SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Furosemid Hexal 40 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 40 mg furosemide.

Excipients with known effect
Each tablet contains 61,8 mg lactose (as monohydrate).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

White, round tablet, lightly convex with one sided score notch.

The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

1) Treatment of oedema associated with
- **cardiac disease**
- **liver disease**
- **renal disease including nephrotic syndrome; in patients with nephrotic syndrome, therapy of the underlying disorder has priority.**

Treatment of pulmonary oedema.

2) Arterial hypertension

4.2 Posology and method of administration

Posology
The usual initial adult dose is 20−40 mg daily; however the dose may need adjusting on an individual basis until an effective dose is achieved.

The subsequent dose guidelines apply to adults:

Hypertension
The usual dose is 40 mg furosemide once daily.
In severe cases up to 60 mg furosemide per day. In case of insufficient response combination with non-diuretic antihypertensives is recommended.

Oedema associated with cardiac or hepatic diseases
The usual initial dose in adults is 20−40 mg furosemide. If the diuretic response is not satisfactory, the single dose can be doubled to 80 mg furosemide after 6 hours. If there is still inadequate diuresis, an additional dose of 160 mg furosemide can be given after a further 6 hours.

The daily maintenance dose is usually 40−80 mg furosemide.

Oedema associated with renal diseases
The usual initial dose in adults is 40 mg furosemide. If the diuretic response is not satisfactory, the single dose can be doubled to 80 mg furosemide after 6 hours. If there is still inadequate diuresis, an additional dose of 160 mg furosemide can be given after a further 6 hours.

The daily maintenance dose is usually 40−80 mg furosemide.

A higher dose (IV administration) may be required in patients with renal insufficiency.
In patients with nephrotic syndrome, the dose must be determined with caution, because of the risk of a higher incidence of adverse reactions.

Paediatric population
The usual initial dose for oral furosemide in infants and children is 2 mg/kg body weight given as a single dose. If the diuretic response is not satisfactory after the initial dose, dose may be increased by 1 or 2 mg/kg no sooner than 6 to 8 hours after the previous dose (maximum of 40 mg daily).

Elderly
The dose recommendations for adults apply. In general furosemide is eliminated more slowly in elderly patients; the dose should be titrated until a satisfactory response is achieved.

Renal impairment
In case of renal insufficiency less furosemide will reach the renal tubules.
An increase of dose may be necessary to obtain the same diuretic effect.

Hepatic impairment
No dose adjustment is needed for patients with mild hepatic impairment; however the dose may require adjustment in cases of moderate to severe hepatic impairment.

Method of administration
For oral administration.

It is recommended that furosemide tablets are taken on an empty stomach, and with plenty of liquid.

4.3 Contraindications

Furosemide must not be administered in cases of:
- **hypersensitivity to the active substance, sulphonamides (possible cross-reacting allergy with furosemide) or to any of the excipients listed in section 6.1,**
- **renal failure with anuria not responding to furosemide treatment,**
- **hepatic coma and precoma associated with hepatic encephalopathy,**
- **severe hypokalaemia (see section 4.8),**
- **severe hyponatraemia,**
- **hypovolaemia or dehydration,**
- **breast-feeding women.**

4.4. Special warnings and precautions for use

Particularly careful monitoring is necessary in case of:

- **hypotension,**
- **manifest or latent diabetes mellitus (regular monitoring of blood glucose values),**
- **gout (regular monitoring of uric acid in serum),**
- **urinary obstruction (e.g. prostatic hypertrophy, hydronephrosis, ureterostenosis),**
- **hypoproteinaemia, e.g. in nephrotic syndrome (careful titration of the dose),**
- **hepatorenal syndrome (rapidly progressive renal insufficiency associated with severe liver disease, e.g. liver cirrhosis),**
- **patients who are at special risk from a pronounced fall in blood pressure, e.g. patients with cerebrovascular perfusion disorders or coronary heart disease,**
- **premature infants (risk of development of nephrocalcinosis/nephrolithiasis; control measures: check of renal function, renal sonography).**

In premature infants with respiratory distress syndrome, diuretic treatment with furosemide during the first weeks of life can increase the risk of persistent ductus arteriosus Botalli.

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.

Furosemide may be used in patients with impaired micturition (e.g. in prostatic hypertrophy) only if diuresis is not impaired, as sudden polyuria may lead to ischuria with overextension of the bladder.

Impairment of electrolyte and fluid balance as a consequence of increased electrolyte excretion are commonly observed during therapy with furosemide. Regular monitoring of serum electrolytes (especially potassium, sodium and calcium) is therefore indicated.

In particular during long-term therapy with furosemide, regular monitoring of serum electrolytes (especially potassium, sodium, calcium), bicarbonate, creatinine, urea and uric acid, as well as blood glucose is recommended.

An especially close monitoring is necessary in patients with a high risk of developing electrolyte disorders or in case of higher fluid losses (e.g. due to emesis, diarrhoea or intense diaphoresis). Hypovolaemia or dehydration as well as considerable electrolyte disorders or disorders in the acid-base balance must be corrected. This may require treatment to be discontinued temporarily.

Possible development of electrolyte disorders is influenced by underlying disorders (e.g. hepatocirrhosis, heart failure), concomitant medication (see section 4.5) and nutrition.

The weight loss caused by increased urinary excretion should not exceed 1 kg/day, irrespective of the extent of urinary excretion.

Cautious dosing is required in case of nephrotic syndrome due to the risk of increasing adverse events.

During long-term treatment with furosemide, a potassium rich diet is always indicated (e.g. potatoes, bananas, tomatoes, spinach, dry fruits). Sometimes a medicinal substitution of potassium is recommended. In other cases (i.e. liver cirrhosis), it is indicated to prevent hypokalaemia and metabolic alkalosis by administering a potassium sparing agent.

<u>Concomitant use with risperidone</u>
In risperidone placebo-controlled trials in elderly patients with dementia, a higher incidence of mortality was observed in patients treated with furosemide plus risperidone

(7.3%; mean age 89 years, range 75−97 years) when compared to patients treated with risperidone alone (3.1%; mean age 84 years, range 70−96 years) or furosemide alone (4.1%; mean age 80 years, range 67−90 years). Concomitant use of risperidone with other diuretics (mainly thiazide diuretics used in low dose) was not associated with similar findings.

No pathophysiological mechanism has been identified to explain this finding, and no consistent pattern for cause of death observed. Nevertheless, caution should be exercised and the risks and benefits of this combination or co-treatment with other potent diuretics should be considered prior to the decision to use. There was no increased incidence of mortality among patients taking other diuretics as concomitant treatment with risperidone. Irrespective of treatment, dehydration was an overall risk factor for mortality and should therefore be avoided in elderly patients with dementia (see section 4.3).

The possibility exists of exacerbation or activation of systemic lupus erythematosus.

Special warnings regarding excipients
This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of other medicinal products on furosemide

Co-administration of furosemide and glucocorticoids, carbenoxolone or laxatives may lead to enhanced losses of potassium with the risk of developing hypokalaemia. Large amounts of liquorice have the same effect in this regard like carbenoxolone.

Non-steroidal antiphlogistics (e.g. indomethacin and acetylsalicylic acid) can reduce the effect of furosemide. In patients developing hypovolaemia on furosemide therapy or in case of dehydration, concurrent administration of non-steroidal antiphlogistics may induce acute renal failure.

Probenecid, methotrexate and other medicinal products – with like furosemide considerable tubular secretion in the kidneys – can diminish the effect of furosemide. Conversely, furosemide can reduce the renal elimination of probenecid, methotrexate and other medicinal products with like furosemide considerable tubular secretion in the kidneys. In high-dosed treatment (especially with furosemide as well as with other medicinal products), this may lead to elevated serum levels of furosemide or adjuvant medication and a higher risk of side effects.

In concurrent administration of phenytoin, an attenuated effect of furosemide was described.

Furosemide and sucralfate must not be taken within 2 hours of each other because sucralfate decreases the absorption of furosemide from the intestine and so reduces its effect.

Effects of furosemide on other medicinal products

Cardiac glycosides and other medicinal products which may induce prolongation of the QT interval (e.g. terfenadine, some antiarrhythmic of classes I and III): induced hypokalaemia and/or hypomagnesaemia may potentiate the effect of cardiac glycosides and aggravate the risk of ventricular arrhythmias.

The toxicity of high-dosed salicylates can be potentiated in concomitant use of furosemide.

Furosemide can enhance the toxic effects of nephrotoxic antibiotics (e.g. aminoglycosides, cephalosporins, polymyxins).

Impairment of renal function may develop in patients receiving concurrent treatment with furosemide and high doses of certain cephalosporins.

The ototoxicity of aminoglycosides (e.g. kanamycin, gentamicin, tobramycin) and other ototoxic medicinal products may be increased in concurrent administration of furosemide. Dysacusis can be irreversible. Concomitant use of the above named medicinal products should therefore be avoided.

If furosemide is used concomitantly with cisplatin, the possibility of auditory damage is to be expected. If forced diuresis with furosemide is aimed at during cisplatin treatment, furosemide may be administered only at low dose (e.g. 40 mg in normal renal function) and in positive fluid balance. Otherwise, increased nephrotoxicity of cisplatin may occur.

Co-administration of furosemide and lithium leads to an increase in the cardiotoxic and neurotoxic effects of lithium via reduced lithium excretion. It is therefore recommended to carefully monitor the lithium plasma level of patients receiving this combination.

A marked fall in blood pressure should be expected on concomitant administration of furosemide with other antihypertensives, diuretics or medicinal products with the potential to decrease the blood pressure. Massive reduction in blood pressure to the point of shock in extreme cases and worsening of renal function (acute renal failure in isolated cases) 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 high dose. If possible, furosemide therapy should be temporarily discontinued or the furosemide dose should be reduced for three days before therapy with an ACE inhibitor is initiated or the dose of an ACE inhibitor is increased.

The effect of theophylline or curariform muscle relaxants can be potentiated due to furosemide.

The effect of antidiabetics or pressor amines (e.g. epinephrine, norepinephrine) can be attenuated in concomitant use of furosemide.

Caution should be exercised and the risks and benefits of the combination or co-treatment of risperidone with furosemide or with other potent diuretics should be considered prior to the decision to use (see section 4.4 regarding increased mortality in elderly patients with dementia concomitantly receiving risperidone).

Concomitant administration of carbamazepine or aminoglutethimide may increase the risk of hyponatraemia.

<u>Other interactions</u>

Concomitant use of ciclosporin A and furosemide is associated with increased risk of gouty arthritis secondary to furosemide-induced hyperuricaemia and ciclosporin impairment of renal uric excretion.

In patients at high risk for radiocontrast nephropathy, furosemide led to a higher incidence of deterioration in renal function after receiving radiocontrast compared to high-risk patients who received only intravenous hydration prior to receiving radiocontrast.

In isolated cases, heat sensation, increased sweating, agitation, nausea, rise in blood pressure and tachycardia may occur after intravenous administration of furosemide within 24 hours after intake

of chloral hydrate. Concomitant administration of furosemide and chloral hydrate is therefore to be avoided.

4.6 Fertility, pregnancy and lactation

Pregnancy

Furosemide is to be used during pregnancy only for a short-term period and after especially strict diagnosis, since furosemide crosses the placenta.
Diuretics are not suitable for routine therapy of hypertension and oedemas during pregnancy, since they impair placental perfusion and consequently intrauterine growth.

If furosemide must be used in case of cardiac or renal insufficiency of the pregnant woman, careful monitoring of electrolytes and haematocrit as well as of foetal growth is required. Displacement of bilirubin from albumin binding and thus elevated risk of nuclear icterus in hyperbilirubinaemia is discussed for furosemide.

Furosemide passes the placenta and reaches 100% of the maternal serum concentration in cord blood. No malformations in humans which might be associated with exposure to furosemide have been reported to date. However, there is insufficient experience to allow a concluding evaluation of a potential damaging effect in the embryo/foetus. Animal studies have shown reproductive toxicity (see section 5.3). The potential risk for humans is unknown.
In utero **urinary production can be stimulated in the foetus. Urolithiasis has been observed after treatment of premature infants with furosemide.**

Breast-feeding

Furosemide passes into breast milk and may inhibit lactation. Women must not breast-feed if they are treated with furosemide. If necessary, breastfeeding should be discontinued (see also section 4.3).

4.7 Effects on ability to drive and use machines

Furosemide may elicit diverse individual reactions which might impair the ability to drive and use machines, especially at the beginning of therapy, and on increasing the dose.

4.8 Undesirable effects

The following convention is used for the frequency classification of adverse reactions: 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)

The frequencies are derived from literature data referring to studies where furosemide is used in a total of 1,387 patients, at any dose and in any indication.

System Organ Class	Very common	Common	Uncommon	Rare	Very rare	Frequency no known
Blood an lymphatic system disorders		Haemocon entration (i case c excessive diuresis)	Thrombocyt penia	Eosinophilia leukopenia	Haemolytic anaemia, aplastic anaemia, agranulocy osis[1]	
Immune system disorders			Allergic dermal an mucosal	Severe anaphylactic and		Exacerbation c activation c

System Organ Class	Very common	Common	Uncommon	Rare	Very rare	Frequency no known
			reactions (see skin an subcutaneou s tissu disorders)	anaphylactoi d reaction such a anaphylactic shock[2] (fo treatment se section 4.9)		systemic lupu erythematosus
Metabolism and nutritio disorders	Electrolyt disturban es (including symptoma tic), dehydrati n an hypovolae mia (particula y in elderl patients), blood triglyceric e increased	Hyponatrae mia[3] an hypochlora emia (particularl in case c limited sodium chloride intake), hypokalaer ia[4] (particularl when th supply c potassium is concomitar tly reduce and/or extrarenal potassium losses ar increased, e.g. i vomiting c chronic diarrhoea), blood cholesterol increased, hyperurica mia an attacks c gout	Glucose tolerance impaired an hyperglycae mia. This ma lead to deterioration of th metabolic status i patients wit manifest diabetes mellitus. Latent diabetes mellitus ma become manifest (se section 4.4)			Hypocalcaemia[5], hypomagnesaer ia[6], metaboli alkalosis, Pseudo-Bartter syndrome (i association wit abuse and/c long-term treatment wit furosemide)
Nervous system disorders		Hepatic encephalop athy i patients with hepati insufficienc y (se section 4.3)		Paraesthesia		Dizziness, fainting and los of consciousnes (caused b symptomatic hypotension), headache
Ear an labyrinth disorders			Usually reversible hearing	Tinnitus		

System Organ Class	Very common	Common	Uncommon	Rare	Very rare	Frequency nc known
			disorders, especially i patients wit renal insufficiency or hypoprotein emia (e.g. i nephrotic syndrome) and/or associated with too rapi intravenous injection, deafness (sometimes irreversible)			
Vascular disorders	Hypotens on including orthostati hypotensi on (ver common with I infusion, see section 4.4)[7]			Vasculitis		Thrombosis (particularly i elderly patients)
Gastrointest nal disorder			Nausea	Vomiting, diarrhoea	Acute pancreatitis	
Hepatobiliar y disorders					Intrahepati cholestasis increase i hepatic transamina ses	
Skin an subcutaneou s tissu disorders			Pruritus, urticaria, rash, bullou exanthema, erythema multiforme, bullous pemphigoid, dermatitis exfoliative, purpura, photosensiti vity			Stevens-Johnso syndrome, toxi epidermal necrolysis, acut generalised exanthematous pustulosis (AGEP), dru rash wit eosinophilia an systemic symptoms (DRESS)
Musculoske etal an						Rhabdomyolysis (in associatio

System Organ Class	Very common	Common	Uncommon	Rare	Very rare	Frequency no known
connective tissue disorders						with sever hypokalaemia)
Renal an urinary disorders	Increase i serum creatinine	Increased urine volume		Interstitial nephritis		Urine sodiur increased, urin chloride increased, bloo urea increased symptoms o urinary outflo obstruction (e.g in prostati hypertrophy, hydronephrosis, ureteral stenosis up to urinar retention wit secondary complications (see section 4.4) nephrocalcinosis /nephrolithiasis in prematur infants (se section 4.4), rena failure (se section 4.5)
Congenital, familial an genetic disorders						Increased risk o persistence o patent ductu arteriosus Botal when furosemid is administere to prematur infants during th first weeks of life
General disorders and administrati n sit conditions				Fever		

1 Typical signs of agranulocytosis include fever with chills, sore throat, changes of the mucous membranes.

2 First signs of shock include skin reactions such as flushing or urticaria, agitation, headache, sweating, nausea, cyanosis.

3 Commonly observed symptoms of sodium deficiency are apathy, systremma, inappetence, asthenia, somnolence, vomiting and confusion.

4 Hypokalaemia is manifested as neuromuscular (myasthenia, paraesthesia, paresis), intestinal (vomiting, constipation, meteorism), renal (polyuria, polydipsia) and cardiac (impaired pace setting and conduction disorders) symptoms. Severe potassium losses may lead to paralytic ileus or disturbed consciousness, up to coma.

5 Hypocalcaemia may induce tetany in rare cases.
6 Tetany or cardiac arrhythmia were observed in rare cases as a consequence of hypomagnesaemia.
7 In excessive diuresis, circulatory complaints up to circulatory collapse may occur, particularly in elderly patients and in children. These are predominantly manifested as headache, vertigo, dysopia, xerostomia and thirst, hypotension and orthostatic dysregulation.

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 an acute or chronic overdose depends on the extent of the water and electrolyte losses. Overdose may lead to hypotension, orthostatic dysregulations, electrolyte disturbances (hypokalaemia, hyponatraemia, hypochloraemia) or alkalosis. Major loss of fluid can result in marked hypovolaemia, dehydration, circulatory collapse and haemoconcentration with diathesis to thrombosis. Delirious states may occur in connection with rapid losses of water and electrolytes.

An anaphylactic shock is rare (symptoms: increased sweating, nausea, cyanosis, pronounced drop in blood pressure, depression of consciousness up to coma etc.).

Management
Overdose or signs of hypovolaemia (hypotension, orthostatic dysregulations) necessitate immediate discontinuation of treatment with furosemide.

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 impaired micturition (e.g. patients with prostatic hyperplasia), unrestricted urinary outflow must be ensured, since sudden polyuria can lead to ischuria accompanied by hyperextension of the bladder.

Therapy in cases of hypovolaemia: **volume substitution**

Therapy in cases of hypokalaemia: **potassium substitution**

Therapy in circulatory collapse: **shock positioning; if necessary shock therapy.**

Emergency measures in case of anaphylactic shock
At the first signs (e.g. cutaneous reactions such as urticaria or flush, agitation, headache, sudden increased sweating, nausea, cyanosis):
- **create a venous access**
- **in addition to other common emergency measures, head-chest down position, ensure airways are clear, administration of oxygen!**
- **if necessary, initiate further - possibly also intensive care - measures (among others administration of epinephrine, volume replacement, 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 the re-absorption of $Na^+/2Cl^-/K^+$ in the ascending part of Henle's loop by blocking the ion carrier for these ions. The fractional sodium excretion can amount to 35% of the glomerularly filtrated sodium. Increased sodium excretion leads secondarily to increased urinary excretion and to increased distal-tubular K^+-secretion attributable to osmotically bound water. The excretion of Ca^{2+} and Mg^{2+} ions is also increased. Besides the losses of the above-mentioned electrolytes, excretion of uric acid may be reduced, and a shift of the acid-base balance towards metabolic alkalosis may occur.

Furosemide interrupts the tubuloglomerular feedback mechanism at the macula densa, so that the saluretic efficacy is not attenuated.

Pharmacodynamic effects

Furosemide leads to dose-dependent stimulation of the renin-angiotensin-aldosterone system. In case of cardiac insufficiency, furosemide leads to an acute reduction of the cardiac preload through dilatation of the venous capacitance vessels. This early vascular effect seems to be mediated through prostaglandins and requires sufficient renal function with activation of the renin-angiotensin-aldosterone system as well as intact prostaglandin synthesis.

Furosemide has an antihypertensive effect as a consequence of increased excretion of sodium chloride and reduced responsiveness of vascular smooth muscle cells to vasoconstrictive stimuli, and a reduction in blood volume.

5.2 Pharmacokinetic properties

Absorption

Furosemide is a weak carboxylic acid which exists mainly in the dissociated form in the gastro-intestinal tract. Furosemide is rapidly but incompletely absorbed (60-70%) on oral administration and its effect is largely over within four hours. The optimal absorption site is the upper duodenum at pH 5.0.

Distribution and biotransformation

Furosemide is bound to plasma albumin and little biotransformation takes place. Regardless of route of administration, 69-97% of activity from a radio-labelled dose is excreted in the first 4 hours after the furosemide is given.

Elimination

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.

Special populations

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 Tablets, but less than 20% residual renal function increases the elimination time.

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, possibly due to immature tubular function.

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.

In studies of reproductive toxicology in foetal rats, a reduced number of differentiated glomeruli, skeletal anomalies of the scapulae, humerus and ribs (induced by hypokalaemia), as well as hydronephrosis occurred in foetal mice and rabbits after administration of high doses.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Microcrystalline cellulose
Lactose monohydrate
Magnesium stearate
Maize starch
Sodium starch glycollate

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

3 years

6.4. Special precautions for storage

Blister
Keep the blister in the outer carton in order to protect from light.

Bottle
This medicinal product does not require any special storage conditions.

6.5. Nature and contents of container

The tablets are packed in polypropylen/aluminium blisters and inserted in a carton, or packed in a HDPE bottle.

Blister: 10, 12, 14, 20, 28, 30, 50, 56, 60, 84, 100 and 250 tablets
Bottle: 100, 250 and 500 tablets

Not all pack sizes or pack types may be marketed.

6.6 Special precautions for disposal

No special requirements

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION / RENEWAL OF AUTHORISATION

Date of first authorisation: {DD month YYYY}
Date of latest renewal: {DD month YYYY}

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

2024-01-18