1 or 2 tablets) a day, together with the usual dosage of other diuretic agents. If diuresis is not achieved with minimal dosage of both agents, the dosage of both may be gradually increased, but that of Amiloride should not exceed 20mg (4 tablets) a day. Once diuresis has been achieved, reduction in dosage of both agents may be attempted for maintenance therapy. The dosage of both agents should be determined by the diuretic response and the plasma potassium level.

Hypertension

Amiloride is given at a dosage of 5mg or 10mg (1 or 2 tablets) a day, together with the usual antihypertensive dosage of thiazides. It is not usually necessary to exceed 10mg of Amiloride a day; in any event, not more than 20mg (4 tablets) of Amiloride a day should be given.

Hepatic cirrhosis with ascites

Treatment should be started with a small dose of Amiloride, i.e. 5mg (1 tablet), plus a low dosage of the other diuretic agent. If necessary, dosage of both agents may be increased gradually until there is effective diuresis.

The dosage of Amiloride should not exceed 20mg (4 tablets) a day. Maintenance doses may be lower than those required to initiate diuresis; reduction in the daily dosage should therefore be attempted when the patient's weight is stabilised.

Gradual weight reduction in cirrhotic patients is especially desirable to reduce the likelihood of untoward reactions.

Elderly:

Because the elderly are more susceptible to electrolyte imbalance and because renal reserve may be reduced, they are more likely to experience hyperkalaemia. The dosage should be adjusted according to renal function, blood electrolytes and diuretic response.

Children:

The use of Amiloride is not recommended in children.

Taken by mouth.

4.3 Contraindications

Hyperkalaemia (plasma potassium over 5.5mmol/l). Other potassium-conserving agents or potassium supplements; anuria, acute renal failure, severe progressive renal disease, diabetic nephropathy. Sensitivity to Amiloride.

4.4 Special warnings and precautions for use

Diabetes Mellitus: To minimise the risk of hypokalaemia in known or suspected diabetic patients, the status of renal function should be determined before initiating therapy. Amiloride should be discontinued at least three days before a glucose tolerance test.

Metabolic or respiratory acidosis: Potassium-conserving therapy should be initiated only with caution in severely ill patients in whom metabolic or respiratory acidosis may occur, e.g. patients with cardiopulmonary disease of decompensated diabetes. Shifts in acid-base balance alter the balance of extracellular-intracellular potassium and the development of acidosis may be associated with rapid increases in plasma potassium.

Hyperkalaemia: This has been observed in patients receiving Amiloride Hydrochloride, alone or with other diuretics. These patients should be observed carefully for clinical, laboratory and ECG evidence of hyperkalaemia.

Some deaths have been reported in this group of patients. Hyperkalaemia has been noted particularly in the elderly and in hospital patients with hepatic cirrhosis or cardiac oedema who have known renal involvement who were seriously ill, or were undergoing vigorous diuretic therapy. Neither potassium-conserving agents nor a diet rich in potassium should be used with Amiloride except in severe and/or refractory cases of hypokalaemia. If the combination is used, plasma potassium levels must be continuously monitored.

Impaired renal function: Patients with increases in blood urea over 10mmol/l, serum creatinine over 130umol/l, or with diabetes mellitus, should not receive Amiloride Hydrochloride without careful frequent monitoring of serum

electrolytes and blood urea levels. In renal impairment, use of a potassium-conserving agent may result in rapid development of hyperkalaemia.

Electrolyte imbalance and blood urea increases: Hyponatraemia and hypochloraemia may occur when Amiloride Hydrochloride is used with other diuretics. Reversible increases in blood urea levels have been reported accompanying vigorous diuresis, especially when diuretics were used in seriously ill patients, such as those with hepatic cirrhosis with ascites and metabolic alkalosis, or those with resistant oedema. Careful monitoring of serum electrolytes and blood urea levels should therefore be carried out when Amiloride is given with oral diuretics to such patients.

Cirrhotic patients: Oral diuretic therapy is more frequently accompanied by side effects in patients with hepatic cirrhosis with or without ascites, because these patients are intolerant of acute shifts in electrolyte balance, and because they often already have hypokalaemia as a result of associated aldosteronism.

Hepatic encephalopathy has been reported in patients with pre-existing severe liver disease.

4.5 Interaction with other medicinal products and other forms of interaction

Lithium should not be given with diuretics because they reduce its renal clearance and add a high risk of lithium toxicity. When combined with thiazide diuretics Amiloride can act synergistically with chlorpropamide to increase the risk of hyponatraemia. There is an increased risk of hyperkalaemia with cyclosporin and the hormone antagonist trilostane; likewise with potassium salts. Amiloride antagonises the ulcer healing effect of carbenoxolone.

The risk of hyperkalaemia may be increased when Amiloride is administered concomitantly with angio-tensin-converting enzyme inhibitor. Accordingly, when concomitant use of these agents is indicated, because of demonstrated hypokalaemia, frequent monitoring of serum potassium should be instituted and caution should be exercised with the use of these agents.

4.6 Pregnancy and lactation

Amiloride is not recommended for use during pregnancy. The potential benefits of the drug must be weighed against possible hazards to a foetus if it is administered to women of child bearing age.

It has been found that the routine use of diuretics in otherwise healthy pregnancy women with or without mild oedema is not indicated because they

may be associated with hypovolaemia, increased blood viscosity and decreased placental perfusion. Foetal and neonatal jaundice, foetal bone depression and thrombocytopenia have also been described.

Nursing Mothers: It is not known whether Amiloride is excreted in human Milk. Because of the potential for serious adverse reactions in the nursing infant a decision should be made whether the mother should stop nursing or whether she should stop taking the drug.

4.7 Effects on ability to drive and use machines

None stated

4.8 Undesirable effects

Nausea/anorexia, abdominal pain, flatulence and mild skin rashes have been reported and are probably related to Amiloride. Other adverse experiences that have been reported with Amiloride are generally those known to be associated with diuresis, or with the underlying disease being treated.

Body as a whole: Headache, weakness, fatigue, back pain, chest pain, neck/shoulder ache, pain in extremities.

Cardiovascular: Angina pectoris, orthostatic hypotension, arrhythmias, palpitation, one patient with a partial heart block developed complete heart block.

Digestive: Anorexia, nausea, vomiting, diarrhoea, constipation, abdominal pain, GI bleeding, jaundice, thirst, dyspepsia, heartburn, flatulence.

Metabolic: Hyperkalaemia (plasma potassium levels over 5.5 mmol/l).

Integumentary: Pruritus, rash, dryness of mouth, alopecia.

Musculoskeletal: Muscle cramps, joint pain.

Nervous: Dizziness, vertigo, paraesthesia, tremor, encephalopathy.

Psychiatric: Nervousness, mental confusion, insomnia, decreased libido, depression, somnolence.

Respiratory: Cough, dyspnoea.

Special senses: Nasal congestion, visual disturbances, increased intra-ocular pressure, tinnitus.

Urogenital: Impotence, polyuria, dysuria, bladder spasms, urinary frequency.

Unknown causal relationship: Other reactions have been reported but occurred under circumstances where a causal relationship could not be excluded. These rare observations are listed to serve as alerting information.

In reactions where no causal relationship could be found were activation of likely pre-existing peptic ulcer, aplastic anaemia, neutropenia and abnormal liver function tests. In some cirrhotic patients jaundice associated with the underlying disease has deepened, but the drug relationship is not certain.

4.9 Overdose

It is not known whether the drug is dialysable. Dehydration and electrolyte imbalance should be treated by established procedures. Amiloride should be stopped and the patient observed closely. No specific antidote is available. Gastric lavage should be performed if of recent ingestion. Treatment is symptomatic and supportive. Plasma potassium levels should be reduced if hyperkalaemia occurs.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Amiloride takes effect about two hours after administration by mouth and its diuretic action persists for about 24 hours. It acts mainly on the distal renal tubules. It increases the excretion of sodium and chloride and reduces the excretion of potassium.

Amiloride enhances the natriuretic and diminishes the kaliuretic effects of other diuretics.

5.2 Pharmacokinetic properties

Amiloride is completely absorbed from the gastro-intestinal tract. Biological half-life in the circulation is about six hours. It is excreted unchanged in the urine.

Peak serum concentrations are reached in about four hours after a dose. About half of a dose is excreted unchanged in the urine within 72 hours.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose BP
Calcium hydrogen phosphate BP
Pregelatinised maize starch BP
Maize starch BP
Magnesium stearate BP
Purified water BP

6.2 Incompatibilities

None stated.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 25°C in a dry place in well closed containers.
Protect from light.

6.5 Nature and contents of container

High density polystyrene with polythene lids and/or polypropylene containers with polypropylene or polythene lids and polyurethane polythene inserts.

Pack sizes: 100 and 500

Blister pack:

20 micron hard-tempered aluminium foil, coated on the dull side with 6-7 GSM heat-seal lacquer and printed on the bright side; 250micron rigid, green PVC Pharmaceutical Grade.

Pack sizes: 28 and 84

(1 x 28 tablets Calendar Pack in a carton
3 x 28 tablets Calendar Packs in a carton)

6.6 Special precautions for disposal

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Goldshield Pharmaceuticals Limited
NLA Tower, 12-16 Addiscombe Road
Croydon, Surrey, CR0 0XT
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 12762/0419

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

12/11/1997

10 DATE OF REVISION OF THE TEXT

11 DOSIMETRY (IF APPLICABLE)

**12 INSTRUCTIONS FOR PREPARATION OF
RADIOPHARMACEUTICALS (IF APPLICABLE)**