SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Amiloride 5 mg Tablets BP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 5.7mg Amiloride Hydrochloride Dihydrate equivalent to 5.0mg anhydrous Amiloride Hydrochloride.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

Off white to creamy white, round, flat, uncoated tablets with beveled edges and debossed with "C" and "G" on either side of breakline and another side is plain.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Potassium- conserving agent;diuretic.
Although Amiloride Hydrochloride may be used alone, its principal indication is as concurrent therapy with thiazides or more potent diuretics in order to conserve potassium during periods of vigorous diuresis and during long-term maintenance therapy.

In congestive heart failure, Amiloride Hydrochloride may be effective alone, but its principal indication is for concomitant use in patients receiving thiazides or more potent diuretic agents.
In hypertension, it is used as an adjunct to prolonged therapy with thiazides and similar agents to prevent potassium depletion.
In hepatic cirrhosis with ascites, Amiloride Hydrochloride usually provides adequate diuresis, with diminished potassium loss and less risk of metabolic alkalosis, when used alone. It may be used with more potent diuretics when a greater diuresis is required while maintaining a more balanced serum electrolyte pattern.

4.2 Posology and method of administration

Adults

Amiloride Hydrochloride alone.The initial dosage is 10 mg (as a single dose or 5mg twice a day). The total daily dose should not exceed 20mg (4 tablets) per day. After diuresis has been achieved, the dosage may be reduced by 5mg increments to the least amount required.

Amiloride Hydrochloride with other diuretic therapy

When Amiloride is used with a diuretic which is given on an intermittent basis, it should be given at the same time as the diuretic.

Hypertension

Usually half 'Amiloride' tablet (2.5mg) given once a day together with the usual antihypertensive dosage of the thiazide concurrently employed. If necessary, increase to 5mg (one 'Amiloride' tablet) given once a day or in divided doses.

Congestive heart failure

Initially half 'Amiloride' tablet (2.5mg) a day together with the usual dosage of the diuretic concurrently employed, subsequently adjusted if required, but not exceeding two 'Amiloride' tablets (10mg) a day. Optimal dosage is determined by diuretic response and the plasma potassium level. Once an initial diuresis has been achieved, reduction in dosage may be attempted for maintenance therapy. Maintenance therapy may be on an intermittent basis.

Hepatic cirrhosis with ascites

Treatment should be started with a low 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 two 'Amiloride' tablets (10 mg) a day. Maintenance dosages 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 associated with diuretic therapy.

Elderly

The elderly are more susceptible to electrolyte imbalance and are more likely to experience hyperkalaemia since renal reserve may be reduced. The dosage

should be carefully adjusted according to renal function, blood electrolytes and diuretic response.

Children:

The use of Amiloride in children under 18 years of age is not recommended as safety and efficacy have not been established.

4.3 Contraindications

Hypersensitivity to Amiloride or any of the excipients listed in section 6.1. Hyperkalaemia (plasma potassium over 5.5mmol/l), other potassium conserving agents or potassium supplements (see precautions); Addison's disease; anuria, acute renal failure, severe progressive renal disease, diabetic nephropathy (see Precautions); prior sensitivity to this product. Safety for use in children is not established. See also 'Use in pregnancy' and 'Use in the breast feeding mother'.

4.4 Special warnings and precautions for use

Diabetes Mellitus: To minimise the risk of hyperkalaemia in known or suspected diabetic patients, the status of renal function should be determined before initiating therapy. Amiloride hydrochloride should be discontinued for at least three days before a glucose tolerance test. In diabetic patients, insulin requirements may change; latent diabetes may become manifest during treatment.

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 or 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 10 mmol/l, serum creatinine over 150 µmol/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.

Treatment of Hyperkalaemia

If hyperkalaemia occurs, Amiloride hydrochloride should be discontinued immediately and, if necessary, active measures taken to reduce the plasma potassium level.

Electrolyte imbalance and Reversible 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 other 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.

In patients with pre-existing severe liver disease, hepatic encephalopathy manifested by tremors, confusion, coma and increased jaundice, has been reported in association with diuretics, including Amiloride hydrochloride.

Paediatric patients: It has not been established that amiloride can be safely used in children. Its use in children should therefore be discouraged.

Excipients
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 (23mg) sodium per tablet, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

- Lithium should not generally be given with diuretics because they reduce the renal clearance of lithium 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.

- When amiloride is administered concurrently with an angiotensin converting enzyme inhibitor, NSAIDs or ciclosporin the risk of hyperkalaemia may be increased. Therefore, if concomitant use of these agents is indicated because of demonstrated hypokalaemia, they should be used with caution and with frequent monitoring of serum potassium. In patients receiving amiloride with NSAIDs or ciclosporin the risk of nephrotoxicity may also be increased.
- Tacrolimus – risk of increased hyperkalaemia when potassium=sparing diuretics and aldosterone antagonist give with tacrolimus.
- Angiotensin II antagonists (losartan, valsartan) – enhanced hypotensive effects when diuretics given with Angiotensin II receptor antagonists
- Beta Blockers (Sotalol) – enhanced hypotensive effect when diuretics given with betablockers, hypokalaemia caused by loop diuretics or thiazides and related diuretics increased risk of ventricular arrhythmias with Sotalol
- Calcium channel blockers (Amlodipine, Diltiazem) – enhanced hypotensive effect when diuretics given with calcium channel blockers
- Adrenergic neurone blockers – enhanced hypotensive effect when given with adrenergic neurone blockers
- Alpha blockers (prazosin) enhanced hypotensive effect when diuretics given with Alpha blockers
- Clonidine enhanced hypotensive effect when diuretics given with clonidine
- Diazoxide enhanced hypotensive and hyperglycaemic effect when diuretics given with diazoxide
- Methyldopa enhanced hypotensive effect when diuretics given with methyldopa
- Moxonidine enhanced hypotensive effect when diuretics given with moxonidine
- Vasodilator Antihypertensive (Hydralazine, Minoxidil, Sodium nitroprusside) enhanced hypotensive effect when diuretics given with hydralazine, minoxidil, sodium nitroprusside. Diuretics should be discontinued 2-3 days before starting treatment with an ACE inhibitor to reduce the risk of hypotension after the first dose.
- Antidepressants – increased risk of postural hypotension with tricyclics. Enhanced hypotensive effect with monoamine oxidase inhibitors (MAOIs)
- St John's Wort – avoid concomitant use; increased risk of postural hypotension when diuretics given with tricyclics
- Carbamazepine – increased risk of hyponatremia
- Aldesleukin enhanced hypotensive effect when diuretics given with aldesleukin
- General Anaesthetic – enhanced hypotensive effect when diuretics given with general anaesthetic
- Antipsychotics – avoid concomitant use with antipsychotics – hypokalaemia caused by diuretics increases risk of ventricular arrhythmias with Amisulpride, enhanced hypotensive effect when diuretics given with phenothiazines, hypokalaemia caused by diuretics increases risk of ventricular arrhythmias with Pimozide.

- Anxiolytics and hypnotics – enhanced hypotensive effect when given with diuretics.
- Atomoxetine – hypokalaemia caused by diuretics increases risk of ventricular arrhythmias with Atomoxetine
- Corticosteroids increased risk of hypokalaemia when diuretics and related diuretics given with corticosteroids
- Levodopa enhanced hypotensive effect when diuretics given with levodopa
- Moxisylyte enhanced hypotensive effect when diuretics given with moxisylyte
- Muscle relaxants enhanced hypotensive effect when diuretics given with baclofen or tizanidine
- Nitrates enhanced hypotensive effect when diuretics given with nitrates
- Oestrogen – diuretics effect of diuretics antagonised by oestrogen
- Drospirenone – risk of hyperkalaemia when potassium sparing diuretics are given with drospirenone (monitor serum potassium during first cycle)
- Alprostadil enhanced hypotensive effect when diuretics given with alprostadil
- Potassium salts – increased risk of hyperkalaemia when potassium sparing diuretics given with potassium salts
- Alcohol – enhanced hypotensive effect when diuretics given with alcohol
- Trilostane – increased risk of hyperkalaemia
- Prostaglandin synthetase inhibitors - In some patients, administration of a prostaglandin synthetase inhibitor may reduce the diuretic, natriuretic and antihypertensive effect of diuretics. Concomitant administration of prostaglandin synthetase inhibitors and potassium-sparing agents, including amiloride HCl, may cause hyperkalaemia and renal failure, especially in elderly patients. Therefore, when amiloride HCl and prostaglandin synthetase inhibitors are used simultaneously, renal function and serum potassium should be carefully monitored.

4.6 Fertility, pregnancy and lactation

Pregnancy

Because clinical experience is limited, 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 pregnant 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 marrow depression and thrombocytopenia have also been described.

Breast-feeding

It is not known whether Amiloride is excreted in human milk. Because many drugs are excreted by this route and because there is a risk that it might take this route of excretion and that it might then cause serious side effects in the breast feeding infant,

the mother should either stop breast feeding or stop taking the drug. The decision depends on the importance of the drug to the mother.

4.7 Effects on ability to drive and use machines

Reduced mental alertness may impair ability to drive or operate dangerous machinery.

4.8 Undesirable effects

The following adverse reactions may occur during the use of Amiloride. The side effects are listed below by system/organ class and frequency. Frequencies are defined as follows:
Very common (≥1/10 patients)
Common (≥1/100, <1/10 patients)
Uncommon (≥1/1,000, <1/100 patients)
Rare (≥1/10,000, <1/1,000 patients)
Very rarely (<1/10,000 patients)
Not known (cannot be determined with available data).

Amiloride Hydrochloride is normally well tolerated, although minor side effects are reported relatively frequently. Except for hyperkalaemia, significant side effects are infrequent. Nausea, anorexia, abdominal pain, flatulence and mild skin rashes have been reported and are probably related to Amiloride: but other side effects are generally associated with diuresis, or with the underlying disease being treated.

Blood and lymphatic system disorders
Not known: Aplastic anaemia, neutropenia.

Nervous system disorders
Not known: Tremors, encephalopathy.

Eye disorders
Not known: Increased eye pressure.

Balance organ and ear disorders
Not known: Tinnitus.

Cardiac disorders[1]
Not known: Palpitations.

Respiratory, thoracic and mediastinal disorders
Not known: Coughing.

Gastrointestinal disorders
Not known: Activation of probably pre-existing peptic ulcer, dyspepsia, dry mouth.

Liver and bile disorders
Not known: Hepatic function abnormalities, jaundice.

Skin and subcutaneous tissue disorders
Not known: Hair loss

Kidney and urinary tract disorders
Not known: Polyuria, pollakiuria, bladder spasms.

Reproductive system and breast disorders
Not known: Decreased libido.

General disorders and administration site disorders
Not known: Pain in neck and shoulder, pain in extremities.

Description of selected side effects
[1] Cardiac disorders: One patient with partial heart block suffered total heart block.

Reactions in which no causal relationship could be established were activation of probable pre-existing peptic ulcer, aplastic anaemia, neutropenia and abnormal liver function tests. In a few cirrhotic patients, jaundice associated with the underlying disease had deepened, but the drug relationship is uncertain.

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 website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

No data are available; and it is not known whether the drug is dialysable.
The most likely signs and symptoms are dehydration and electrolyte imbalance which should be treated by established procedures. Therapy should be discontinued and the patient observed closely. No specific antidote is available. If ingestion is recent, emesis should be induced or gastric lavage should be performed.

Treatment is symptomatic and supportive. If hyperkalaemia occurs, active measures should be taken to reduce plasma potassium levels.

The plasma half life of amiloride is about six hours.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Aldosterone antagonists and other Potassium sparing agents, ATC code: C03DB01.

Amiloride prevents, in the distal tubule and in the transition to the cortical collecting duct, the reabsorption of sodium and, especially as a result, the secretion of potassium and hydrogen ions to the urine.

The potassium-retaining action of amiloride occurs within the first 2 hours after administration and reaches a maximum about 6-10 hours after oral administration. The effective efficacy of the drug persists for at least 12 hours and the antikaliuretic action is noticeable for 24 hours.

5.2 Pharmacokinetic properties

Absorption
Amiloride is absorbed from the gastrointestinal tract by approximately 50% after oral administration. Concomitant food intake reduces absorption by approximately 30%.

Distribution
Peak serum concentrations are achieved about 3-4 hours after administration by mouth.

Metabolism
Amiloride does not bind to proteins and the volume of distribution is approximately 5 l/kg.

Elimination
Amiloride is not metabolised and is excreted by ± 50% in the urine and by ± 40% in the faeces. The plasma half-life is approximately 6-9 hours.

5.3 Preclinical safety data

None stated

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Dibasic calcium phosphate dihydrate
Pregelatinised starch
Maize starch
Magnesium stearate

Sodium starch glycolate

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Tablet containers: Do not store above 25°C. Keep in the original container. Keep the container tightly closed.
Blister packs: Do not store above 25°C. Store in the original package in order to protect from light.

6.5 Nature and contents of container

Container pack:

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

Pack sizes: 100 and 500 tablets

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; 250 micron rigid, green PVC Pharmaceutical Grade.

Pack sizes: 28 and 84 tablets
1 x 28 tablets Calendar Pack in a carton
3 x 28 tablets Calendar Packs in a carton

Blister pack:

PVC/PVDC Opaque white (250/90)/Plain Aluminium foil 0.025MM
Pack size: 28 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Not applicable

7 MARKETING AUTHORISATION HOLDER

Accord Healthcare Limited

Sage house, 319 Pinner Road

North Harrow, Middlesex, HA1 4HF

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 20075/0031

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17/02/2009

10 DATE OF REVISION OF THE TEXT

13/11/2024