SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Furosemide Teva 125 mg, tabletten
Furosemide Teva 250 mg, tabletten
Furosemide Teva 500 mg, tabletten

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 125 mg of furosemide.
Each tablet contains 250 mg of furosemide.
Each tablet contains 500 mg of furosemide.

Excipient with known effect
Each tablet contains 32.1 mg of lactose monohydrate.
Each tablet contains 64.2 mg of lactose monohydrate.
Each tablet contains 128.4 mg of lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

125 mg: White or almost white, round, biconvex tablets, breakline on one side, the other side is plain. Diameter: approx. 9 mm
250 mg: White or almost white, round, biconvex tablets, with two crossed breaklines on one side of the tablet, the other side is plain. Diameter: approx. 11 mm
500 mg: White or almost white, round, biconvex tablets, with two crossed breaklines on one side of the tablet, the other side is plain. Diameter: approx. 14 mm

The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[Product name] tablets are indicated in adult patients with oedema and severely reduced glomerular filtration (glomerular filtration rate (GFR) < 20 ml/min).

4.2 Posology and method of administration

Posology

The dosage should be adjusted individually, predominantly on the basis of response to treatment. The lowest effective dose should always be used.

Adults

For nephrotic syndrome, the dose is generally 250 mg to 500 mg furosemide daily. For other indications, the dose may vary from 250 mg to 1500 mg furosemide daily.

The dose should be carefully adjusted in patients with chronic renal insufficiency in order to gradually resolve oedema.

The patient's hydration status and serum electrolytes should be monitored and the response to treatment periodically evaluated.

The duration of treatment depends on the nature and severity of the disease.

Paediatric population

The safety and efficacy of [Product name] 125 mg, 250 mg and 500 mg strengths in children and adolescents under 18 years of age have not been established. No data are available. Other pharmaceutical forms/strengths may be more appropriate for administration to this population.

Elderly

Cautious titration starting with low dose is recommended until the required response is achieved.

Method of administration
For oral administration. The tablets should be swallowed without chewing with plenty of liquid and on an empty stomach.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Patients who are allergic to sulfonamides (e.g. sulfonamide antibiotics or sulfonylureas) may have cross sensitivity to furosemide.
- Normal renal clearance and reduced renal function with GFR > 20 ml/min, due to risk of severe fluid and electrolyte loss in such cases
- Precoma or coma associated with hepatic encephalopathy
- Renal failure with anuria
- Hypokalaemia
- Hyponatremia
- Hypovolaemia or dehydration
- Lactation
- Cardiac glycoside (e.g. digoxin, digitoxin) intoxication
- Addison's disease

4.4 Special warnings and precautions for use

The diuretic effect should be monitored regularly.

Particularly careful monitoring is required in patients with:

- Hypotension
- Gout (serum uric acid should be monitored regularly)
- Urinary tract obstruction (*e.g.* prostate hypertrophy, hydronephrosis, ureteral stenosis)
- Hypoproteinaemia, *e.g.* in nephrotic syndrome (the dose should be carefully titrated)
- Hepatic cirrhosis and concomitant renal impairment
- Patients at particular risk from a sudden, unexpected drop in blood pressure, *e.g.* patients with cerebrovascular disorders or coronary heart disease
- In premature infants (risk of developing nephrocalcinosis/nephrolithiasis; the renal function should be monitored and renal sonography carried out).

Furosemide should only be used in patients with a clear reduction in glomerular filtration. Otherwise there is a risk of excessive fluid and electrolyte loss.

Photosensitivity reactions have been reported with furosemide (see section 4.8). If photosensitivity reactions occur during treatment, it is recommended that treatment be discontinued. If re-

administration of treatment is necessary, it is recommended that areas exposed to the sun or artificial UVA light be protected.

In premature children with respiratory distress syndrome, diuretic treatment with furosemide in the first weeks of life may increase the risk of a patent *ductus arteriosus*.

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 represent a risk of hypotension.

Serum electrolytes (mainly potassium, sodium, calcium, magnesium, chloride), bicarbonate, creatinine, urea, uric acid and blood glucose should be monitored regularly during long-term treatment with furosemide. Regular monitoring is necessary in patients at high risk of developing electrolyte disorders or in the event of significant fluid loss (e.g. due to vomiting, diarrhoea or intense sweating). Hypovolemia, dehydration, significant electrolyte disorders and acid-base disorders should be corrected and treatment discontinued if necessary.

Hypokalemia

Hypokalemia should be taken into account, especially in elderly patients, patients with liver cirrhosis, concomitant treatment with corticosteroids, one-sided diet and laxative abuse. It is advisable to always regularly monitor the plasma potassium concentration, especially at higher doses and in patients with renal impairment, and to provide additional potassium therapy if necessary. This is particularly important during concurrent treatment with digoxin, because a potassium deficiency can provoke or worsen the symptoms of digitalis intoxication. With long-term use of [Product name], it is recommended to prescribe a potassium-rich diet (potatoes, bananas, tomatoes, citrus fruits, fruit juices, dried fruits, cauliflower and spinach).

Blood glucose

The hyperglycaemic effect is modest. Blood glucose control monitoring should be reinforced in diabetics and pre-diabetics.

Renal function

Strong diuresis with impaired renal function can cause reversible renal function impairment. Adequate fluid administration is necessary in such patients. Renal function should therefore be monitored regularly.
Urinary outflow must be guaranteed. In patients with partial obstruction of the urinary tract (for example patients with hydronephrosis, nephrolithiasis, bladder disorders, prostatic hyperplasia or ureteral stricture), increased urine production can cause or worsen complaints. These patients should be closely monitored, especially during the initial phase of treatment.

Metabolism

A pre-existing metabolic alkalosis may worsen during treatment with [Product name] (e.g. in decompensated liver cirrhosis).
During treatment with [Products name], the uric acid level of the plasma may increase; This only exceptionally leads to gout symptoms.
The cholesterol and triglyceride levels in the blood may also be temporarily increased. With continued treatment, the values usually return to normal within six months.

Hypercalcemia

In acute hypercalcemia, the patient will often be dehydrated as a result of vomiting and diuresis. Therefore, one should correct the dehydration condition before administering [Product name]. Treatment of hypercalcemia with high dose furosemide will result in fluid and electrolyte loss.

Accurate fluid replacement and electrolyte correction is necessary with this treatment.

Levothyroxine

High doses of furosemide can hinder (inhibit) the protein binding of thyroid hormones, which may initially lead to an increased level of free thyroid hormone, which progresses to a general decrease in the total thyroid hormone level. Thyroid hormone levels should be monitored.

The weight loss resulting from increased urine excretion should not exceed 1 kg/day independently from the degree of urine excretion.

The dose should be adjusted with caution in patients with nephrotic syndrome owing to the increased risk of adverse events.

Concomitant administration with risperidone

A higher incidence of mortality was observed in placebo-controlled studies in elderly patients with dementia in individuals treated with furosemide and risperidone (7.3%, average age 89 years, range 75-97 years) compared to those on risperidone alone (3.1%, average age 84 years, range 70-96 years) or furosemide alone (4.1%, average age 80 years, range 67-90 years). The concomitant administration of risperidone with other diuretics (mostly low-dose thiazides) was not associated with a similar finding.

No pathophysiological mechanism and no single causal pattern for the deaths emerged from these observations. Consequently, caution is required, and the risks and indication of this combination or the association of other potent diuretics with risperidone should be weighed before initiating treatment. The incidence of mortality was not increased in patients treated with other diuretics in combination with risperidone. Independently from treatment, dehydration was a general risk factor for mortality and should therefore be avoided in elderly patients with dementia (see section 4.3).

There is a possibility of exacerbation or activation of systemic lupus erythematosus.

Furosemide is not recommended for preventative diuresis in patients at high risk for radiocontrast nephropathy (see section 4.5).

Excipient(s)

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

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say it is essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

The concomitant administration of furosemide and glucocorticoids, carbenoxolone or laxatives may lead to increased potassium loss with the risk of hypokalaemia. Large quantities of liquorice act like carbenoxolone in this respect.

Concomitant administration of carbamazepine may increase the risk of hyponatraemia

Non-steroidal anti-inflammatory agents (NSAIDs) (*e.g.* indomethacin, acetylsalicylic acid) may reduce the effect of furosemide. NSAIDs may lead to acute renal failure in patients on furosemide who develop hypovolaemia or dehydration.

Probenecid, methotrexate and other agents which undergo significant renal tubular secretion like furosemide may reduce its effect. Furosemide may reduce the renal elimination of such substances which may result in increased serum levels and a higher risk of adverse events, especially in patients on high-dose therapy of either furosemide or the associated agent.

The concomitant administration of phenytoin has been reported to reduce the effect of furosemide.

As sucralfate reduces the intestinal uptake of furosemide and therefore reduces its effect, the two substances should be administered at least 2 hours apart.

It should be taken into account that myocardial sensitivity to cardiac glycosides may be increased owing to furosemide-induced hypokalaemia and/or hypomagnesaemia. The risk of ventricular arrhythmias (including *torsades de pointes*) may be increased in combination with agents associated with long QT syndrome (*e.g.* terfenadine, some class I and III anti-arrhythmic agents) and in the presence of electrolyte disorders.

The toxicity of high-dose salicylates may be increased during concomitant treatment with furosemide.

Furosemide may increase the adverse effects of nephrotoxic agents (*e.g.* antibiotics such as aminoglycosides, cephalosporins, polymyxins).

Deterioration of renal function may occur in patients receiving furosemide concomitantly with high doses of some cephalosporins.

The ototoxicity of aminoglycosides (*e.g.* kanamycin, gentamicin, tobramycin) and other ototoxic agents may be increased when they are used concomitantly with furosemide. The resulting hearing disturbances may be irreversible. The association of these agents should therefore be avoided.

The possibility of hearing disorders should be taken into account when administering cisplatin and furosemide together. If forced diuresis with furosemide is considered necessary during treatment with cisplatin, furosemide should only be used in low doses (*e.g.* 40 mg for normal renal function) and within patients with a positive fluid balance. Otherwise, the nephrotoxicity of cisplatin may be increased.

The combination of furosemide and lithium leads to reduced lithium excretion and consequently to an increase in the cardio- and neurotoxic effects of lithium. Lithium levels should therefore be carefully monitored in patients requiring such combined treatment.

A marked fall in blood pressure should be expected on concomitant administration of furosemide with other antihypertensives, diuretics or agents with the potential to decrease the blood pressure. In particular, massive reductions in blood pressure to the point of shock and worsening of renal function (in isolated cases acute renal failure) have been reported when angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARB) were administered for the first time, or for the first time at a higher dose. Where possible, furosemide should therefore be temporarily discontinued or at least the dose reduced for 3 days prior to the initiation or up-titration of ACE inhibitor or ARB treatment.

Furosemide may increase the effect of theophylline and curare-type muscle relaxants.

Furosemide may reduce the effect of anti-diabetic agents and sympathomimetics (*e.g.* epinephrine, norepinephrine).

Caution should be exercised in patients treated with risperidone, and the risks and benefits of combination or concomitant treatment with furosemide or other potent diuretics should be weighed prior to the decision to use (see section 4.4).

High doses of furosemide can inhibit the binding of thyroid hormones (*e.g.* levothyroxine) to transport

proteins. This can result in an initial, transient increase in free thyroid hormone, followed by an overall decrease in total thyroid hormone levels. Thyroid hormone levels should be monitored.

Concomitant use of ciclosporin A and furosemide is associated with an increased risk of uric arthritis as a result of furosemide-induced hyperuricemia and impairment of renal uric acid excretion by ciclosporin.

Patients under treatment with furosemide were more likely to experience kidney damage from X-ray contrast agents than those at risk who received only intravenous fluid (Hydration) before contrast examination.

In isolated cases, hot flushes, perspiration, unrest, nausea, increases in blood pressure and tachycardia have been observed within 24 hours after the administration of chloral hydrate and intravenous furosemide. The concomitant use of furosemide and chloral hydrate should therefore be avoided.

Aliskiren reduces the plasma concentration of orally administered furosemide. It is recommended to monitor the diuretic effect of furosemide when starting and adjusting the dose of concomitant treatment with aliskiren.

4.6 Fertility, pregnancy and lactation

Pregnancy

Furosemide should only be used during pregnancy for short periods if absolutely necessary, as it crosses the placenta.

Diuretics are not routinely indicated for the treatment of hypertension and oedema in pregnancy since they reduce placental perfusion and consequently intra-uterine growth.

If furosemide is required to treat cardiac or renal insufficiency in pregnancy, electrolyte and haematocrit levels and fetal growth must be monitored closely. Displacement of bilirubin from albumin binding and a resulting increase in the risk of nuclear jaundice in hyperbilirubinaemia have been reported with furosemide.

Furosemide crosses the placenta and reaches 100% of maternal serum concentrations in umbilical blood. No malformations have been reported in humans to date which could be linked to exposure to furosemide. There are insufficient data to definitively determine its potential harmful effects on the embryo/fetus. Fetal urine production *in utero* may be stimulated. Urolithiasis has been reported in premature infants treated with furosemide.

Breast-feeding

Furosemide is excreted in breast milk and inhibits lactation. Furosemide should therefore not be given to breast-feeding women. Otherwise, breast-feeding should be discontinued (see section 4.3).

4.7 Effects on ability to drive and use machines

Furosemide has minor influence on the ability to drive and use machines. It may elicit diverse individual reactions which might impair the ability to drive and use machines, especially at the beginning therapy, on increasing the dose or changing the treatment and in association with alcohol.

4.8 Undesirable effects

Adverse events are categorised by following frequencies:

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)
Not known	(cannot be estimated from the available data)

Blood and lymphatic system disorders

Common:	Haemoconcentration (with excessive diuresis)
Uncommon:	Thrombocytopenia
Rare:	Eosinophilia, leucopenia
Very rare:	Haemolytic anaemia, aplastic anaemia, agranulocytosis

Immune system disorders

Uncommon:	Pruritus, skin and mucous membrane reactions (see skin and subcutaneous disorders)
Rare:	Severe anaphylactic and anaphylactoid reactions such as anaphylactic shock (see section 4.9)
Not known:	Exacerbation or activation of systemic lupus erythematosus

Endocrine disorders:
The glucose tolerance may deteriorate with furosemide and hyperglycaemia may develop. In patients with manifest diabetes mellitus this may lead to worsening of the metabolic situation. Latent diabetes mellitus may become manifest.

Metabolism and nutrition disorders (see section 4.4)

Very common:	Electrolyte disorders (including symptomatic), dehydration and hypovolaemia (especially in elderly patients), increased blood triglycerides
Common:	Hyponatraemia, hypochloraemia, hypokalaemia, increased blood cholesterol, increased blood uric acid and gout attacks
Not known:	Hypocalcaemia, hypomagnesaemia, hyperglycaemia, metabolic alkalosis, pseudo-Bartter syndrome

Fluid and electrolyte disorders are frequently observed during treatment with furosemide owing to the increased electrolyte excretion. Regular monitoring of serum electrolytes (in particular potassium, sodium and calcium) is therefore recommended.

The possibility of electrolyte disorders depends on co-morbidities (*e.g.* hepatic cirrhosis, cardiac insufficiency), concomitant therapy (see section 4.5) and nutrition.

Hyponatraemia and corresponding symptoms may result from increased renal sodium loss, in particular in the presence of reduced sodium intake. The commonest symptoms of sodium depletion are apathy, leg cramps, loss of appetite, vomiting and confusion.

Hypokalaemia, which may be associated with neuromuscular (muscle weakness, paraesthesia, paresis), intestinal (vomiting, constipation, tympanites), renal (polyuria, polydipsia) and cardiac (pacemaker and conduction disorders) symptoms, may result from increased renal potassium loss, especially with concomitant reduced potassium intake and/or increased extra-renal potassium loss (*e.g.* with vomiting or chronic diarrhoea). Severe potassium loss may lead to paralytic ileus or loss of consciousness and coma.

Increased calcium loss may lead to hypocalcaemia. In rare cases this may result in tetany.

Increased renal magnesium loss may lead to hypomagnesaemia and, in rare cases, result in tetany or cardiac rhythm disorders.

Metabolic alkalosis may develop or worsen as a consequence of electrolyte and fluid loss during treatment with furosemide.

Hyperuricaemia commonly develops during treatment with furosemide, which may lead to gout in predisposed patients.

Serum cholesterol and triglyceride levels may increase during treatment with furosemide.

Nervous system disorders

Common:	Hepatic encephalopathy in patients with hepatic insufficiency
Rare:	Paraesthesia, Hyperosmolar coma
Not known:	Dizziness, fainting and loss of consciousness (caused by symptomatic hypotension), headache

Ear and labyrinth disorders

Uncommon:	Deafness (sometimes irreversible), hearing impairment (usually reversible), particularly in patients with renal insufficiency or hypoproteinaemia (*e.g.* in nephrotic syndrome) and/or when intravenous injection is too rapid
Rare:	Tinnitus

Vascular disorders

Very common:	(With intravenous infusion) Hypotension, including orthostatic syndrome (see section 4.4)
Rare:	Vasculitis
Not known:	Thrombosis (especially in elderly)

Excessive diuresis may lead to circulatory disorders, especially in the elderly and children, which manifest primarily as headache, dizziness, visual disturbances, mouth dryness and thirst, hypotension and orthostatic regulation disorders. Dehydration, circulatory collapse due to hypovolaemia and haemoconcentration may occur. The latter may increase the risk of thrombosis, particularly in the elderly.

Gastrointestinal disorders

Uncommon:	Nausea
Rare:	Vomiting, diarrhoea.

Hepatobiliary disorders

Very rare:	Acute pancreatitis, intra-hepatic cholestasis, increased hepatic transaminase levels

Skin and subcutaneous tissue disorders

Uncommon:	Pruritus, skin and mucous membrane reactions (*e.g.* bullous exanthema, urticaria, rash, purpura, erythema multiforme, bullous pemphigoid, exfoliative dermatitis, photosensitivity)
Very rare:	Stevens-Johnson syndrome, toxic epidermal necrolysis
Not known:	Acute generalised exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms *(*DRESS), lichenoid reactions.

Musculoskeletal and connective tissue disorders

Not known:	Cases of rhabdomyolysis have been reported, often in association with severe hypokalaemia (see section 4.3)

Renal and urinary disorders

Very common:	Increased blood creatinine
Common:	Increased urine volume
Rare:	Interstitial nephritis
Not known:	Increased urine sodium, increase urine chloride, increase blood urea, symptoms of urinary tract obstructions (*e.g.* in prostate hyperplasia, hydronephrosis, ureteral stenosis) up to urinary obstruction (urinary retention) with secondary complications (see section 4.4), renal failure (see section 4.5)

Pregnancy, puerperium and perinatal conditions
Nephrolithiasis and/or nephrocalcinosis may occur in premature infants treated with furosemide.

In premature children with respiratory distress syndrome, diuretic treatment with furosemide in the first weeks of life may increase the risk of a patent *ductus arteriosus*.

General disorders and administration site conditions
Rare: Fever

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 national reporting system listed in Appendix V.

4.9 Overdose

Symptoms

The clinical picture of acute or chronic overdose depends on the degree of fluid and electrolyte loss. Overdose may lead to hypotension, orthostatic regulation disorders, electrolyte disorders (hypokalaemia, hyponatraemia, hypochloraemia) or alkalosis. Severe fluid loss may result in marked hypovolaemia, dehydration, circulatory collapse and haemoconcentration with risk of thrombosis. Delirium may occur with rapid fluid and electrolyte loss. Anaphylactic shock (symptoms: perspiration, nausea, cyanosis, severe hypotension, loss of consciousness, coma) may rarely develop.

Treatment

Furosemide must be immediately discontinued in the event of overdose or on development of signs of hypovolaemia (hypotension, orthostatic regulation disorders).

Primary poison management measures (induced vomiting, gastric lavage) and measures to reduce absorption (medicinal charcoal) should be taken if the overdose is recent.

In severe cases, vital signs must be monitored and the fluid, electrolyte and acid-base balance, blood glucose and renally excreted substances repeatedly evaluated, and any necessary corrective measures taken.

In patients with micturition disorders (*e.g.* prostate hypertrophy), an unobstructed flow of urine must be maintained, as a sudden flux of urine could lead to anuria with over-extension of the bladder.

Treatment of hypovolaemia: volume expansion
Treatment of hypokalaemia: potassium substitution
Treatment of circulatory collapse: shock position, if necessary, shock therapy
Immediate treatment measures in the event of anaphylactic shock: at the first signs (*e.g.* cutaneous reactions such as urticaria, flush, unrest, headache, perspiration, nausea, cyanosis)
- maintain circulation
- maintain patent airway, administer oxygen
- further measures, including intensive care measures, may be required (including administration of epinephrine, volume substitution, glucocorticoids).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diuretics, high-ceiling diuretics, sulfonamides, plain

ATC code: C03CA01

Mechanism of action
Furosemide is a potent, short- and rapid-acting loop diuretic. It inhibits sodium, chloride and potassium re-absorption in the ascending limb of the loop of Henle by blocking the $Na^+/2Cl^-/K^+$ transporter. Fractional sodium excretion may thus reach 35% of glomerular sodium filtration. As a result of the increased sodium excretion, urine secretion and distal tubular potassium secretion are augmented secondary to osmotic water movement. Calcium and magnesium excretion are similarly increased. Uric acid excretion may be reduced and the acid-base balance disrupted towards metabolic alkalosis in parallel with these electrolyte losses.

Pharmacodynamic effects
Furosemide interrupts the tubulo-glomerular feedback mechanism to the macula densa, so the diuretic effect is not reduced.

Furosemide causes dose-dependent stimulation of the renin-angiotensin-aldosterone system.

In heart failure, furosemide acutely reduces the cardiac preload by dilating venous capacity vessels. This early vascular effect seems to be mediated by prostaglandins and presupposes and sufficient renal function with activation of the renin-angiotensin-aldosterone system and intact prostaglandin synthesis.

Furosemide reduces blood pressure by increasing sodium excretion and reducing the reactivity of vascular smooth muscle to vasoconstrictive stimulation as well as by reducing blood volume.

5.2 Pharmacokinetic properties

Absorption
After oral administration, 60-70% of furosemide is absorbed from the gastrointestinal tract. This may be reduced to less than 30% in patients with chronic heart failure or nephrotic syndrome.

The onset of the effect of furosemide occurs after approximately 30 minutes. Peak plasma concentrations occur within approximately an hour after ingestion of a tablet.

Distribution
The plasma protein binding of furosemide is approximately 95%. This may be reduced to 10% in renal insufficiency. The relative volume of distribution is approximately 0.2 l/kg body weight (0.8 l/kg body weight in neonates).

Biotransformation
Furosemide is only slightly metabolised in the liver (approximately 10%) and is mostly excreted unchanged.

Elimination
Its elimination is two thirds renal, and one third biliary/faecal. The elimination half-life is approximately 1 hour with normal renal function; it may be increased up to 24 hours in terminal renal insufficiency.

5.3 Preclinical safety data

Acute oral toxicity was low in all species tested. Chronic toxicity studies in the rat and dog led to renal alterations (among others fibrous degeneration and renal calcification).

In vitro and *in vivo* tests of genetic toxicology did not reveal any clinically relevant evidence of a genotoxic potential of furosemide.

Long-term studies in mice and rats did not yield any relevant evidence of a tumorigenic potential.

Reproduction toxicity studies with high doses revealed a reduced number of differentiated glomeruli, skeletal abnormalities in the scapula, humerus and ribs due to hypokalaemia in rat fetuses, and hydronephrosis in mouse and rabbit fetuses.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cellulose, microcrystalline E460
Lactose monohydrate
Povidone K90 E1201
Sodium starch glycolate Type A
Magnesium stearate E470b

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in the original package in order to protect from light. Keep blisters in the outer carton.

6.5 Nature and contents of container

[*125 mg*]
PVC-Alu blisters containing 10, 20, 30, 50 or 100 tablets and unit-dose blisters containing 10x1, 20x1, 30x1, 50x1 or 100x1 tablets.

HDPE bottles with PP cap with aluminium seal containing 50, 100, 105 or 200 tablets.

[*250 mg*]
PVC-Alu blisters containing 10, 20, 30, 50 or 100 tablets and unit-dose blisters containing 10x1, 20x1, 30x1, 50x1 or 100x1 tablets.

HDPE bottles with PP cap with aluminium seal containing 50, 100, 105 or 200 tablets.

[*500 mg*]
PVC-Alu blisters containing 20, 30, 50 or 100 tablets.

HDPE bottles with PP cap with aluminium seal containing 50, 100, 105 or 200 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Teva B.V.
Swensweg 5
2031 GA Haarlem
Nederland

8. MARKETING AUTHORISATION NUMBER(S)

RVG 133838 – 125 mg, tabletten
RVG 133839 – 250 mg, tabletten
RVG 133840 – 500 mg, tabletten

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Datum van eerste verlening van de vergunning: 9 december 2025

10. DATE OF REVISION OF THE TEXT