

# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Amiloride Hydrochloride 5 mg Tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains amiloride hydrochloride, equivalent to 5 mg anhydrous amiloride hydrochloride

Excipient with known effect:

Also contains 75.0 mg lactose per tablet. For the full list of excipients, see section 6.1

## 3 PHARMACEUTICAL FORM

Tablet

Flat cream coloured bevelled tablets, odourless. Engraved MP48 on one side and scored on the other.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

While Amiloride may be used independently, its main indication is for concurrent therapy with either thiazide diuretics such as hydrochlorothiazide or loop diuretics such as furosemide in order to conserve potassium in those at risk from hypokalaemia during episodes of vigorous diuresis and during long-term maintenance therapy.

Amiloride is indicated in the treatment of:

- (i) Congestive heart failure
- (ii) Hypertension, as an adjunctive agent
- (iii) Oedema associated with hepatic cirrhosis (including ascites)

### 4.2 Posology and method of administration

### Posology:

#### **Adults:**

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

#### **Amiloride with other diuretic therapy**

##### Congestive heart failure:

Amiloride may be started at a dosage of 2.5 mg (½ tablet) 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 10 mg (2 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 2.5 mg to 10 mg (½ to 2 tablets) a day, together with the usual antihypertensive dosage of thiazides.

##### Hepatic cirrhosis with ascites

Treatment should be started with a small dose of Amiloride, i.e. 5 mg (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 10 mg (2 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.

#### **Older People:**

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.

**Paediatric Population:**

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

Method of Administration: Oral

**4.3 Contraindications**

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Hyperkalaemia (plasma potassium over 5.5 mmol/l), other potassium conserving agent or potassium supplements (see section 4.4).

Anuria.

Acute renal failure, severe renal impairment, diabetic nephropathy (see section 4.4).

Addison's disease.

Safety for use in children is not established

**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

should be discontinued at least three days before a glucose tolerance test

because of

the risks of provoking severe hyperkalaemia.

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, 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, (see section 4.3).

It is also important to bear in mind that administration of a potassium-sparing diuretic to a patient receiving an ACE inhibitor or an angiotensin-II receptor antagonist can cause severe hyperkalaemia, (see section 4.5).

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

#### Impaired renal function:

Patients with increases in blood urea over 10 mmol/l, serum creatinine over 130 µmol/l, or with diabetes mellitus, should not receive Amiloride 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, (see section 4.3).

#### Electrolyte imbalance and blood urea increases:

Hyponatraemia and hypochloraemia may occur when Amiloride 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.

#### Hepatic impairment:

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, (see section 5.2). Hepatic encephalopathy has been reported in patients with pre-existing severe liver disease.

#### Excipient warnings:

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

#### 4.5 Interaction with other medicinal products and other forms of interaction

##### Antimania

Lithium should not be given with diuretics because they reduce its renal clearance and add a high risk of lithium toxicity.

##### Drugs to treat diabetes

When combined with thiazide diuretics Amiloride can act synergistically with chlorpropamide to increase the risk of hyponatraemia. Canagliflozin might increase the risk of hypotension. Hypotensive and hyperglycaemic effects may be enhanced when diuretics are given with diazoxide.

##### Anti-epileptics:

There is an increased risk of hyponatraemia when diuretics are given with carbamazepine.

##### Immunosuppressants:

There is an increased risk of hyperkalaemia with ciclosporin and tacrolimus. Concomitant use with platinum compounds may increase the risk of nephrotoxicity and ototoxicity. Aldesleukin may produce an enhanced hypotensive effect when given with diuretics.

##### Analgesics:

There is a risk of decreased renal function and the development of hyperkalaemia with NSAIDs (e.g. indometacin). The effects of diuretics are antagonised by ketorolac.

##### Anti-hypertensives:

The risk of hyperkalaemia may be increased when amiloride is administered concomitantly with ACE inhibitors or angiotensin-II-converting enzyme inhibitors (losartan, valsartan).

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. There is an increased risk of hyperkalaemia when potassium-sparing diuretics are given with aliskiren.

Hypokalaemia caused by loop diuretics or thiazides and related diuretics increases the risk of ventricular arrhythmias with the beta blocker, sotalol.

Concurrent administration of ACE inhibitors, adrenergic neurone blockers, alpha blockers, angiotensin-II receptor antagonists (losartan, valsartan), beta blockers (sotalol), calcium channel blockers, clonidine, hydralazine, methyldopa, minoxidil, moxislyte, moxonidine, nitrates, sodium nitroprusside may enhance the hypotensive effect.

##### Anti-depressants:

There is an increased risk of postural hypotension when diuretics are given with tricyclic antidepressants or MAOIs.

Corticosteroids:

Corticosteroids antagonize the diuretic effect of diuretics.

Antibiotics:

Amiloride can cause a small reduction in the absorption of amoxicillin. Lymecycline should be avoided because of its association with rises in blood urea nitrogen levels. The nephrotoxic effects of tetracyclines may be exacerbated by diuretics. Trimethoprim may cause hyperkalaemia and this may be additive with the effects of potassium-sparing diuretics.

Anti-protozoals:

Pentamidine is structurally similar to amiloride and therefore use with potassium-sparing diuretics may result in severe hyperkalaemia.

Ulcer-healing agents:

Amiloride can oppose the ulcer healing effect of carbenoxolone.

Cardiac glycoside (Digoxin):

Amiloride has little effect on digoxin levels in healthy subjects, but it might reduce its inotropic effects, and in patients with renal impairment amiloride possibly raises digoxin levels.

Alcohol:

Alcohol may enhance the hypotensive effect of diuretics.

Prostaglandins:

There is an enhanced hypotensive effect when diuretics are given with alprostadil.

General anaesthetics

There is an enhanced hypotensive effect when diuretics are given with general anaesthetics.

Anxiolytics and Hypnotics:

There is an enhanced hypotensive effect when diuretics are given with anxiolytics and hypnotics.

Muscle relaxants:

There is an enhanced hypotensive effect when diuretics are given with baclofen or tizanidine.

Anti-Parkinsonism drugs:

There is an enhanced hypotensive effect when diuretics are given with levodopa, co-beneldopa or co-careldopa.

Anti-psychotics:

Avoid concomitant use with antipsychotics – hypokalemia 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

Hormones:

The diuretic effect of diuretics is antagonised by oestrogens. There is a risk of hyperkalaemia when potassium-sparing diuretics are given with drospirenone and the hormone antagonist trilostane.

Total Parenteral Nutrition:

There are reports of patients receiving total parenteral nutrition (TPN) are developing metabolic acidosis associated with concurrent use of amiloride; it is suggested that the reason for this is because the diuretics prevented the kidneys from responding normally to the acid load from the TPN. Caution is advised during the concurrent use.

Potassium Supplements:

There is an increased risk of hyperkalaemia when amiloride is given with potassium supplements or with other potassium-sparing diuretics.

CNS Stimulants

Hypokalaemia caused by diuretics increases risk of ventricular arrhythmias with Atomoxetine

## **4.6 Fertility, pregnancy and lactation**

Pregnancy:

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 childbearing 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.

Breast-feeding:

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 mothers should stop taking the drug.

## **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, although minor side-effects are reported relatively frequently. Apart from hyperkalaemia, significant adverse reactions have been infrequently reported. Nausea/anorexia, abdominal pain, flatulence and mild skin rash are probably due to amiloride; but other side-effects are generally associated with diuresis or with the underlying disease being treated.

##### Blood and lymphatic system disorders:

Rise in blood urea-nitrogen concentrations, (\*aplastic anaemia, \*neutropenia).

##### Metabolism and nutrition disorders:

Anorexia, hyperkalaemia (plasma potassium levels over 5.5 mmol/l), hyponatraemia (when used with other diuretics), metabolic acidosis, Serum uric acid levels may rise during treatment with amiloride and acute attacks of gout may be precipitated

##### Psychiatric disorders:

Nervousness, agitation, mental confusion, insomnia, decreased libido, somnolence, depression, minor psychiatric changes

##### Nervous system disorders:

Headache, dizziness, paraesthesia, tremor, encephalopathy, somnolence

##### Eye disorders:

Minor visual disturbances, increased intra-ocular pressure

##### Ear and labyrinth disorders

Tinnitus, vertigo.

##### Cardiac disorders:

Angina pectoris, arrhythmias, palpitation.

One patient with a partial heart block developed complete heart block.

##### Vascular disorders:

Orthostatic hypotension.

##### Respiratory, thoracic and mediastinal disorders:

Cough, nasal congestion, dyspnoea.

##### Gastrointestinal disorders:

Nausea, vomiting, diarrhoea, constipation, abdominal pain, thirst, dyspepsia, heartburn, flatulence, dry mouth, GI bleeding, (\*activation of likely pre-existing peptic ulcer)

Hepatobiliary disorders:

Jaundice (\*abnormal liver function tests).

Skin and subcutaneous

tissue disorders:

Mild skin rashes, pruritus, alopecia. Musculoskeletal

and connective tissue

disorders:

Muscle cramps, joint pain, back pain, chest pain, neck/shoulder ache, pain in extremities.

Renal and urinary disorders:

Urinary disturbances: polyuria, dysuria, bladder spasms, urinary frequency.

Reproductive system and breast disorders:

Sexual dysfunction, impotence.

General disorders and administration site conditions:

Weakness, fatigue, malaise

*\*Unknown causal relationship*

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

#### **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. If ingestion is recent, gastric lavage should be performed. Treatment is symptomatic and supportive. Plasma potassium levels should be reduced if hyperkalaemia occurs.

## **5 PHARMACOLOGICAL PROPERTIES**

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other Potassium sparing agents, ATC code: C03DB01

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 incompletely absorbed from the gastro-intestinal tract; bioavailability is about 50% and is reduced by food. It is not significantly bound to plasma proteins and has a plasma half-life of 6 to 9 hours; the terminal half-life may be 20 hours or more. It is excreted unchanged in the urine.

Peak serum concentrations are reached in about four hours after a dose.

### Hepatic impairment:

In patients with acute hepatitis the terminal half-life of amiloride was 33 hours compared with 21 hours in healthy subjects. The proportion of the dose excreted in the urine was increased from 49 to 80%.

### Renal impairment:

Studies of the pharmacokinetics of amiloride have reported an increase in terminal elimination half-life from 20 hours in healthy subjects to 100 hours in patients with end-stage renal disease. The natriuretic effect of amiloride was reduced in patients with creatinine clearance below 50 mL/minute. In patients with renal impairment amiloride could aggravate potassium retention due to renal disease. Studies in elderly patients have found increased half-life and steady state concentrations associated with reduced renal function.

## 5.3 Preclinical safety data

No relevant information additional to that contained elsewhere in the SPC.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Lactose monohydrate

Calcium hydrogen phosphate dihydrate

Maize starch,

Pregelatinized starch

Magnesium stearate

## **6.2 Incompatibilities**

None stated.

## **6.3 Shelf life**

2 years

## **6.4 Special precautions for storage**

- a) Containers: Do not store above 25°C. Keep the container tightly closed. Store in the original container.
- b) Strips: Do not store above 25°C. Store in the original package. Keep in the outer carton.

## **6.5 Nature and contents of container**

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

PVC / Aluminium foil strips. 250 micron pharmaceutical grade green PVC and 20 micron hard-tempered aluminium foil coated on the dull side with 6-7 gsm heat seal lacquer and printed on the bright side.

Containers and Strips of 28, 30, 50, 56, 60, 84, 100, 250, 500 & 1000 tablets.

## **6.6 Special precautions for disposal**

Not Applicable

## **7 MARKETING AUTHORISATION HOLDER**

Genethics Europe Limited

41 - 43 Klimentos

Klimentos Tower

Nicosia 1061

Cyprus

**8    MARKETING AUTHORISATION NUMBER(S)**

PL 42976/0063

**9    DATE OF FIRST AUTHORISATION/RENEWAL OF THE  
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11/02/2025

**10   DATE OF REVISION OF THE TEXT**

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