**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 the active substance, furosemide or any of the 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 (see section 4.4)
- Digitalis intoxication (see also section 4.5)
- Breast-feeding women (see section 4.6).

### 4.4. Special warnings and precautions for use

**Conditions requiring correction before furosemide is started** (see also section 4.3)

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

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.

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

- elderly patients
- difficulty with micturition/potential obstruction in the urinary tract including prostatic hypertrophy (increased risk of acute retention)
- diabetes mellitus (latent diabetes may become overt: insulin requirements in established diabetes may increase: stop furosemide before a glucose tolerance test)
- gout (furosemide may raise uric acid levels/precipitate gout)
- patients with hepatorenal syndrome
- impaired hepatic function (see section 4.3 and below – monitoring required)
- impaired renal function (see section 4.3 and below – monitoring required)
- hypoproteinaemia e.g. nephrotic syndrome (effect of furosemide may be impaired and its risk of ototoxicity potentiated – cautious dose titration required)
- in moderate liver congestion dosage adjustment may be needed
- patients who are at risk of pronounced fall in blood pressure.

**Avoidance with other medicines** (see also section 4.5 for other interactions)

- concurrent NSAIDs should be avoided – if not possible diuretic effect of furosemide may be attenuated
- ACE-inhibitors & Angiotensin II receptor antagonists – severe hypotension may occur – dose of furosemide should be reduced/stopped (3 days) before starting or increasing the dose of these.

**Laboratory monitoring requirements**

- Serum sodium

Particularly in the elderly or in patients liable to electrolyte deficiency.

- Serum potassium

The possibility of hypokalaemia should be taken into account, in particular in patients with cirrhosis of the liver, those receiving concomitant treatment with corticosteroids, those with an unbalanced diet and those who abuse laxatives. Regular monitoring of the potassium, and if necessary treatment with a potassium supplement, is recommended in all cases, but is essential at higher doses and in patients with impaired renal function. It is especially important in the event of concomitant treatment with digoxin, as potassium deficiency can trigger or exacerbate the symptoms of digitalis intoxication (see section 4.5).

A potassium-rich diet is recommended during long-term use.

Frequent checks of the serum potassium are necessary in patients with impaired renal function and creatinine clearance below 60ml/min per 1.73m$^2$ body surface area as well as in cases where furosemide is taken in combination with certain other drugs which may lead to an increase in potassium levels (see section 4.5 & refer to section 4.8 for details of electrolyte and metabolic abnormalities).

- Renal function

Frequent BUN in first few months of treatment, periodically thereafter. Long- term/high-dose BUN should regularly be measured. Marked diuresis can cause reversible impairment of kidney function in patients with renal dysfunction. Adequate fluid intake is necessary in such patients.

Serum creatinine and urea levels tend to rise during treatment

- Glucose

Adverse effect on carbohydrate metabolism - exacerbation of existing carbohydrate intolerance or diabetes mellitus. Regular monitoring of blood glucose levels is desirable.

- Other electrolytes

Patients with hepatic failure/alcoholic cirrhosis are particularly at risk of hypomagnesia (as well as hypokalaemia). During long-term therapy (especially at high doses) magnesium, calcium, chloride, bicarbonate and uric acid should be regularly measured.

**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.

**Other alterations in lab values**

- Serum cholesterol and triglycerides may rise but usually return to normal within 6 months of starting furosemide.

**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

- **ACE Inhibitors** - enhanced hypotensive effect when given with diuretics. A marked falls in blood pressure and deterioration in renal function may be seen when ACE inhibitors are added to furosemide therapy. The dose of furosemide should be reduced for at least three days, or the drug stopped, before initiating the ACE inhibitor or increasing the dose of an ACE inhibitor.
- **Alpha-blockers** - enhanced hypotensive effect when diuretics are given with alpha- blockers, also increased risk of a first-dose hypotension with post-synaptic alpha blockers such as prazosin.
- **Beta-blockers** - there is an enhanced hypotensive effect when diuretics are given with beta-blockers. Hypokalaemia caused by loop diuretics increases the risk of ventricular arrhythmias with sotalol.
- **Angiotensin-II Receptor Antagonists** - enhanced hypotensive effect when diuretics given with angiotensin-II receptor antagonists.
- **Antipsychotics** - hypokalaemia caused by diuretics increase the risk of ventricular arrhythmias with amisulpride or sertindole. An enhanced hypotensive effect may be seen when diuretics are given with phenothiazines. Hypokalaemia caused by diuretics increases risk of ventricular arrhythmias with pimozide (avoid concomitant use).
- **Risperidone -** when administering risperidone, caution should be exercised and the risks and benefits of the combination or co-treatment with furosemide or with other potent diuretics should be considered prior to the decision to use. Increased mortality has been observed in elderly patients with dementia concomitantly receiving risperidone.
- **Anti-arrhythmics** - hypokalaemia caused by loop diuretics increases cardiac toxicity with amiodarone, disopyramide, flecainide and antagonises the action of lidocaine and mexiletine.
- **Cardiac glycosides** - hypokalaemia caused by loop diuretics increases cardiac toxicity with cardiac glycosides.
- **Other diuretics** - there is an increased risk of hypokalaemia when loop diuretics are given with acetazolamide. Profound diuresis is possible when metolazone is given with furosemide. There is an increased risk of hypokalaemia when loop diuretics are given with thiazides and related diuretics.
- **Renin inhibitors** - aliskiren reduces 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.
- **Lithium** - loop diuretics reduce the excretion of lithium, which may lead to increased plasma concentrations and a risk of toxicity. Therefore, it is recommended that lithium levels are carefully monitored and where necessary the lithium dosage is adjusted in patients receiving this combination.
- **Potassium salts** - there is an increased risk of hyperkalaemia when given with potassium salts.
- **Sucralfate** - furosemide and sucralfate must not be taken within 2 hours of each other as sucralfate decreases the absorption of furosemide from the intestine and so reduces its effect.
- **Lipid regulating drugs** – **Bile acid sequestrants** *(*e.g. colestyramine, colestipol) - reduced absorption of furosemide - administer 2 to 3 hours apart.
- **Analgesics** - diuretics can increase the risk of nephrotoxicity of NSAIDs, also antagonism of diuretic effect. Antagonism of diuretic effect (especially with indometacin and ketorolac). Salycylic toxicity may be increased by furosemide.
- **Antibacterials** - avoid the use of diuretics in lymecycline treatment. There is an increased risk of ototoxicity when loop diuretics are given with aminoglycosides, polymyxins or vancomycin. Since this may lead to irreversible damage, these drugs must only be used with furosemide if there are compelling medical reasons. Impairment of renal function may

develop in patients receiving concurrent treatment with furosemide and high doses of certain cephalosporins.

- **Ciclosporin** - there is an increased risk of nephrotoxicity and possibly hypermagnesaemia when diuretics are given with ciclosporin.

  **Antidepressants** - possible increase of hypokalaemia when loop diuretics are given with reboxetine. There is an enhanced hypotensive effect when diuretics are given with MAOIs. There is an increased risk of postural hypotension when diuretics are given with tricyclic antidepressants.
- **Antiepileptics** - there is an increased risk of hyponatraemia when diuretics are given with carbamazepine. The effects of furosemide are antagonized by phenytoin.
- **Antifungals** - there is an increased risk of hypokalaemia when loop diuretics are given with amphoterecin.
- **Antivirals** - plasma concentration of diuretics may be increased by nelfinavir, ritonavir or saquinavir.
- **Atomoxetine** - hypokalaemia caused by diuretics increases the risk of ventricular arrhythmias with atomoxetine.
- **Barbiturates** - plasma concentrations of diuretics may be decreased. There may be an increased risk of osteomalacia when diuretics are taken in combination with Phenobarbital.
- **Corticosteroids** - the diuretic effect of diuretics is antagonized by corticosteroids. There is an increased risk of hypokalaemia when loop diuretics are given with corticosteroids.
- **Cisplatin** - there is a risk of increased ototoxic effects if cisplatin and furosemide are given concomitantly. In addition, nephrotoxicity of cisplatin may be enhanced if furosemide is not given in low doses (e.g. 40mg in patients with normal renal function) and with positive fluid balance when used to achieve forced diuresis during cisplatin treatment.
- **Dopaminergics** - enhanced hypotensive effect with levodopa.
- **Muscle relaxants** - enhanced hypotensive effect with baclofen or tizanidine.
- **Oestrogens and progestogens** - diuretic effect antagonized.
- **Prostaglandins** - enhanced hypotensive effect with alprostadil.
- **Sympathomimetics, Beta$_2$** - there is an increased risk of hypokalaemia when loop diuretics are given with high doses of beta$_2$ sympathomimetics.
- **Tacrolimus** - there is an increased risk of hypokalaemia when given with tacrolimus.
- **Theophylline** - there is an increased risk of hypokalaemia when loop diuretics are given with theophylline.
- **Warfarin and clofibrate** - warfarin and clofibrate compete with furosemide in the binding to serum albumin. This may have clinical significance in patients with low serum albumin levels (e.g. in nephrotic syndrome). Furosemide does not change the pharmacokinetics of warfarin to a significant extent, but a strong diuresis with associated dehydration may weaken the antithrombotic effect of warfarin.
- **Probenecid, methotrexate and other drugs** which, like furosemide, undergo significant renal tubular secretion may reduce the effect of furosemide. Conversely, furosemide may decrease renal elimination of these drugs. In case of high-dose treatment (in particular, of both furosemide and the other drugs), this may lead to increased serum levels and an increased risk of adverse effects due to furosemide or the concomitant medication.
- **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.
- **Carbenoxolone, prolonged use of laxatives, liquorice** - may increase the risk of developing hypokalaemia.

## 4.6. Fertility, pregnancy and lactation

### Pregnancy

There is clinical evidence of safety of the drug in the third trimester of human pregnancy; however, furosemide crosses the placental barrier. It must not be given during pregnancy unless there are compelling medical reasons. Treatment during pregnancy requires monitoring of foetal growth.

### Breast-feeding

Furosemide passes into breast milk and may inhibit lactation. Women must not breastfeed if they are treated with furosemide.

### 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 so affected should not drive or operate machinery.

## 4.8. Undesirable effects

The following classification of CIOMS frequencies according to the MedDRA database is used where applicable: 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).

| | | |
|---|---|---|
| **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), nephrocalcinosis in infants |
| | 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 |
| **Psychiatric disorder** | Rare | psychiatric disorder |
| **Nervous system disorders** | Rare | paraesthesia, confusion, headache, dizziness |
| **Eye disorders** | Uncommon | visual disturbance, blurred vision, yellow vision |
| | 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) |
| **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 |
| **Musculoskeletal and connective tissue disorders** | Uncommon | muscle cramps, muscle weakness |
| | Uncommon | reduced diuresis, urinary incontinence, urinary obstruction (in patients with hyperplasia of the prostate, bladder inability to empty, urethral stricture unspecified) |
| | Rare | nephrocalcinosis (in pre-term infants treated with furosemide), interstitial nephritis, acute renal failure |
| **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 |

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

### a) Signs and symptoms

The clinical picture in acute or chronic over dosage depends primarily on the extent and consequences of loss of electrolytes and fluids (e.g. hypovolemia, dehydration, hemoconcentration, cardiac arrhythmia - including A-V block and ventricular fibrillation). Symptoms of these changes include: severe hypotension (and progression to shock), acute renal failure, thrombosis, delirious states, flaccid paralysis, apathy and confusion.

### b) Treatment

There is no known specific antidote for furosemide. If ingestion is very Attempts may be made to limit more extensive systemic absorption of active substance, through measures such as gastric lavage or other measures intended to reduce absorption (e.g. use of activated charcoal).

Changes in clinically relevant fluid and electrolyte balance must be corrected. Together with the prevention and treatment of serious complications resulting from such imbalances and other effects on the body, this corrective action may require intensive generalist and specific medical monitoring, as well as of therapeutic measures

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Diuretics, Diuretics of loop. ATC code: C03CA01

**Mechanism of action:**Furosemide is a potent, fast-acting diuretic with a rapid onset of action. From the pharmacological point of view, furosemide inhibits co-transport system (reabsorption) of the Na +, K + and – Cl 2 electrolytes, located of the luminal cell membrane of the ascending branch of the Hanley loop consequently, the efficacy of the saluretic action of furosemide depends on the product reaches the tubular lumen through a transport mechanism anionic. Diuretic action results from the inhibition of sodium chloride reabsorption in this segment of the loop of Henle. As a result, the fraction of sodium excreted may to 35% of glomerular sodium filtration. Side effects of excretion increased urinary excretion and increased distal secretion of potassium at the level of the distal tubule. The excretion of calcium and magnesium ions is increased.

Furosemide disrupts the tubulo-glomerular feedback mechanism in the macula dense, resulting in non- attenuation of saluretic activity. Furosemide causes dose-dependent stimulation of the renin-angiotensin-aldosterone system.

In case of heart failure, furosemide causes an acute reduction in preload (by increasing the capacitance of blood vessels). This vascular effect seems to be mediated by prostaglandins and with the activation of the renin-angiotensin system and an intact synthesis of prostaglandins. Apart from the fact that, given its furosemide decreases the vascular reactivity to catecholamines, which is increased in hypertensive patients.

The antihypertensive efficacy of furosemide is attributable to increased excretion of sodium, blood volume reduction and vascular smooth muscle response to the stimulus vasoconstrictor.

### 5.2. Pharmacokinetic properties

Furosemide is rapidly absorbed from the gastrointestinal tract. The tmax is 1 to 1.5 hours in the case of Furosemide 40 mg. Absorption of the drug denotes a broad intra and interindividual variability.

The bioavailability of furosemide in healthy volunteers is approximately 50%-70% for tablets. In the case of sick individuals, the bioavailability of drug is influenced by several factors, including concomitant diseases, can be reduced by around 30% (for example in the case of nephrotic).

The fact that the absorption of furosemide may be affected by food intake and effect seems to depend on the pharmaceutical formulation in question. The volume of distribution of furosemide is 0.1 to 1.2 liters per kg of body weight.

The plasma protein binding (mostly to albumin) is greater than 98%. Furosemide is mostly eliminated in the non-conjugated form, mainly by secretion at the level of the proximal tubule. Following intravenous administration, 60% to 70% of the furosemide dose is excreted in this way. The glucuronic metabolite of furosemide represents 10% to 20% of the substances recovered in the urine.

The remaining dose is excreted in the faeces, probably after biliary secretion.

The terminal half-life of furosemide after intravenous administration is approximately 1 to 1.5 hours. Furosemide is excreted in breast milk.
Furosemide crosses the barrier the placenta slowly transferring to the fetus.

Furosemide reaches concentrations identical in the mother and in the fetus or newborn.

Renal insufficiency

In case of renal insufficiency, the elimination of furosemide is slower and its half-life is prolonged, the terminal half-life may reach 24 hours in patients with severe renal impairment. In case of nephrotic syndrome, the lower concentration of plasma proteins leads to that higher concentrations of unconjugated (free) furosemide are achieved. Per On the other hand, the efficacy of furosemide is reduced in these patients, due to the intratubular albumin and decreased tubular secretion.

Furosemide is poorly dialysable in patients receiving hemodialysis, dialysis peritoneal or CAPD (Chronic Ambulatory Peritoneal Dialysis).

Hepatic insufficiency

In case of hepatic impairment, the half-life of furosemide in the order of 30% to 90%, mainly due to the higher volume of high. In addition, in this group of patients there is pharmacokinetic parameters. Congestive heart failure, severe hypertension, elderly elimination of furosemide is slowed due to reduced renal function in patients with congestive heart failure, severe hypertension or in the elderly.

Premature and new born infant

Depending on the maturity of the kidney, elimination of furosemide may be slower. The metabolism of the drug is also reduced in the case of children with insufficiency of glucuronization capacity. The terminal half-life is less than 12 hours in children with a post-conception age greater than 33 weeks. In children with terminal age is equal to that of adults.

### 5.3. Preclinical safety data

Not applicable.

## 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 Israel Ltd.
124 Dvora HaNevi'a St.,
Tel Aviv, 6944020.

## 8. REGISTRATION NUMBER

020.20.20472

**The leaflet was revised in September 2024**