**SUMMARY OF PRODUCT CHARACTERISTICS**

# FUSID TABLETS

Tablets

## 1. Name of the medicinal product

Fusid tablets

## 2. Qualitative and quantitative composition

Each tablet contains 40 mg Furosemide

For the full list of excipients, see section Error! Reference source not found..

## 3. Pharmaceutical form

White, round flat tablet, engraved "TEVA" on one side and bisected on the other side of the tablets.

## 4. Clinical particulars

### 4.1. Therapeutic Indications

If gastrointestinal absorption is impaired or oral administration is not practical for any reason, and for patients in emergency clinical situations, Fusid is indicated by the intravenous or the intra-muscular route. Parenteral use should be replaced with oral Fusid as soon as practical.

- Treatment of edema associated with congestive heart failure, cirrhosis of the liver and renal disease, including the nephrotic syndrome.
- Adjunctive therapy in acute pulmonary edema.
- Treatment of hypertension.

### 4.2. Posology and method of administration

*Posology*

Since furosemide is a potent diuretic which, if given in excessive amounts, can lead to profound diuresis with water and electrolyte depletion, careful medical supervision is required. Dosage should be adjusted to the individual needs of each patient.

*Adults*

*Edema:* The usual initial dose is 20-80 mg/day administered as a single dose. Usually, prompt diuresis ensues. Depending on the response, a second dose should be administered 6-8 hours later. If the diuretic response is unsatisfactory, the dose should be increased by increments of 20 or 40 mg, no sooner than 6-8 hours after previous dose, until the desired diuretic effect has been obtained. This individually-determined dose should then be administered 1-2 times a day. In patients with severe edema, dosage may be titrated up to 600 mg/day.
Mobilization of edema may be most efficiently and safely accomplished with an intermittent dosage schedule. Furosemide should be administered on 2-4 consecutive days, each week. With doses exceeding 80 mg/day, clinical and laboratory observations are recommended.

*Hypertension*: The usual initial dosage is 40 mg, twice a day. Dosage should be adjusted according to response. If a patient does not respond, other antihypertensive agents should be

added. Blood pressure changes should be observed when used with other antihypertensives, especially during initial therapy. The dosage of other agents should be reduced by at least 50% as soon as furosemide is added, to prevent excessive drop in blood pressure. As blood pressure falls, either the dose should be reduced or the other antihypertensives discontinued.

*Infants and Children*

The usual initial dose of furosemide in infants and children is 2 mg/kg body weight. If diuretic response after the initial dose is unsatisfactory, dosage may be increased by 1-2 mg/kg body weight, but no sooner than 6-8 hours after the first dose. Doses greater than 6 mg/kg are not recommended. For maintenance therapy, the dose should be adjusted to the minimum effective level.

## 4.3. Contraindications

Furosemide is contraindicated in the following circumstances:

- Hypersensitivity to furosemide, any of its excipients listed in section 6.1, sulfonamides, sulfonamide derivatives/amiloride
- Anuria and impaired renal function (creatinine clearance below 30mL/min per 1.73 m2 body surface area) and renal failure resulting from poisoning by nephrotoxic and/or hepatotoxic agents
- Electrolyte disturbances (severe hyponatraemia: severe hypokalaemia, hypovolaemia), dehydration and/or hypotension (see section 4.4)
- Concomitant potassium supplements or potassium sparing diuretics (see section 4.5)
- Pre-coma/coma associated with hepatic cirrhosis or encephalopathy
- Addison's disease
- Digitalis intoxication (see also section 4.5)
- Breast-feeding women (see section 4.6)

## 4.4. Special warnings and precautions for use

*Hypotension and/or hypovolaemia (see also section 4.3)*

These and any acid-base disturbances should be corrected before furosemide is started.

Symptomatic hypotension leading to dizziness, fainting or loss of consciousness can occur in patients treated with furosemide, particularly in the elderly, patients on other medications which can cause hypotension and patients with other medical conditions that are risks for hypotension.

*Dose titration/adjustment (see section 4.2)*

- Patients with hypoproteinaemia (such as associated with the nephrotic syndrome) require careful dose titration (reduced furosemide effect: increased risk of ototoxicity)
- In moderate liver congestion dosage adjustment may be needed

*Caution required*:

Caution needed in the following circumstances:

- impaired hepatic function (see sections ~~4.2 &~~ 4.3 and below – monitoring required)
- impaired renal function and hepato-renal syndrome (see section 4.3 and below –monitoring required)
- diabetes mellitus (latent diabetes may become overt insulin requirements in established diabetes may increase)
- elderly patients
- difficulty with micturition/potential obstruction in the urinary tract including prostatic hypertrophy (increased risk of acute retention).
- gout (increased risk of hyperuricaemia)

- patients at risk of pronounced fall in blood pressure.

*Clinical monitoring requirements (see also section 4.8)*:

Regular monitoring for:

- blood dyscrasias. If these occur, stop furosemide immediately
- liver damage
- idiosyncratic reactions

In premature infants there is a risk of development of nephrocalcinosis/ nephrolithiasis. Renal function must be monitored and renal ultrasonography performed.

*Laboratory monitoring requirements*:

- frequent BUN in first few months of treatment, periodically thereafter
- serum electrolytes with replacement as appropriate

*Other alterations in lab values*

- Serum creatinine and urea levels tend to rise during treatment
- Serum cholesterol and triglycerides may rise but usually return to normal within 6 months of starting furosemide.
- Furosemide should be discontinued before a glucose tolerance test

*Excipients*

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

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

- ***Antihypertensives*** – enhanced hypotensive effect possible with all types. Concurrent use with ACE inhibitors can result in marked falls in blood pressure. Furosemide should be stopped or the dose reduced before starting an ACE inhibitor. There is a risk of a first-dose effect with post-synaptic alpha blockers e.g. prazosin. Furosemide may interact with ACE inhibitors causing impaired renal function.
- ***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.
- ***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.
- ***Drugs associated with QT prolongation*** – cardiac toxicity may be increased by furosemide-induced hypokalaemia and/or hypomagnesaemia.
- ***Cardiac Glycosides*** – hypokalaemia and electrolyte disturbances (including magnesium) increases the risk of cardiac toxicity.
- ***Vasodilators*** – enhanced hypotensive effect with moxisylyte (thymoxamine) or hydralazine.
- ***Renin inhibitors*** – aliskiren reduces plasma concentrations of furosemide.
- ***Nitrates*** – enhanced hypotensive effect.
- ***Lithium***– Furosemide reduces lithium excretion with increased plasma lithium concentrations (risk of toxicity). Avoid concomitant administration unless plasma levels are monitored.
- ***Chelating agents*** – sucralfate may decrease the gastro-intestinal absorption of furosemide – the 2 drugs should be taken at least 2 hours apart.
- ***Lipid regulating drugs*** – ***Bile acid sequestrants*** *(*e.g. colestyramine, colestipol) – reduced absorption of furosemide - administer 2 to 3 hours apart.

- ***NSAIDs*** – increased risk of nephrotoxicity (especially if there is hypovolaemia). Indometacin and ketorolac may antagonise the effects of furosemide. In patients with dehydration or hypovolaemia, NSAIDs may cause acute renal insufficiency.
- ***Salicylates*** – effects may be potentiated by furosemide.
- ***Antibiotics*** – increased risk of ototoxicity with aminoglycosides, polymixins or vancomycin. Increased risk of nephrotoxicity with aminoglycosides or cefaloridine. Furosemide can decrease vancomycin serum levels after cardiac surgery.
- ***Antidepressants*** – enhanced hypotensive effect with MAOIs. Increased risk of postural hypotension with TCAs (tricyclic antidepressants). Possible increased risk of hypokalaemia with reboxetine.
- ***Antidiabetics*** –hypoglycaemic effects antagonised by furosemide.
- ***Insulin*** – requirements may be increased (see section 4.4).
- ***Antiepileptics*** – increased risk of hyponatraemia with carbamazepine. Diuretic effect reduced by phenytoin.
- ***Antihistamines*** – hypokalaemia with increased risk of cardiac toxicity.
- ***Antifungals*** – increased risk of hypokalaemia with amphoterecin.
- ***Anxiolytics and hypnotics*** – enhanced hypotensive effect. Chloral or triclorfos may displace thyroid hormone from binding site.
- ***CNS stimulants (drugs used for ADHD)*** – hypokalaemia increases the risk of ventricular arrhythmias.
- ***Corticosteroids*** – diuretic effect antagonised (sodium retention) and increased risk of hypokalaemia.
- ***Cytotoxics*** – increased risk of nephrotoxicity and ototoxicity with platinum compounds.
- ***Other diuretics*** – profound diuresis possible when furosemide given with metolazone. Increased risk of hypokalaemia with thiazides.
- ***Dopaminergics*** – enhanced hypotensive effect with levodopa.
- ***Immunomodulators*** – enhanced hypotensive effect with aldesleukin.
- ***Muscle relaxants*** – enhanced hypotensive effect with baclofen or tizanidine (see also *Anaesthetic agents* below – curare).
- ***Oestrogens and progestogens*** – diuretic effect antagonized.
- ***Prostaglandins*** – enhanced hypotensive effect with alprostadil.
- ***Sympathomimetics*** – increased risk of hypokalaemia with high doses of beta$_2$ sympathomimetics (such as bambuterol, femoterol, salbutamol, salmeterol and terbutaline).
- ***Theophylline*** – enhanced hypotensive effect.
- ***Probenecid*** – reduced renal clearance of furosemide and decreased diuretic effect.
- ***Anaesthetic agents*** – general anaesthetic agents may enhance the hypotensive effects of furosemide. The effects of curare may be enhanced by furosemide.
- ***Alcohol*** – enhanced hypotensive effect.
- ***Laxative abuse*** - increases the risk of potassium loss.
- ***Liquorice*** - excess intake may increase the risk of hypokalaemia

### 4.6. Pregnancy and lactation

The teratogenic and embryotoxic potential of furosemide in humans is unknown. There is little evidence of safety of high dose furosemide in human pregnancy, although the results of animal work, in general, show no hazardous effects.

The drug should not be used in pregnant women unless the benefits to the patient outweigh the possible risk to the foetus which includes persistence of patent ductus arteriosus (section 4.8).

Furosemide may inhibit lactation or may pass into the breast milk, it should therefore be used with caution in nursing mothers.

### 4.7. Effects on Ability to Drive and Use Machines

Patients should be warned that reduced mental alertness may impair ability to drive or operate dangerous machinery.

### 4.8. Undesirable effects

Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); Frequency not known (cannot be estimated from the available data).

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| **Blood and lymphatic system disorders:** | Uncommon: | aplastic anaemia |
| | Rare: | bone marrow depression (necessitates withdrawal of treatment), eosinophilia, leucopenia. |
| | Very rare: | haemolytic anaemia, agranulocytosis, thrombocytopenia |
| **Metabolism and nutritional disorders:** | Very common: | dehydration, hyponatraemia, hypochloremic metabolic alkalosis, hypocalcaemia, hypomagnesemia (incidences of the last three are reduced by triamterene) |
| | Common: | Hypovolaemia, hypochloraemia |
| | Uncommon: | impaired glucose tolerance (by hypokalaemia) hyperuricaemia, gout, reduction of serum HDL- cholesterol, elevation of serum LDL-cholesterol, elevation of serum triglycerides, hyperglycaemia |
| | Very rare: | tetany |
| | Frequency not known: | aggravated pre-existing metabolic alkalosis (in decompensated cirrhosis of the liver), fluid and electrolyte disturbances, excretion of potassium increased* |
| **Psychiatric disorder:** | Rare: | psychiatric disorder NOC |
| **Nervous system disorders:** | Rare: | paraesthesia, confusion, headache |
| | Not known: | dizziness, fainting and loss of consciousness (caused by symptomatic hypotension) |
| **Eye disorders:** | Uncommon: | visual disturbance, blurred vision, yellow vision. |
| **Ear and labyrinth disorders:** | Uncommon: | deafness (sometimes irreversible) |
| | Rare: | tinnitus and reversible or irreversible loss of hearing (although usually transitory, particularly in patients with renal failure, hypoproteinaemia (e.g. in nephritic syndrome)) |
| **Cardiac disorders:** | Uncommon: | orthostatic intolerance, cardiac arrhythmias, increased risk or persistence of patent ductus arteriosus in premature infants. |
| **Vascular disorders:** | Very common: | hypotension, (which, if pronounced may cause signs and symptoms such as impairment of concentration and reactions, light-headedness, sensations of pressure in the head, headache, drowsiness, weakness, disorders of vision, dry mouth, orthostatic intolerance). |
| | Rare: | vasculitis, thrombosis, shock |
| **Gastrointestinal disorders:** | Uncommon: | dry mouth, thirst, nausea, bowel motility disturbances, vomiting, diarrhoea, constipation |
| | Rare: | acute pancreatitis (in long-term diuretic treatment, including furosemide). |

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| **Hepatobiliary disorders:** | Rare: | pure intrahepatic cholestasis (jaundice), hepatic function abnormal. |
| **Skin and subcutaneous tissue disorders:** | Rare: | rash, pruritus, photosensitivity, toxic epidermal necrolysis. |
| | Frequency not known: | urticaria, erythema multiforme, purpura, exfoliative dermatitis, itching, allergic reactions, such as skin rashes, various forms of dermatitis including urticaria, bullous lesions, acute generalised exanthematous pustulosis (AGEP). When these occur treatment should be withdrawn, Stevens- Johnson syndrome. |
| **Musculoskeletal and connective tissue disorders:** | Uncommon: | muscle cramps, muscle weakness. |
| **Renal and urinary disorders:** | Very common: | nephrocalcinosis in infants |
| | Uncommon: | reduced diuresis, urinary incontinence, urinary obstruction (in patients with hyperplasia of the prostate, bladder inability to empty, urethral stricture unspecified). |
| | Rare: | acute renal failure. |
| | Very rare: | interstitial nephritis |
| **Congenital, familial and genetic disorders:** | Rare: | patent ductus arteriosus |
| **General disorders and administration site conditions:** | Uncommon: | Fatigue |
| | Rare: | malaise, fever, severe anaphylactoid or anaphylactic reactions (e.g. with shock). |
| **Investigations:** | Common: | creatinine increased, blood urea increased |
| | Rare: | Transaminases increased, blood |

* Potassium deficiency manifests itself in neuromuscular symptoms (muscular weakness, paralysis), intestinal symptoms (vomiting, constipation, meterorism), renal symptoms (polyuria) or cardiac symptoms. Severe potassium depletion can result in paralytic ileus or confusion, which can result in coma.

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il

### 4.9. Overdosage

Symptoms include dehydration and electrolyte depletion due to excessive diuresis. In cirrhotic patients, overdosage may precipitate hepatic coma.

Treatment should be aimed at fluid replacement and correction of the electrolyte imbalance. The drug should be discontinued and electrolyte and water replacement instituted immediately; adjustment should be on the basis of careful monitoring.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamic properties

ATC code: CO3C A01

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 and a hypotonic or isotonic urine produced.

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

### 5.2. Pharmacokinetic properties

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.

### 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 of the SPC.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1. List of excipients

Also contains:
Lactose, microcrystalline cellulose, starch, crospovidone, povidone, colloidal silicon dioxide, magnesium stearate, propylparaben, butylparaben.

Lactose content per tablet: 36 mg.

### 6.2. Incompatibilities

None known.

### 6.3. Shelf life

The expiry date of the product is indicated on the packaging materials.

### 6.4. Special precautions for storage

Store in a cool and dry place, below 25°C.

### 6.5. Nature and contents of container

The product is supplied in PVC/aluminum blisters packed in carton box of: 25, 30, 50 and 1000 tablets.

Not all pack sizes may be marketed.

### 6.6. Special precautions for disposal and other handling

Not applicable.

## 7. LICENSE HOLDER AND MANUFACTURER

Teva Pharmaceutical Industries Ltd.
P.O.Box 3190, Petach-Tikva.

## 8. REGISTRATION NUMBER

020.20.20472

**The leaflet was revised in December 2020**