

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Impugan 20 mg tablets

Impugan 40 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Impugan 20 mg tablet contains: 20 mg furosemide

Each Impugan 40 mg tablet contains: 40 mg furosemide

Excipient with known effect

Each Impugan 20 mg tablet contains: 28 mg lactose

Each Impugan 40 mg tablet contains: 56 mg lactose

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

Tablets 20 mg: white to yellowish, biconvex, 6 mm in diameter, engraved with CDL.

Tablets 40 mg: white to yellowish, flat, with a single score line, 8 mm in diameter, engraved with CJJ

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Acute pulmonary oedema. Cardiac, renal, hepatic and other forms of oedema. Hypertension.

4.2 Posology and method of administration

Posology

Adults

Oedema of different genesis: 20-40 mg orally in the morning is usually enough. Sometimes higher doses are required, 80-160 (240) mg daily, preferably divided into 2-3 doses. Dose is increased gradually until satisfactory effect is obtained.

Hypertension: 20-80 mg daily. Impugan can be combined with other antihypertensive drugs, whereby the daily dose of each drug may often be reduced.

Paediatric population

The suggested oral dose is 1-3 mg/kg of body weight.

Treatment control

During long-term treatment should regular checks of plasma electrolytes be performed, especially during simultaneous digitalis medication and at the beginning of the treatment.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Patients who are allergic to sulphonamides
- Patients with hypovolaemia or dehydration
- Patients with precomatose or comatose conditions associated with hepatic encephalopathy.

- Patients with severe toxic renal damage (at high doses) and/or with anuric renal insufficiency

4.4 Special warnings and precautions for use

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.

Strict sodium restricted diet should be avoided during treatment with diuretics.

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 essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Combinations that should be avoided

Gentamicin

Concomitant i.v. administration of gentamicin (80 mg) and furosemide (40 mg) decreases the clearance of gentamicin with approximately 40%, with elevated plasma concentrations as a result. Simultaneous i.v. administration of these drugs should be avoided.

Furosemide may intensify the ototoxicity of aminoglycosides and other ototoxic drugs.

Combinations that may require dose adjustment

Digitalis glycosides

Induced hypokalemia may enhance digitalis effect (intoxication risk).

Sotalol

Hypokalemia associated with thiazide therapy is thought to increase the risk of arrhythmias triggered by sotalol (syncope, prolonged QT).

Nonsteroidal anti-inflammatory / antirheumatic agents, NSAIDs

Antiphlogistics of NSAID-type (indomethacin, propionic acid) have been shown to counteract the diuretic effect of furosemide and bumetanide, possibly via inhibition of prostaglandin synthesis. They can also counteract the antihypertensive effect of thiazides. This interaction is not likely to occur with sulindac and is possibly insignificant for selective COX-2 inhibitors. In patients with dehydration or hypovolaemia, non-steroidal anti-inflammatory drugs may cause acute renal insufficiency.

Lithium

Thiazides reduce renal excretion of lithium, which can result in increased plasma concentrations with unchanged lithium dosages. A recent study suggests that loop diuretics (furosemide) have little such effect.

ACE inhibitors

Studies on patients with chronic heart failure show that captopril (and probably other ACE inhibitors) reduces the diuretic and sodium effect of furosemide. Patients receiving diuretic therapy may develop severe hypotension and impaired renal function when an ACE inhibitor is used for the first time or is first used in a higher dose ("first-dose hypotension").

Aliskiren

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.

Other interactions

The antihypertensive effect increases when combined with specific antihypertensive drugs. Concomitant administration of furosemide, in high doses, and cephalothin / cephaloridine has occasionally been reported to enhance the nephrotoxic effect of cephalothin / cephaloridine. In patients with high salicylate intake, furosemide can cause salicylate toxicity by inhibiting renal salicylate excretion.

4.6 Fertility, pregnancy and lactation

Pregnancy

Generally furosemide should only be used for specific indications during pregnancy.

Thiazides, thiazide diuretics and loop diuretics may pass to the fetus and cause electrolyte imbalance. Cases of neonatal thrombocytopenia have been described with thiazide and thiazide-diuretics. Even with the usage of loop diuretics such as furosemide and bumetanide this risk probably also exists. During the last trimester Impugan should only be given after careful consideration and in the lowest appropriate dose.

Breastfeeding

Furosemide passes into breast milk in quantities that may affect the child even in therapeutic doses. Diuretics inhibit lactation and are therefore unsuitable for breastfeeding women.

4.7 Effects on ability to drive and use machines

Furosemide has minor or insignificant influence on the ability to drive and use machines.

4.8 Undesirable effects

Adequate majority of side effects are dose dependent. The most common are disorders of electrolyte and fluid balance (about 5%), which are associated with the physiological effect that primarily occurs in patients with impaired hepatic function and in patients with renal insufficiency that take high doses .

BLOOD AND LYMPHATIC SYSTEM DISORDERS	
Uncommon ($\geq 1/1,000$ to $< 1/100$)	Aplastic anaemia
Rare ($\geq 1/10,000$ to $< 1/1,000$)	Leukopaenia, agranulocytosis, thrombocytopaenia
METABOLISM AND NUTRITION DISORDERS	
Common ($\geq 1/100$ to $< 1/10$)	Hypomagnesaemia, hypokalaemia, hyperuricaemia, hypochloraemia, hyponatraemia, hypocalcaemia
Uncommon ($\geq 1/1,000$ to $< 1/100$)	Dehydration
Rare ($\geq 1/10,000$ to $< 1/1,000$)	Hyperglycaemia

NERVOUS SYSTEM DISORDERS	
Not known (cannot be estimated from the available data)	Dizziness, fainting and loss of consciousness (caused by symptomatic hypotension)
EAR AND LABYRINTH DISORDERS	
Uncommon ($\geq 1/1,000$ to $< 1/100$)	Deafness (sometimes irreversible)
Rare ($\geq 1/10,000$ to $< 1/1,000$)	Tinnitus and reversible deafness (in high plasma concentrations)
VASCULAR DISORDERS	
Common ($\geq 1/100$ to $< 1/10$)	Hypovolaemia in intensive therapy
Uncommon ($\geq 1/1,000$ to $< 1/100$)	Hypotension
Rare ($\geq 1/10,000$ to $< 1/1,000$)	Vasculitis
GASTROINTESTINAL DISORDERS	
Uncommon ($\geq 1/1,000$ to $< 1/100$)	Nausea, vomiting
Not known (cannot be estimated from the available data)	Acute pancreatitis
HEPATOBIILIARY DISORDERS	
Rare ($\geq 1/10,000$ to $< 1/1,000$)	Hepatic reactions such as elevated hepatic enzymes
Not known (cannot be estimated from the available data)	Intrahepatic cholestasis
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	
Rare ($\geq 1/10,000$ to $< 1/1,000$)	Rash, pruritus, urticaria, exfoliative dermatitis, erythema multiforme, purpura, Stevens-Johnsons syndrome. Toxic epidermal necrolysis, photosensitization
Not known (cannot be estimated from the available data)	Acute generalised exanthematous pustulosis (AGEP), drug reaction with eosinophilia and systemic symptoms (DRESS)
RENAL AND URINARY DISORDERS	
Very common ($\geq 1/10$)	Nephrocalcinosis in infants
Not known (cannot be estimated from the available data)	Interstitial nephritis, worsening of renal dysfunction

At lower doses, typically used in treatment of e.g. cardiac and renal edema, the serum electrolytes are usually within normal ranges.

Hypokalemia, possibly with hypochloremic alkalosis may occur particularly with forced diuresis, special consideration should be taken when in digitalis medication.

Hypovolemia may occur at higher oral doses. At serum concentrations higher than 50 micrograms/ ml hearing loss has been reported. This is usually reversible.

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

Toxicity: 80 mg to 1-2 year olds gave mild intoxication, and 240-320 mg for 2 year olds gave moderate intoxication. 600-800 mg to 14 year olds gave moderate intoxication, 420-500 mg in the elderly caused mild to moderate intoxication.

Symptoms: Disorders of electrolyte and fluid balance, thirst, dehydration, metabolic alkalosis. Initial polyuria, with big losses of fluids oliguria, anuria. Secondary to fluid and electrolyte losses, headache, confusion, dizziness, paresthesias, muscle weakness, possible. Convulsions and coma, orthostatic hypotension, syncope, ECG changes, arrhythmias. Nausea, vomiting, abdominal pain.

Treatment: Gastric lavage if needed, coal. Rehydration adjustment of electrolyte and acid-base balance. Continuous ECG- monitoring for severe dehydration/electrolyte disturbance. Other symptomatic therapy.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: High-ceiling diuretics, ATC code: C03CA01

Furosemide is a sulfonamide and a diuretic such as "high-ceiling" which means a dose-dependent effect over a wide dose range. The effect has a rapid onset and short duration. Furosemide acts primarily through inhibition of chloride absorption in the ascending limb of Henle's loop, but also exerts an effect in the proximal and distal tubules. In parallel with the increased chloride excretion, the excretion of sodium, calcium, potassium and magnesium is increased. In addition, potassium excretion increases, while excretion of bicarbonate is practically unaffected. The resulting diuresis is strong with a subsequent, usually weak, blood pressure lowering effect. In pulmonary oedema, furosemide before the onset of diuresis induces a rapid increase in venous capacity, bringing about a fall in the filling pressure in the left chamber.

Furosemide has also, usually weak, antihypertensive effect that sets in later and lasts longer than the diuretic effect.

Since the blood pressure lowering effect is weaker with loop diuretics than with thiazides then hypertension treatment should only be used to potentiate other drugs, by giving a greater diuresis. Indication for loop diuretics is primarily when renal function is impaired. A normal blood pressure is not affected or only slightly affected.

5.2 Pharmacokinetic properties

Furosemide is absorbed rapidly from the gastrointestinal tract. Peak serum concentrations are reached after ½-2 hours after oral administration. The absorption of furosemide may be delayed and reduced

with concomitant food intake. In the case of severe oedema, reduced bioavailability has been reported, probably due to reduced absorption from the gastrointestinal tract. The diuretic effect is normally set in after ½-1 hour and is maximal after 1-2 hours. It lasts 4-6 hours. Protein binding has been estimated at 91-99%.

The half-life is normally 1-2 hours and longer in infants as well as in patients with liver and kidney disease. The main part is excreted within 10 hours after a dose. 24 hours after a single dose there are no measurable amounts of furosemide in the urin. 2/3 of furosemide is excreted unchanged by glomerular filtration and tubular secretion and the remainder via faeces.

5.3 Preclinical safety data

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6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate 28 mg resp 56 mg
Magnesium stearate
Croscarmellose sodium
Talk
Corn starch
Cellulose, microcrystalline
Starch pregelatinised

6.2 Incompatibilities

Not applicable

6.3 Shelf life

5 years

6.4 Special precautions for storage

Store in the outer carton in order to protect from light.

6.5 Nature and contents of container

Tablets 20 mg:

24 tablets: Blister (PVC/ Aluminum)

50 x 1 tablets: Blister (PVC/ Aluminum)

100 tablets: Bottle (Polyethylene) with child-resistant screw cap (Polyethylene)

Tablets 40 mg:

24 tablets: Blister (PVC/ Aluminum)

50 x 1 tablets: Blister (PVC/ Aluminum)

100 tablets: Bottle (Polyethylene) with child-resistant screw cap (Polyethylene)

250 tablets: Bottle (Polyethylene) with child-resistant screw cap (Polyethylene)

1000 tablets: Bottle (Polyethylene) with child-resistant screw cap (Polyethylene)

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

7. MARKETING AUTHORISATION HOLDER

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

2024-07-12