

SUMMARY OF PRODUCT CHARACTERISTICS

1. PRODUCT NAME

Gutron 2.5 mg Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 2.5 mg of midodrine hydrochloride.

Full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gutron is presented in tablet form for oral administration.

4. CLINICAL INFORMATION

4.1. Therapeutic indications

Orthostatic hypotension:

- Orthostatic hypotension, particularly refractory;
- Reduction of blood pressure due to treatment with neuroleptics and antidepressants;
- In hypersensitivity to tension changes related to atmospheric conditions;
- Hypotension after anesthesia in infections and hemodialysis.

Urological indications:

Females:

- Effort Urinary Incontinence type III (Blaivas, McGuire) (sphincter dysfunction).
- As an adjunct in the remaining stress urinary incontinence with mild or moderate urethral hypermobility.

Males:

- Retrograde ejaculation.
- In the involuntary loss of urine resulting from sphincter hypotonia, namely postoperative.

4.2. Dosage and method of administration

Children: not recommended the use of Gutron in patients aged less than 12 years, taking into account the lack of experience in treating children (see section 5.1 Pharmacodynamic properties and 5.2 Pharmacokinetic properties).

Orthostatic hypotension: 1 tablet 2 to 3 times a day.

This dose should be adjusted gradually after about 3 days of treatment

depending on the patient response, and may be decreased to 1/2 tablet 2 to 3 times daily, increased to 2 tablets or 2 to 3 times a day.

The maintenance dose should be chosen individually for each patient in order to obtain the optimum therapeutic effect together with a minimum side effects.

The administration of Gutron must be taken during the day when the patient is in operation. It is suggested the administration Interval 3-4 hours immediately after rising in the morning, at midday and in the evening, at least 4 hours before bedtime, to prevent the risk of supine hypertension.

The maximum daily dose is 30 mg.

Urologic indications: 1 to 2 tablets 2 to 3 times a day (the last dose should be taken at least 4 hours before bedtime).

Ingestion of the tablets must be made with a glass of water.

In case of omitting one or more doses, the patient should continue treatment as prescribed by the doctor without taking the previous dose.

4.3. Contraindications

- Hypersensitivity to, midodrine, or any of the excipients.
- Gutron is contraindicated in cases of hypertension, pheochromocytoma, acute nephritis, severe perturbation of renal function, narrow-angle glaucoma, prostatic hypertrophy with significant residue, mechanical obstruction to the bladder emptying or hyperthyroidism.
- Gutron should be administered with caution in the presence of organic changes of the heart or coronary vessels in cardiac arrhythmias and renal failure.

Patients with renal impairment: No specific studies have been conducted on a possible dose reduction in patients with renal insufficiency. In general, midodrine hydrochloride is contraindicated in patients with severe acute renal failure.

Patients with hepatic impairment: No specific experience in the administration of Gutron in this group of patients.

Elderly: No specific studies have been conducted in the elderly that allow substantiate the need for dose reduction in this patient group.

4.4. Special warnings and precautions for use

In patients receiving prolonged treatment is advised monitoring renal function and blood pressure.

Concomitant administration of Gutron with other drugs that have a direct or indirect effect on blood pressure or heart rate (guanethidine, β -1 agonists, and nonselective β -blockers) requires frequent monitoring of blood pressure and heart rate.

4.5. Drug interactions and other forms of interaction

Gutron activity can be inhibited by direct-blocking agents (prazosin, phentolamine) or indirect agents α - blockers (reserpine).

Concurrent use of digitalics is not recommended because of the possible potentiation of bradycardia or intracardiac conduction defects caused by these agents.

4.6. Pregnancy and lactation

Although studies in animals have not shown embryotoxic or teratogenic effects, there are no well-controlled studies in humans, so use during pregnancy should only be considered when the potential benefits to the mother outweigh the possible risks to the fetus.

Gutron should be used with caution, and only after due consideration of the risk / benefit, during lactation, since there are no studies available on midodrine passing into breast milk. In these cases, the newborn should be careful monitoring.

4.7. Effects on the ability to drive and use machines

Not described.

4.8. Undesirable effects

In some individual cases, there may be complaints of angina, cardiac arrhythmias and rashes.

Higher doses can lead to the appearance of skin reactions, especially in the posterior neck and scalp, feeling cold, urinary urgency or urinary retention.

Can appear a decrease in the heart rate reflex (bradycardia reflex) that can be treated with atropine.

4.9. Overdose

Overdose produces skin reactions, dose-related, especially in the posterior neck and scalp, feeling cold, reflex bradycardia, increase in blood pressure with cephalic congestion and urinary urgency or urinary retention.

Antidote:

α -receptor blockers such as competitive antagonists, e.g., Phentolamine. Bradycardia and conduction defects may be antagonized by atropine.

5. Pharmacological Properties

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Group 3.3 Cardiovascular. Sympathomimetic.

ATC code: C01CA17

Midodrine hydrochloride is an inactive pro drug which, through an enzymatic hydrolysis slowly releases the active metabolite desglimidodrine. This has an α -selective sympathomimetic peripheral action that causes shrinkage mainly on the peripheral venous and, to a lesser extent, the arterioles. There are substantial increase in the peripheral resistance and a decrease in venous blood accumulation in the periphery, which causes an elevation in blood pressure when it is reduced and thus improves the symptoms of orthostatic hypotension Symptomatic hypotension and other related clinical situations.

At the proximal urethra and bladder neck, midodrine hydrochloride increases muscle tone by stimulating the α -1 receptors. This action results in an increase of the maximum urethral closing pressure, which leads to an improvement in some cases of urinary incontinence.

Midodrine hydrochloride doesn't have β -mimetic properties, does not cause tachycardia, as it happens with some similar drugs.

5.2. Pharmacokinetic properties

This drug hardly crosses the blood brain barrier and has no effects on the central nervous system.

After oral administration, midodrine hydrochloride is rapidly and almost completely absorbed.

The bioavailability is 93%.

As midodrine hydrochloride is a prodrug of the active metabolite, desglimidodrine the onset of action is relatively slow. The plasma concentration peak is achieved after 1 hour and the plasma half-life is 3 hours.

Desglimidodrine can be detected in plasma 10 hours after administration.

Midodrine hydrochloride and its active metabolite are excreted almost entirely through the urine in 24 hours, 5% unchanged as midodrine hydrochloride, approximately 40% as active metabolite and the remaining 55% as pharmacologically inactive metabolites.

5.3. Data from preclinical safety

Studies in animals showed no embryotoxic or teratogenic alterations effects.

6. PHARMACEUTICAL INFORMATION

6.1. List of excipients

Magnesium stearate, talc, colloidal anhydrous silica, microcrystalline cellulose and corn starch.

6.2. Incompatibilities

Not described.

6.3. Shelf life

5 years.

6.4. Special precautions for storage

Store below 25 ° C.

6.5. Nature and contents of container

Gutron tablet is packed in PVC / aluminum, and comes in packs of 20, 60 and 100 tablets.

It is possible that not all pack sizes may be marketed.

6.6. Special precautions for disposal

No special requirements.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

BLUEMED Unipessoal, Lda

Rua Poeta Adriano Correia de Oliveira,233

4510-698 Fânzeres - Portugal

8. NUMBER (S) OF THE MARKETING AUTHORISATION

Registration no. ° 9464602: 20 Tablets, 2.5 mg, blister.

Registration no. ° 5013420: 60 Tablets, 2.5 mg, blister.

Registration no. ° 4640090: 100 Tablets, 2.5 mg, blister.

9. DATE OF FIRST AUTHORISATION / RENEWAL OF PERMISSION MARKETING

Date of first authorization in the market: 03 de Outubro de 1977

10. DATE OF REVISION OF THE TEXT

28-06-12