CORE SAFETY PROFILE
BUFFOMEDIL HYDROCHLORIDE

PRODUCT NAME

Buflomedil hydrochloride

Brand Names

Loftyl, Lofton, Bufedil

4.3 - CONTRAINDICATIONS

Buflomedil hydrochloride is contraindicated in individuals who have previously shown hypersensitivity to the drug or to any of the inactive ingredients.

Buflomedil hydrochloride must not be given to patients with severe renal impairment (defined as creatinine clearance <30 mL/min).

Buflomedil hydrochloride is also contraindicated immediately postpartum or in the presence of arterial bleeding.

4.4 - WARNINGS AND PRECAUTIONS

Pregnancy

Due to a lack of appropriate clinical safety data, the safety of buflomedil during pregnancy and lactation has not been established. The use of buflomedil is therefore not recommended.

Elderly patients

Clinical experience has not shown any differences between elderly and younger patients in terms of response. In general, the dose for elderly patients should be chosen with caution, starting with a low dose and not exceeding 600 mg/day.

Children

Since no clinical data are available, the safety and efficacy of buflomedil in this group have not been established, and the use of this medicinal product in children under 18 is therefore not advised.
In view of the narrow therapeutic index of buflomedil, the maximum recommended dose must not be exceeded. Exceeding the maximum dose or a lack of dose modification in patients with renal or hepatic impairment can result in overdose, which can manifest as serious neurological and cardiovascular effects (see sections Adverse reactions and Overdosage). For dosage adjustment in patients with renal impairment see Dosage and administration.

Measurement of renal function
Renal function should be determined prior to starting treatment and at regular intervals during treatment; at least once a year in patients with normal renal function and at least twice a year in patients with renal impairment, patients over 65, and patients weighing less than 50 kg (see section Dosage and administration).

Loftyl should be used with caution in patients with:
- Acute myocardial infarction
- Severe hypotension (systolic pressure of < 90 mmHg).
- Hepatic impairment
- Renal impairment
- Severe hypotony
- Cardiac conduction disturbances
- Seizures

4.5 - DRUG INTERACTIONS

There is a greater risk of undesirable neurological effects (convulsions) when buflomedil is administered concomitantly with CYP2D6 inhibitors (e.g. fluoxetine, paroxetine, quinidine) in patients with renal or hepatic impairment (see section 5.2).

Buflomedil may potentiate the hypotensive effect of vasodilators, calcium antagonists (e.g. amlodipine, diltiazem and verapamil), antihypertensive agents and alcohol.

In one study, decreases of blood glucose levels were observed in diabetic patients simultaneously treated with oral antidiabetic drug. However, a double-blind study with buflomedil and glibenclamide did not support this observation.

4.6 - PREGNANCY AND LACTATION

Studies in animals have not shown evidence of any teratogenic effect.

Due to a lack of appropriate clinical safety data, the safety of buflomedil during pregnancy and lactation has not been established. The use of buflomedil is therefore not recommended.

4.7 - EFFECTS ON THE ABILITY TO DRIVE AND USE MACHINES
Given the individually different reactions to buflomedil, the ability to drive or use machines may be affected, especially at the beginning of the treatment, after dose adjustment or together with alcohol.

### 4.8 - ADVERSE REACTIONS

In the majority of cases the adverse events are relatively minor. The adverse reactions most commonly reported by patients treated in clinical trials with buflomedil are, in order of decreasing incidence: vertigo, headache, gastrointestinal disorders, nausea, vasodilation and dizziness.

From post-marketing surveillance the following adverse events have been described:

* **Skin and subcutaneous tissue disorders**: rash, psoriasis

* **Immune system disorders**: allergic reactions (e.g. rash, tachycardia, hypotension/shock)

* **Cardiac disorders**: atrial fibrillation

* **Renal and urinary disorders**: polyuria

* **Vascular disorders**: hypertension

* **Nervous system disorders**: somnolence

* **Respiratory, thoracic and mediastinal disorders**: epistaxis

* **Reproductive system and breast disorders**: menorrhagia

* **Musculoskeletal and connective tissue disorders**: increased creatinaemia

### 4.9 - OVERDOSAGE

In the event of intentional or accidental overdose, neurological effects (seizures, status epilepticus) may occur rapidly (within 15-90 minutes) and be followed by cardiovascular reactions (sinus tachycardia, hypotension, severe ventricular arrhythmias, and conduction disturbances mainly affecting the ventricles). The patient can quickly lapse into a coma and/or experience cardiac arrest.

The clinical presentation is very similar to that of an overdose with an imipramine-type antidepressant.

An intentional or accidental overdose of buflomedil can be fatal.
Management:
The patient should be immediately transported to a hospital for continuous neurological and electrocardiograph monitoring and respiratory assistance.

If the patient is agitated or experiencing seizures, a benzodiazepine (e.g. diazepam) can be used.

Treatment should be commenced as soon as the first signs or symptoms appear.