SUMMARY OF PRODUCT CHARACTERISTICS FUROSEMIDE 40 MG TABLETS

1. **Name of the Medicinal Product**

   Furosemide 40 mg Tablets

2. **Qualitative and Quantitative Composition**

   Each tablet contains 40 mg of Furosemide.

3. **Pharmaceutical Form**

   Uncoated Tablet

4. **Clinical Particulars**

4.1 Therapeutic Indications

Furosemide is a potent diuretic with rapid action.

Furosemide tablets are indicated for:

• The treatment of fluid retention associated with heart failure, including left ventricular failure, cirrhosis of the liver and renal disease, including nephrotic syndrome.

• The treatment of mild to moderate hypertension when brisk diuretic response is required. Alone or in combination with other anti-hypertensive agents in the treatment of more severe cases.

4.2 Posology and Method of administration

For oral administration.

Adults: The initial adult dose is 40mg daily, reduced to 20mg daily or 40mg on alternative days. In some patients daily doses of 80mg or higher (given in divided doses) may be required.

Elderly: Caution is advised as furosemide is excreted more slowly in the elderly. Treatment should be started with 20mg and titrated upwards as required

4.3 Contraindications

- Hypersensitivity to furosemide, amiloride, sulphonamides or sulphonamide derivatives, and/or any of the excipients of the product.

- Hypovolaemia and dehydration (with or without accompanying hypotension)

- Severe hypokalaemia: severe hyponatraemia.

- Comatose or pre-comatose states associated with hepatic cirrhosis.

- Anuria or renal failure with anuria not responding to furosemide, renal failure as a result of poisoning by nephrotoxic or hepatotoxic agents or renal failure associated with hepatic coma

- Addison's disease.

- Children and adolescents under 18 years of age (safety in this age group has not yet been established).

- Digitalis intoxication.

- Concomitant potassium supplements or potassium sparing diuretics.

- Porphyria

- Breast-feeding women.

4.4 Special warnings and precautions for use

• Hypotension.

• Hypovolaemia.

• Severe electrolyte disturbances – particularly hypokalaemia, hyponatraemia and acid-base disturbances.

Furosemide is not recommended

• In patients at high risk for radiocontrast nephropathy - it should not be used for diuresis as part of the preventative measures against radiocontrast-induced nephropathy.

• In patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption.

***Particular caution and/or dose reduction required*:**

• Elderly patients (lower initial dose as particularly susceptible to side-effects –

• Difficulty with micturition including prostatic hypertrophy (increased risk of urinary retention: consider lower dose). Closely monitor patients with partial occlusion of the urinary tract

4.5 Interaction with other medicinal products and other forms of interaction

General- The dosage of concurrently administered cardiac glycosides, diuretics, anti-hypertensive agents, or other drugs with blood-pressure-lowering potential may require adjustment as a more pronounced fall in blood pressure must be anticipated if given concomitantly with furosemide.

The toxic effects of nephrotoxic drugs may be increased by concomitant administration of potent diuretics such as furosemide.

Some electrolyte disturbances (e.g. hypokalaemia, hypomagnesaemia) may increase the toxicity of certain other drugs (e.g. digitalis preparations and drugs inducing QT interval prolongation syndrome).

Antihypertensives – enhanced hypotensive effect possible with all types. Concurrent use with ACE inhibitors or Angiotensin II receptor antagonists can result in marked falls in blood pressure, furosemide should be stopped or the dose reduced before starting an ACE-inhibitor or Angiotensin II receptor antagonists

Antipsychotics – furosemide-induced hypokalaemia increases the risk of cardiac toxicity. Avoid concurrent use with pimozide. Increased risk of ventricular arrhythmias with amisulpride or sertindole. Enhanced hypotensive effect with phenothiazines.

When administering risperidone, caution should be exercised and the risks and benefits of the combination or co-treatment with furosemide or with other potent diuretics should be considered prior to the decision to use.

Anti-arrhythmics (including amiodarone, disopyramide, flecanaide and sotalol) - risk of cardiac toxicity (because of furosemide-induced hypokalaemia). The effects of lidocaine, tocainide or mexiletine may be antagonised by furosemide.

Cardiac glycosides – hypokalaemia and electrolyte disturbances (including hypomagnesia) increase the risk of cardiac toxicity.

Drugs that prolong Q-T interval – increased risk of toxicity with furosemide-induced electrolyte disturbances

Vasodilators – enhanced hypotensive effect with moxisylyte (thymoxamine) or hydralazine

Other diuretics – profound diuresis possible when furosemide given with metolazone. Increased risk of hypokalaemia with thiazides. Contraindicated with potassium sparing diuretics (eg Amiloride spironolactone) - increased risk of hyperkalaemia

Renin inhibitors – aliskiren reduces plasma concentrations of furosemide

4.6 Pregnancy and lactation

Pregnancy

There is clinical evidence of safety of the drug in the third trimester of human pregnancy & furosemide has been given after the first trimester of pregnancy for oedema, hypertension and toxaemia of pregnancy without causing fetal or newborn adverse effects. However, furosemide crosses the placental barrier and should not be given during pregnancy unless there are compelling medical reasons. It should only be used for the pathological causes of oedema which are not directly or indirectly linked to the pregnancy. The treatment with diuretics of oedema and hypertension caused by pregnancy is undesirable because placental perfusion can be reduced, so, if used, monitoring of fetal growth is required.

Lactation

Furosemide is contraindicated as it passes into breast milk and may inhibit lactation.

4.7 Effects on ability to drive and use machines

Reduced mental alertness, dizziness and blurred vision have been reported, particularly at the start of treatment, with dose changes and in combination with alcohol. Patients should be advised that if affected, they should not drive, operate machinery or take part in activities where these effects could put themselves or others at risk.

4.8 Undesirable Effects

Blood and lymphatic system disorders:

Uncommon:

• thrombocytopenia

Rare:

• Eosinophilia

• Leukopenia

• Bone marrow depression (necessitates withdrawal of treatment). The haemopoietic status should be therefore be regularly monitored.

Very Rare:

• aplastic anaemia or haemolytic anaemia

• agranulocytosis

Nervous system disorders

Rare:

• paraesthesia

• hyperosmolar coma

Not known :

Dizziness, fainting and loss of consciousness

5 Overdose

Features

Overdose can cause massive diuresis resulting in dehydration, volume depletion and electrolyte disturbances with consequent hypotension and cardiac toxicity. The clinical picture in acute or chronic overdose depends primarily on the extent and consequences of electrolyte and fluid loss, e.g. hypovolaemia, dehydration, haemoconcentration, cardiac arrhythmias due to excessive diuresis. Symptoms of these disturbances include severe hypotension (progressing to shock), acute renal failure, thrombosis, delirious states, flaccid paralysis, apathy and confusion. High doses have the potential to cause transient deafness and may precipitate gout (disturbed uric acid secretion).

Management

• Benefits of gastric decontamination are uncertain. In patients presenting within 1 hour of ingestion, consider activated charcoal (50g for adults: 1g/kg for children)

• Observe for a minimum of 4 hours - monitor pulse and blood pressure.

• Treat hypotension and dehydration with appropriate IV fluids

6 Pharmacological Properties

6.1 Pharmacodynamic Properties

The evidence from many experimental studies suggests that furosemide acts along the entire nephron with the exception of the distal exchange site. The main effect is on the ascending limb of the loop of Henley with a complex effect on renal circulation. Blood-flow is diverted from the juxta-medullary region to the outer cortex.

The principle renal action of furosemide is to inhibit active chloride transport in the thick ascending limb. Re-absorption of sodium, chloride from the nephron is reduced hypotonic or isotonic urine produced.

It has been established that prostaglandin (PG) biosynthesis the renin-angiotensin system are affected by furosemide administration and that furosemide alters the renal permeability of the glomerulus to serum proteins.

6.2 Pharmacokinetic Properties

Approximately 65% of the dose is absorbed after oral administration. The plasma half-life is biphasic with a terminal elimination phase of about 1½ hours. Furosemide is up to 99% bound to plasma proteins and is mainly excreted in the urine, largely unchanged, but also excreted in the bile, non-renal elimination being considerably increased in renal failure. Furosemide crosses the placental barrier and is excreted in the milk.

Furosemide is a weak carboxylic acid which exists mainly in the dissociated form in the gastrointestinal tract. Furosemide is rapidly but incompletely absorbed (60-70%) on oral administration and its effect is largely over within 4 hours. The optimal absorption site is the upper duodenum at pH 5.0. Regardless of route of administration 69-97% of activity from a radio-labelled dose is excreted in the first 4 hours after the drug is given. Furosemide is bound to

plasma albumin and little biotransformation takes place. Furosemide is mainly eliminated via the kidneys (80-90%); a small fraction of the dose undergoes biliary elimination and 10-15% of the activity can be recovered from the faeces.

In renal/ hepatic impairment

Where liver disease is present, biliary elimination is reduced up to 50%. Renal impairment has little effect on the elimination rate of furosemide, but less than 20% residual renal function increases the elimination time.

The elderly

The elimination of furosemide is delayed in the elderly where a certain degree of renal impairment is present.

New born

A sustained diuretic effect is seen in the newborn, possibly due to immature tubular function.

6.3 Preclinical safety data

Not applicable.

7 Pharmaceutical Particulars

7.1 List of Excipients

Lactose BP

Maize Starch BP

Potassium Sorbate BP

Sodium Lauryl Sulphate BP

Croscarmellose sodium BP dried

Magnesium Stearate BP

7.2 Incompatibilities

None

7.3 Shelf life

3 Years

7.4 Special precautions for storage

Store in a dry place below 30°C. Protect from light.

7.5 Nature and contents of container

PVC/ALU blister packing

7.6 Instructions for use, handling and disposal

No special requirements

8 Registrant

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9 Manufacturer

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