SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Furosemid Medical Valley 20 mg tablets
Furosemid Medical Valley 40 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each <invented name> 20 mg tablet contains 20 mg of furosemide.
Each <invented name> 40 mg tablet contains 40 mg of furosemide.

Excipient(s) with known effect
Each <invented name> 20 mg tablet contains 52.5 mg of lactose monohydrate.
Each <invented name> 40 mg tablet contains 105 mg of lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

<invented name> 20 mg tablets:
White to off white round tablets, 6 mm (approx.) in diameter, marked F 20 on one side and plain on the other side.

<invented name> 40 mg tablets:
White or off white circular tablets, 8 mm (approx.) in diameter, marked F 40 on one side (F and 40 are separated by break line*) and plain on the other side.

The 40 mg 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

Adults

The initial adult dose is 20-40 mg daily. The dose should be adjusted until the lowest effective dose is achieved as a maintenance dose. In some patients, daily doses of 80 mg or higher (given in divided doses) may be required.

Paediatric population
The recommended dose range is 1-3 mg/kg bodyweight.

Elderly
Caution is advised as furosemide is eliminated more slowly in elderly patients. Treatment should be titrated upwards as required (see section 4.4).

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.

Clinical monitoring requirements
Serum potassium should be closely monitored after treatment initiation and in subjects with concomitant treatment with cardiac glycosides, such as digoxin (see also section 4.4).

Method of administration
For oral administration. It is recommended to take tablets on an empty stomach.

4.3 Contraindications

Furosemide is contraindicated in the following circumstances:
- hypersensitivity to the active substance, to sulfonamides, sulfonamide derivatives/amiloride (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
- hypovolaemia or dehydration (with or without accompanying hypotension) (see section 4.4)
- severe hypokalaemia
- severe hyponatraemia
- breast-feeding women (see section 4.6)
- Addison's disease
- pre-coma/coma associated with hepatic cirrhosis or encephalopathy

4.4 Special warnings and precautions for use

The risk of hypokalaemia should be considered, especially in the beginning of the treatment and in patients concomitantly treated with digitalis.

Particularly careful monitoring is necessary in case of:
- hypotension
- patients who are at special risk from a pronounced fall in blood pressure, e.g. patients with cerebrovascular perfusion disorders or coronary heart disease
- latent or manifest diabetes (regular monitoring of blood glucose values)
- hepatorenal syndrome (rapidly progressive renal insufficiency associated with severe liver disease, e.g. liver cirrhosis)
- hypoproteinaemia, e.g. associated with nephrotic syndrome (the effect of furosemide may be weakened and its ototoxicity potentiated). Cautious dose titration is required.
- gout

- premature infants (risk of development nephrocalcinosis nephrolithiasis; renal function must be monitored, and renal ultrasonography performed)

Hypotension and/or hypovolaemia
Symptomatic hypotension leading to dizziness, loss of consciousness can occur in elderly patients treated with furosemide, patients on other medications causing hypotension and patients with other medical conditions that are risks for hypotension (see section 4.3).

Premature infants
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.

Impaired micturition
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.

Electrolyte disorders
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. During long-term therapy with furosemide, regular monitoring of bicarbonate, creatinine, urea and uric acid, as well as blood glucose is also recommended.

An especially close monitoring is necessary in patients with a high risk of developing electrolyte disorders in case of higher fluid losses (e.g. due to emesis, diarrhoea or intense diaphoresis), or due to underlying disorders (e.g. hepatocirrhosis, heart failure), concomitant medication (see section 4.5) and nutrition. 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.

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

The possibility exists of exacerbation or activation of systemic lupus erythematosus hence caution should be taken when administering frusemide to patients with a history of SLE.

Concomitant use with risperidone
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.

Excipients

Lactose
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.

Sodium
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.

Aliskiren reduces the plasma concentration of furosemide given orally. Reduced effect of furosemide might be observed in patients treated with both aliskiren and oral furosemide, and it is recommended to monitor for reduced diuretic effect and adjust the dose accordingly.

Effects of furosemide on other medicinal products

Cardiac glycosides (e.g. digitalis) 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.

Other interactions

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 hyperbilirubinemia 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.

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 (see section 4.8).

Breast-feeding
Furosemide pass into the breast milk and may inhibit lactation. Breast-feeding is contraindicated during treatment with furosemide (see section 4.3).

Fertility
No human data on the effect of furosemide on fertility are available.

4.7 Effects on ability to drive and use machines

Reduced mental alertness and rarely dizziness and blurred vision have been reported. Patients affected should not drive or operate 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); not known (cannot be estimated from the available data).

Blood and lymphatic system disorders:	Common:	Haemoconcentration (in case of excessive diuresis)
	Uncommon:	Thrombocytopenia
	Rare:	Eosinophilia, leukopenia
	Very rare:	Haemolytic anaemia, aplastic anaemia, agranulocytosis[1]
Immune system disorders:	Uncommon:	Allergic dermal and mucosal reactions (see skin and subcutaneous tissue disorders)
	Rare:	Severe anaphylactic and anaphylactoid reactions such as anaphylactic shock[2] (for treatment see section 4.9)
	Not known:	Exacerbation or activation of systemic lupus erythematosus
Metabolism and nutritional disorders:	Very common:	Electrolyte disturbances (including symptomatic), dehydration and hypovolemia (particularly in elderly patients), blood triglyceride increased
	Common:	Hyponatraemia[3] and hypochloraemia (particularly in case of limited sodium chloride intake), hypokalaemia[4] (particularly when the

		supply of potassium is concomitantly reduced and/or extrarenal potassium losses are increased, e.g. in vomiting or chronic diarrhoea), blood cholesterol increased, hyperuricemia and attacks of gout
	Uncommon:	Glucose tolerance impaired and hyperglycaemia. This may lead to a deterioration of the metabolic status in patients with manifest diabetes mellitus. Latent diabetes mellitus may become manifest (see section 4.4).
	Not known:	Hypocalcaemia[5], hypomagnesaemia[6], metabolic alkalosis, Pseudo-Bartter syndrome (in association with abuse and/or long-term treatment with furosemide)
Nervous system disorders:	Uncommon:	Hepatic encephalopathy in patients with hepatic insufficiency (see section 4.3)
	Rare:	Paraesthesia
	Not known:	Dizziness, fainting and loss of consciousness (caused by symptomatic hypotension), headache
Ear and labyrinth disorders:	Uncommon:	Usually reversible hearing disorders, especially in patients with renal insufficiency or hypoproteinaemia (e.g., in nephrotic syndrome) and/or associated with too rapid intravenous injection, deafness (sometimes irreversible)
	Rare:	Tinnitus
Vascular disorders:	Very common:	Hypotension, including orthostatic hypotension (very common with IV infusion, see section 4.4)[7]
	Rare:	Vasculitis
	Not known:	Thrombosis (particularly in elderly patients)
Gastrointestinal disorders:	Uncommon:	Nausea
	Rare:	Vomiting, diarrhoea
	Very rare	Acute pancreatitis
Hepatobiliary disorders:	Very rare:	Intrahepatic cholestasis, increase in hepatic transaminases
Skin and subcutaneous tissue disorders:	Rare:	Rash, pruritus, urticaria, bullous exanthema, erythema multiforme, bullous pemphigoid, dermatitis exfoliative, purpura, photosensitivity
	Not known:	Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis (AGEP), drug rash with eosinophilia and systemic symptoms (DRESS)
Musculoskeletal and connective tissue disorders:	Not known:	Rhabdomyolysis (in association with severe hypokalaemia)
Renal and urinary disorders:	Very common:	Increase in serum creatinine

	Common:	Increased urine volume
	Very rare:	Interstitial nephritis
	Not known:	Urine sodium increased, urine chloride increased, blood urea increased, symptoms of urinary outflow obstruction (e.g. in prostatic hypertrophy, hydronephrosis, ureteral stenosis) up to urinary retention with secondary complications (see section 4.4), nephrocalcinosis /nephrolithiasis in premature infants (see section 4.4), renal failure (see section 4.5)
Congenital, familial and genetic disorders:	Not known:	Increased risk of persistence of patent ductus arteriosus Botalli when furosemide is administered to premature infants during the first weeks of life
General disorders and administration site conditions:	Rare:	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: High-ceiling diuretics, ATC code: CO3C A01

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 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.

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 drug 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, 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 in the new-born, 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

Lactose monohydrate (E1410)
Maize starch

Pregelatinised starch
Sodium starch glycolate (Type A)
Magnesium stearate (E470b)
Water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of 24 months for <invented name> 20 mg tablet.
Shelf life of 36 months for <invented name> 40 mg tablet

6.4 Special precautions for storage

The medicinal product does not require any special temperature storage conditions. Store in the original package in order to protect from light.

6.5 Nature and contents of container

Not all pack sizes may be marketed.

Blister pack: <invented name> is supplied in opaque PVDC /PVC/Aluminium blister of 10 tablets with pack size: 30, 90, 100 tablets.

Bottle pack:
<invented name> 20 mg is also supplied in HDPE bottle with a polypropylene screw cap in pack sizes: 105, 110, 500 tablets.

<invented name> 40 mg is also supplied in a HDPE bottle with a polypropylene screw cap in pack sizes: 105, 110, 270, 500 tablets.

6.6 Special precautions for disposal <and other handling>

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

<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

2024-07-08