SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Amiloride 5mg Tablets BP

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Amiloride hydrochloride (anhydrous equivalent) 5.0mg

For excipients see 6.1

3 PHARMACEUTICAL FORM

Tablet for oral use.

Amiloride 5mg Tablets BP are yellow, round tablets marked AML5 with breakline on one side and CP on the reverse.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Amiloride is a diuretic used alone or as an adjunct to other diuretics in the treatment of oedema and hypertension.

4.2 Posology and method of administration

Adults:

Initially 10mg daily or 5mg twice daily, adjusted according to response. The dosage may be increased up to a maximum of 20mg daily.

Used as an adjunct to other diuretics for hypertension and congestive heart failure:

Initially 5mg or 10mg daily.

Cirrhosis with ascites: Initially 5mg daily.

Elderly:

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

Children under 18 years:

Not indicated.

4.3 Contraindications

Hyperkalaemia, severe renal impairment, prior sensitivity to amiloride. Other potassium-sparing drugs and potassium supplements are contraindicated during amiloride therapy. The safety of amiloride hydrochloride for use in children under 18 years of age has not been established.

4.4 Special warnings and precautions for use

Amiloride should be given with caution to elderly patients, patients likely to develop acidosis, patients with diabetes mellitus and those with impaired hepatic or renal function. Patients with impaired renal function should be monitored carefully for serum electrolytes and blood urea levels, as should seriously ill patients, such as those with hepatic cirrhosis with ascites and metabolic alkalosis or those with resistant oedema who are also taking diuretics. Patients taking amiloride either alone or with other diuretics or angiotensin-converting enzyme inhibitors may develop hyperkalaemia.

Serum electrolytes and blood urea should be monitored periodically. If hyperkalaemia occurs, amiloride hydrochloride should be discontinued immediately and, if necessary, active measures taken to reduce the plasma potassium level.

Amiloride should be discontinued at least three days before a glucose tolerance test because of the risk of provoking severe hyperkalaemia.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Alcohol: Postural hypotension associated with diuretic therapy may be enhanced.

Aldesleukin: Enhanced hypotensive effect may occur when aldesleukin and amiloride are used concomitantly.

Anaesthetics, general: Enhanced hypotensive effect may occur when general anaesthetics and amiloride are used concomitantly.

Analgesics: Diuretics increase the risk of nephrotoxicity with NSAIDs. Indometacin and possibly other NSAIDs increase the risk of hyperkalaemia with potassium-sparing diuretics. Indometacin and ketorolac antagonise the diuretic effect.

Antiarrhythmics: The antiarrhythmic activity of quinidine can be opposed by amiloride.

Antidepressants: increased risk of postural hypotension with tricyclics. Enhanced hypotensive effect with monoamine oxidase inhibitors (MAOIs).

Antidiabetic agents: Chlorpropamide increases the risk of hyponatraemia associated with thiazides in combination with potassium sparing diuretics.

Antiepileptics: increased risk of hyponatraemia with carbamazepine.

Antihypertensives: An enhanced hypotensive effect (which can be extreme) can occur with antihypertensives, including ACE inhibitors, angiotensin-II antagonists, calcium channel blockers, beta blockers, alpha blockers (increased risk of first dose hypotension) or hydralazine. With ACE inhibitors and angiotensin-II antagonists there is also an increased risk of hyperkalaemia.

Antipsychotics: Lithium should not be given with diuretics because they reduce its renal clearance and add a high risk of lithium toxicity. Enhanced hypotensive effect may occur when phenothiazines and amiloride are used concomitantly.

Corticosteroids: Fluid retention associated with corticosteroid use may antagonise the diuretic/antihypertensive response.

Dopaminergics: Enhanced hypotensive effect may occur when levodopa and amiloride are used concomitantly.

Hormones and other endocrine drugs: Combined oral contraceptives and oestrogens may antagonise the diuretic effect. There is an increased risk of hyperkalaemia with trilostane.

Immunosuppressants: increased risk of hyperkalaemia with cyclosporin and tacrolimus. Increased risk of nephrotoxicity with concomitant use of ciclosporin and amiloride.

Muscle relaxants: enhanced hypotensive effect with baclofen and tizanidine.

Nitrates: Enhanced hypotensive effect may occur when nitrates and amiloride are used concomitantly.

Potassium conserving agents, potassium supplements: When amiloride is administered concomitantly with potassium conserving agents or potassium supplements, there is an increased risk of hyperkalaemia (see 4.3 Contraindications).

Prostaglandins: Hypotensive effect may be potentiated by alprostadil.

Ulcer-healing agents: Amiloride antagonises the ulcer-healing effect of carbenoxolone.

Laboratory value alterations: Creatinine clearance: Amiloride blocks the tubular secretion of creatinine, leading to falsely high measurements of creatinine clearance.

4.6 Pregnancy and lactation

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

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

Amiloride is usually well tolerated. Except for hyperkalaemia significant side effects are infrequent. Reported side-effects include the following:

Blood and lymphatic system disorders: Aplastic anaemia and neutropenia have been reported rarely.

Psychiatric disorders: Decreased libido, somnolence, mental confusion, or minor psychiatric changes may occur.

Nervous system disorders: Encephalopathy, paraesthesia.

Eye disorders: Visual changes.

Cardiac disorders: Angina pectoris, arrhythmias, palpitations, postural hypotension**,** dizziness.

Respiratory, thoracic and mediastinal disorders: Dyspnoea, cough.

Gastrointestinal disorders: Nausea, vomiting, constipation or diarrhoea, abdominal pain.

Hepatobiliary disorders: Abnormal liver function. A deepening of jaundice has occurred in cirrhotic patients receiving amiloride hydrochloride alone, but the relationship to amiloride is uncertain.

Skin and subcutaneous tissue disorders: Alopecia, rash, pruritus.

Renal and urinary disorders: Effects on electrolyte balance e.g. hyperkalaemia (particularly in elderly patients, diabetics and patients with renal impairment) and hyponatraemia occasionally occur. Signs include dry mouth, thirst, headache, muscle cramps and weakness. Rises in blood-urea-nitrogen concentrations may occur with amiloride.

Reproductive and breast disorders: Impotence.

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.

4.9 Overdose

Symptoms
The most likely signs and symptoms are dehydration and electrolyte imbalance which should be treated by established methods. Amiloride should be discontinued and the patient observed closely.

Treatment
No specific antidote is available. Patients who present within one hour of overdose may be administered activated charcoal. Treatment should be symptomatic and supportive. If hyperkalaemia occurs, active measures should be taken to reduce plasma potassium levels.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Amiloride is a pyrazinoylguanidine derivative which acts as a potassium-sparing diuretic.

Amiloride interferes with transport of electrolytes in the nephron. As electrogenic sodium transport is interrupted the electrical potential across the tubular epithelium falls. The reduction or elimination of this potential, which is one of the driving forces for secretion of potassium, is probably the basis of the potassium-sparing effect.

5.2 Pharmacokinetic properties

Amiloride is incompletely absorbed from the gastrointestinal tract (approximately 50% is absorbed).

Peak serum concentrations are achieved about three to four hours after oral administration.

Amiloride does not bind to plasma proteins and has an apparent volume of distribution greater than body water. Amiloride is not metabolised.

Amiloride is secreted in the proximal tubule of the kidney and excreted in the urine unchanged.

The half life of amiloride is about 6 hours.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate

Starch

Povidone

Sodium starch glycollate

Magnesium stearate

Dispersed Quinoline Yellow Lake
(E104)

Isopropanol

6.2 Incompatibilities

None known.

6.3 Shelf life

Three years.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Polypropylene or polyethylene tablet container and a polyethylene cap of 100, 250, 500 or 1000 tablets.

Strips of PVC/A1 foil of 10 or 14 tablets in multiple packs.

6.6 Special precautions for disposal

None.

7 MARKETING AUTHORISATION HOLDER

Wockhardt UK Limited

Ash Road North

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Wrexham

LL13 9UF

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 29831/0006

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25th November 1991

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24/08/2015