Gutron Tablets 5 mg

(Midodrine hydrochloride 5mg)

DESCRIPTION
Name: GUTRON (midodrine hydrochloride) Tablets
Dosage Form: 5 mg tablets for oral administration
Active Ingredient: Midodrine hydrochloride, 5 mg

Pharmacological Classification: Vasopressor / Antihypotensive

INDICATIONS
For treatment of idiopathic / neurogenic orthostatic hypotension.

The Indication is based on GUTRON effect on increases in 1-minute standing systolic blood pressure, a surrogate marker considered likely to correspond to a clinical benefit.
At present, however, clinical benefits of GUTRON principally improved ability to perform life activities, have not been established. Further clinical trials are underway to verify and describe the clinical benefits of GUTRON.

After initiation of treatment, GUTRON should be continued only for patients who report significant symptomatic improvement.

Because midodrine can cause marked elevation of supine blood pressure, it should be used in patients whose lives are considerably impaired despite standard clinical care including nonpharmacologic treatment (such as support stockings), plasma volume expansion and lifestyle alterations.

DOSAGE AND ADMINISTRATION
Adults and adolescents (>18 years): Initial dose 2.5 mg 2-3 times a day. The maximum recommended dose should not exceed 30 mg daily.
Treatment should be started under close medical supervision in a controlled clinical setting such as in hospital, in clinic, or in office. Hourly measurements of blood pressure (supine and sitting) should be made for 3 hours after the first dose and also the second dose of a three times daily dosage regimen. This procedure should be followed also when the dose is increased. During the period of close medical supervision, the patient or a person living with the patient should be trained to measure blood pressure. Supine and sitting blood pressures should be measured daily for at least one month after the initiation of treatment and twice per week afterwards. The administration of midodrine should be stopped and the attending physician notified immediately, if blood pressure in either position increases above 180/100 mmHg. It is recommended that treatment begins at the lowest level and be titrated at weekly intervals in small increments until the optimal response is obtained.
Dosing should take place during the daytime hours when the patient needs to be upright pursuing the activities of daily life. A suggested dosing schedule of approximately 4-hour intervals is as follows: shortly before or upon arising in the morning, midday, and the late afternoon (not later than 6 P.M.). Doses may be given in 3-hour intervals, if required, to control symptoms, but not more frequently. Single doses as high as 20 mg have been given to patients, but severe and persistent systolic supine hypertension occur at a high rate (about 45%) at this dose. In order to reduce the potential for supine hypertension during sleep, GUTRON should not be given after the evening meal or less than 4 hours

before bedtime. Total daily doses greater than 30 mg have been tolerated by some patients, but their safety and usefulness have not been studied systematically or established. Because of the risk of supine hypertension, GUTRON should be continued only in patients who appear to attain symptomatic improvement during initial treatment.
The supine and standing blood pressure should be monitored regularly, and the administration of GUTRON should be stopped if supine blood pressure increases excessively.
Because desglymidodrine is excreted renally, dosing in patients with abnormal renal function should be cautious; although this has not been systematically studied, it is recommended that treatment of these patients be initiated using 2.5 mg doses.
Dosing in children has not been adequately studied. Blood levels of midodrine and desglymidodrine were similar when comparing levels in patients 65 or older vs. younger than 65 and when comparing males vs. females, suggesting dose modifications for these groups are not necessary.

CONTRAINDICATIONS
GUTRON is contraindicated in patients with the following conditions/diseases:

- Severe organic heart disease (e.g: bradycardia, ischaemic heart disease, congestive heart failure, cardiac conduction disturbances or aortic aneurism)
- Hypertension
- Serious obliterative or spastic vascular disorders (e.g: cerebrovascular occlusions and spasms)
- Acute renal disease
- Severe renal impairment
- Hypertrophy of the prostate gland with residual volume increased
- Urinary retention
- Proliferative diabetic retinopathy
- Phaechromocytoma
- Hyperthyroidism
- Narrow-angle glaucoma
- Known hypersensitivity to any component of the product

GUTRON should not be used in patients with persistent excessive supine hypertension. GUTRON should not be used in vasovagal hypotension.

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE
Supine Hypertension: The most potentially serious adverse reaction associated with GUTRON therapy is marked elevation of supine arterial blood pressure (supine hypertension). Systolic pressure of about 200 mmHg were seen overall in about 13.4% of patients given 10 mg of GUTRON. Systolic elevations of this degree were most likely to be observed in patients with relatively elevated pre-treatment systolic blood pressures (mean 170 mmHg). There is no experience in patients with initial supine systolic pressure above 180 mmHg, as those patients were excluded from the clinical trials. Use of GUTRON in such patients is not recommended. Sitting blood pressures were also elevated by GUTRON therapy. It is essential to monitor supine and sitting blood pressures in patients maintained on GUTRON.

The potential for supine and sitting hypertension should be evaluated at the beginning of GUTRON therapy. Supine hypertension can often be controlled by preventing: the patient from becoming fully supine, i.e., sleeping with the head of the bed elevated. The patient should be cautioned to report symptoms of supine hypertension immediately (e.g. cardiac awareness, pounding in the ears, headache,

blurred vision, etc). The patient should be advised to discontinue the medication immediately if supine hypertension persists. Patients should be monitored for possible secondary events to hypertension.

Blood pressure should be monitored carefully when GUTRON is used concomitantly with other agents that cause vasoconstriction, such as phenylephrine, ephedrine, dihydroergotamine, phenylpropanolamine, or pseudoephedrine.
A slight slowing of the heart rate may occur after administration of GUTRON primarily due to vagal reflex. Caution should be exercised when GUTRON is used concomitantly with cardiac glycosides (such as digitalis), psychopharmacologic agents, beta blockers or other agents that directly or indirectly reduce heart rate.

Patients who experience any signs or symptoms suggesting bradycardia (pulse slowing, increased dizziness, syncope, cardiac awareness) should be advised to discontinue GUTRON and should be re-evaluated.
GUTRON should be used cautiously in patients with urinary retention problems, as desglymidodrine acts on the alpha-adrenergic receptors of the bladder neck.

GUTRON should be used with caution in orthostatic hypotensive patients who are also diabetic, as well as those with a history of visual problems who are also taking fludrocortisone acetate, which is known to cause an increase in intraocular pressure and glaucoma.

GUTRON use has not been studied in patients with renal impairment. Because desglymidodrine is eliminated via the kidneys, and higher blood levels would be expected in such patients, GUTRON should be used with caution in patients with renal impairment, with a starting dose of 2.5mg (see **Dosage and Administration**). Renal function should be assessed prior to initial use of GUTRON.

GUTRON use has not been studied in patients with hepatic impairment. GUTRON should be used with caution in patients with hepatic impairment, as the liver has a role in the metabolism of midodrine.

Information for Patients: Patients should be told that certain agents in over-the-counter products, such as cold remedies and diet aids, can elevate blood pressure, and therefore, should be used cautiously with GUTRON, as they may enhance or potentiate the pressor effects of GUTRON (see Drug **Interactions**). Patients should also be made aware of the possibility of supine hypertension. They should be told to avoid taking their dose if they are to be supine for any length of time, i.e they should take their last daily dose of GUTRON 3 to 4 hours before bedtime to minimize nighttime supine hypertension.

Laboratory Tests: Since desglymidodrine is eliminated by the kidneys and the liver has a role in its metabolism, evaluation of the patient should include assessment of renal and hepatic function prior to initiating therapy and subsequently, as appropriate.

Interaction with other medications and other forms of interaction
Midodrine is an inhibitor of Cytochrome P450 CYP2D6 and may therefore affect the metabolism of other drugs metabolized by this isoenzyme (e.g. perphenazine, amiodorone, metoclopramide). This may lead to increased systemic exposure and increased effects of these drugs.

Avoid the concomitant use of midodrine together with vasoconstrictor, sympathomimetic pressor agents and other drugs which cause hypertension (such as tricyclic antidepressants, antihistamines,

thyroid hormones, MAO-inhibitors, as well as over-the-counter remedies), as this may cause excessive hypertension.

When administered concomitantly with GUTRON, cardiac glycosides may enhance or precipitate bradycardia, A.V, block or arrhythmia. The use of drugs that stimulate alpha-adrenergic receptors (e.g., phenylephrine, pseudoephedrine, ephedrine, phenylpropanolamine or dihydroergotamine) may enhance or potentiate the pressor effects of GUTRON. Therefore, caution should be used when GUTRON is administered concomitantly with agents that cause vasoconstriction.

GUTRON has been used in patients concomitantly treated with salt-retaining steroid therapy (i.e., fludrocortisone acetate), with or without salt supplementation. The potential for supine hypertension should be carefully monitored in these patients and may be minimized by either reducing the dose of fludrocortisone acetate or decreasing the salt intake prior to initiation of treatment with GUTRON.

Alpha-adrenergic blocking agents, such as prazosin, phentoalmine, terazosin, and doxazosin, can antagonize the effects of GUTRON.
Concomitant use of midodrine and beta-receptor blocking agents, which may reduce the heart rate; require careful monitoring.

Potential for Drug Interactions: It appears possible, although there is no supporting experimental evidence, that the high renal clearance of desglymidodrine (a base) is due to active tubular secretion by the base-secreting system also responsible for the secretion of such drugs as metformin, cimetidine, ranitidine, procainamide, triamterene, flecainide, and quinidine. Thus there may be a potential for drug-drug Interactions with these drugs.

PREGNANCY AND LACTATION

Use in Pregnancy

Pregnancy Category C. GUTRON increased the rate of embryo resorption, reduced fetal body weight in rats and rabbits, and decreased fetal survival in rabbits when given in doses 13 (rat) and 7 (rabbit) times the maximum human dose based on body surface area (mg/m^2). No teratogenic effects have been observed in studies in rats and rabbits.

There are no adequate and well-controlled studies in pregnant women. Any woman getting pregnant during treatment should be withdrawn from the treatment immediately upon established pregnancy.

Use during lactation

It is not known whether this drug is excreted in human milk therefore midodrine should not be used during lactation.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Negligible influence; However, in case of dizziness or light-headedness, care should be taken when driving vehicles or operating machinery.

ADVERSE REACTIONS

The most frequent adverse reactions seen in controlled trials were supine and sitting hypertension; paresthesia and pruritus, mainly of the scalp; goosebumps; chills; urinary urge; urinary retention; urinary frequency; heartburn and stomatitis.

The frequency of these events in a 3-week placebo-controlled trial is shown in the following table:
Adverse Events

	Placebo N=88		Midodrine N=82	
Event	# of reports	% of patients	# of reports	% of patients
Total # of reports	22		77	
Parasthesia[1]	4	4.5	15	18.3
Piloerection	0	0	11	13.4
Dysuria[2]	0	0	11	13.4
Pruritus[3]	2	2.3	10	12.2
Supine hypertension[4]	0	0	6	7.3
Chills	0	0	4	4.9
Pain[5]	0	0	4	4.9
Rash	1	1.1	2	2.4

[1] Includes hyperesthesia and scalp paresthesia
[2] Includes dysuria (1), increased urinary frequency (2), impaired urination (1), urinary retention (5), urinary urgency (2)
[3] Includes scalp pruritus
[4] Includes patients who experienced an increase in supine hypertension
[5] Includes abdominal pain and pain increase

Less frequent adverse reactions were headache; feeling of pressure / fullness in the head; vasodilation / flushing face; confusion / thinking abnormality; dry mouth; nervousness / anxiety and rash. Other adverse reactions that occurred rarely were visual field defect; dizziness; skin hyperesthesia; insomnia; somnolence; erythema multiforme; canker sore; dry skin; dysuria; impaired urination; asthenia; backache; pyrosis; nausea; gastrointestinal distress; flatulence and leg cramps, sleep disorder, restlessness, excitability, irritability, reflex bradycardia, tachycardia, abdominal pain, vomiting, diarrhoea, hepatic function abnormal and raised liver enzymes.

The most potentially serious adverse reaction associated with GUTRON therapy is supine hyertension. The feelings of paresthesia, pruritus, piloerection and chills are pilomotor reactions associated with the action of midodrine on the alpha-adrenergic receptors of the hair follicles. Feelings of urinary urgency, retention and frequency are associated with the action of midodrine on the alpha-receptors of the bladder neck.

OVERDOSAGE

Symptoms
Symptoms of overdose could include hypertension, piloerection (goosebumps) and a sensation of coldness, bradycardia and urinary retention. There are 2 reported cases of overdosage with GUTRON, both in young males. One patient ingested GUTRON drops, 250 mg, experienced systolic blood pressure

of greater than 200 mmHg, was treated with an IV injection of 20 mg of phentolamine, and was discharged the same night without any complaints. The other patient ingested 205 mg of GUTRON (41 5 mg tablets), and was found lethargic and unable to talk, unresponsive to voice but responsive to painful stimuli, hypertensive and bradycardic. Gastric lavage was performed, and the patient recovered fully by the next day without sequelae.
The single doses that would be associated with symptoms of overdosage or would be potentially life-threatening are unknown. The oral LD_{50} is approximately 30 to 50 mg/kg in rats, 675 mg/kg in mice, and 125 to 160 mg/kg in dogs.
Desglymidodrine is dialyzable.

Treatment
Beside basic life support recommended general treatment based on the pharmacology of the drug includes induced emesis and administration of alpha-sympatholytic drugs (e.g., nitroprusside, phentolamine, nitroglycerin). Bradycardia and bradycardic conduction defects can be counteracted by atropine.

Drug abuse and dependence
There is no potential for drug abuse or dependence with midodrine.

PHARMACOLOGICAL PROPERTIES

Mechanism of Action: GUTRON forms an active metabolite, desglymidodrine, that is an alpha-agonist, and exerts its actions via activation of the alpa-adrenergic receptors of the arteriolar and venous vasculature, producing an increase in vascular tone and elevation of blood pressure. Desglymidodrine diffuses poorly across the blood-brain barrier, and is therefore not associated with effects on the central nervous system.

Administration of GUTRON results in a rise in standing, sitting, and supine systolic and diastolic blood pressure in patients with orthostatic hypotension of various etiologies. Standing systolic blood pressure is elevated by approximately 15 to 30 mmHg at 1 hour after a 10mg dose of midodrine, with some effect persisting 2 to 3 hours. GUTRON has no clinically significant effect on standing or supine pulse rates in patients with autonomic -failure.

Pharmacokinetics: GUTRON is a prodrug, i.e., the therapeutic effect of orally administered midodrine is due to the major metabolite desglymidodrine, formed by deglycination of midodrine. After oral administration, GUTRON is rapidly absorbed. The plasma levels of the prodrug peak after about half an hour, and decline with a half-life of approximately 25minutes, while the metabolite reaches peak blood concentrations about 1 to 2hours after a dose of midodrine and has a half-life of about 3 to 4 hours. The absolute bioavailability of midodrine (measured as desglymidodrine) is 93%. The bioavailability of desglymidodrine is not affected by food. Approximately the same amount of desglymidodrine is formed after Intravenous and oral administration of midodrine. Neither midodrine nor desglymidodrine is bound to plasma proteins to any significant extent.

Metabolism and Excretion: Thorough metabolic studies have not been conducted, but it appears that deglycination of midodrine to desglymidodrine takes place in many tissues, and both compounds are metabolized in part by the liver. Neither midodrine nor desglymidodrine is a substrate for monoamine oxidase.

Renal elimination of midodrine is insignificant. The renal clearance of desglymidodrine is of the order of 385mL/minute, most, about 80%, by active renal secretion. The actual mechanism of active secretion has not been studied, but it is possible that it occurs by the base-secreting pathway responsible for the secretion of several other drugs that are bases (see also **Potential for Drug Interactions**).

Preclinical safety data

Pharmacology safety studies and repeat-dose toxicity studies in animals did not reveal safety concerns for humans at the recommended dose levels. The preclinical tests conducted revealed that midodrine is non-teratogenic and non-mutagenic.

In carcinogenic trials in rats an increased tumour incidence in the testicular interstitial cells was observed; the relevance of this for humans is however unclear.

Clinical Studies

Midodrine has been studied in 3 principal controlled trials, one of 3-weeks duration and 2 of 1 to 2 days duration. All studies were randomized, double-blind and parallel-design trials in patients with orthostatic hypotension of any etiology and supine-to-standing fall of systolic blood pressure of at least 15 mmHg accompanied by at least moderate dizziness / lightheadedness. Patients with pre-existing sustained supine hypertension above 180/110 mmHg were routinely excluded. In a 3-week study in 170 patients, most previously untreated with midodrine, the midodrine-treated patients (10 mg t.i.d., with the last dose not later than 6 P.M.) had significantly higher (by about 20 mmHg) 1-minute standing systolic pressure 1 hour after dosing (blood pressure were not measured at other times) for all 3 weeks. After week 1, midodrine treated patients had small improvements in dizziness/ lightheadedness / unsteadiness scores and global evaluations, but these effects were made difficult to interpret by a high) early drop-out rate (about 25% vs. 5% on placebo). Supine and sitting blood pressure rose 16/8 and 20/10 mmHg, respectively, on average. In a 2-day study, after open-label midodrine, known midodrine responders received midodrine 10 mg or placebo at 0, 3, and 6 hours. One-minute standing systolic blood pressures were increased 1 hour after each dose by about 15 mmHg and 3 hours after each dose by about 12 mmHg; 3-minute standing pressures were increased also at 1, but not 3, hours after dosing. There were increases in standing time seen intermittently 1hour after dosing, but not at 3 hours.
In a 1-day, dose-response trial, single doses of 0,2.5, 10, and 20 mg of midodrine were given to 25 patients. The 10 and 20 mg doses produced increases in standing 1-minute systolic pressure of about 30mmHg at 1 hour; the increase was sustained in part for 2 hours after 10 mg and 4 hours after 20mg. Supine systolic pressure was $\geq$ 200 mmHg an 22% of patients on 10 mg and 45% of patients on 20mg; elevated pressures often lasted 6 hours or more.

PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Tablets

Microcrystalline Cellulose, Colloidal anhydrous silica , Magnesium Stearate, Maize Starch, Talc, FD&C Yellow No.6 Lake (5 mg tablet)

Shelf life
36 months

Special precautions for storage
Store below 25°C.
Store in the original package.

Nature and contents of container
Pack Size: 2X 10s & 5 X10s
Not all pack sizes may be marketed.

MANUFACTURER
Takeda GmbH,
Plant Oranienburg,
Lehnizstr. 70-98,
DE-16515 Oranienburg,
Germany

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Patient Information Leaflet

GUTRON Tablet 5 mg
Tablets 5mg
Please read this leaflet before you start to take your medicine.
It is essential to follow your doctor's advice. If there is anything you do not understand, please ask your doctor or pharmacist.
Keep this leaflet until you have finished all your prescribed course of medicine as you may want to read it again.

What is in GUTRON Tablets?
Each GUTRON Tablet contains 5 mg of the active ingredient midodrine hyrochloride. GUTRON Tablets also contain other ingredients which are colloidal anhydrous silica, microcrystalline cellulose, maize starch, talc and magnesium stearate.
There are 20 or 50 tablets in one blister pack.

What type of medicine is this?
Midodrine (MI-doe-dreen) is a medicine used to treat low blood pressure (hypotension). It works by stimulating nerve endings in blood vessels, causing the blood vessels to tighten. As a result, blood pressure is increased.

Who makes the tablets?

GUTRON Tablets are made by Takeda GmbH, Plant Oranienburg, Lehnitzstr. 70-98, DE-16515 Oranienburg, Germany.

What are the tablets for?

GUTRON Tablets are used to stop the fall in your blood pressure which can happen when you sit up or stand up.

This should help to relieve symptoms which you might be suffering such as dizziness, fainting, blurring vision and weakness.

When should you not use the medicine?

The presence of other medical problems may affect the use of midodrine. Make sure you tell your doctor if you have any other medical problems especially:

1. A tumour near the kidney, known as phaeochromocytoma.
2. Overactive thyroid, and if you have a problem with your thyroid gland called thyrotoxicosis.
3. Hypertension (high blood pressure).
4. Vagal hypotension (a form of low blood pressure).
5. Severe organic heart disease (e.g: bradycardia, ischaemic heart disease, congestive heart failure, cardiac conduction disturbances or aortic aneurism).
6. An infection of the kidney, or if you are having problems passing urine (urinary retention), effects of midodrine on the bladder aggravate this condition.
7. Liver disease - effects of midodrine may be increased because of slower removal of the medicine from the body.
8. Narrow-angle glaucoma, visual problems - effects of midodrine may aggravate these problems.
9. Serious obliterative or spastic vascular disorders (e.g cerebrovascular occlusions and spasms)
10. Acute renal disease and severe renal impairment.
11. Hypertrophy of the prostate gland with residual volume increased.
12. Proliferative diabetic retinopathy.
13. Known hypersensitivity to any component of the product.

Consult your doctor when you have any of the above problems.

Before you take GUTRON Tablets

If the answer to any of the following questions is yes, talk to your doctor or pharmacist before taking GUTRON Tablets.

- Have you been told by a doctor that your kidneys are not working properly?
- Are you pregnant or breast feeding?
- Are you taking a medicine for high blood pressure; to increase the force to your heart beat; for depression; to reduce appetite or relieve congestion as these medicine could interfere with the effect of GUTRON Tablets.
- Are you taking a medicine to relieve congestion such as the ones you can buy from a pharmacist without a prescription?
- Are you taking any other medicines?

Very rarely people find that they react to some of the other ingredients in products. Of these other ingredients GUTRON Tablets contain microcrystalline cellulose.

Precautions while using this medicine

Do not take other medicines unless they have been discussed with your doctor. This especially includes over-the- counter medicines for appetite control, asthma, colds, cough, hayfever, or sinus problems, since they may tend to increase your blood pressure.

Used with other medicine
Although certain medicines should not be used together at all, in other cases two different medicines may be used together even if an interaction might occur. In these cases, your doctor may want to change the dose, or other precautions may be necessary. When you are taking midodrine, it is especially important that your health care professional knows if you are taking any of the following:

Digitalis glycoside (eg. Lanoxin) - effects on the heart may be increased.
Steroids that cause sodium retention, such as fludrocortisone.
Vasoconstriction medication, such as dihydroergotamine (eg. Migranal), and ephedrine, phenylephrine (ingredients in many cough & cold combination products) - effects on blood pressure may be increased.
Propanolamine, or pseudoephedrine, phenylephedrine (ingredients in many cough & cold combination products) - effects on blood pressure may be increased.

Proper use of this medicine
The last dose of midodrine should not be taken after the evening meal or less than 3 to 4 hours before bedtime because high blood pressure upon lying down (supine hypertension) can occur, which can cause blurred vision, headache, and pounding in the ears while lying down after taking this medicine. Also, midodrine should not be taken if you will be lying down for any length of time.

Adults, adolescents *and the elderly:*
The usual starting dose is 2.5 mg (% tablet) taken 2-3 times a day. Your doctor may increase this dose each week until the best effect is seen. Most people do not need more than 30 mg a day.

Children:
These tablets should not be given to children. Dosing children has not been studied as patients 18 years or younger were excluded from clinical trial.

DO NOT TAKE MORE THAN THE DOCTOR HAS RECOMMENDED.

Follow your doctor's directions on how and for how long to take GUTRON Tablets.

What if I have taken too much?
If more than the prescribed dose of GUTRON is taken, contact your doctor immediately.

What should I do if I forget to take a dose?
If it is more than half way to your next dose leave out the missed dose completely and continue with the next dose at the normal time it is due.
If you are in any doubt, contact your doctor or pharmacist before you take the missed dose.

What unwanted effects might it have?
Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur, if they do occur they may need medical attention. Check with your doctor as soon as possible if any of the following side effects occur:

More common - Blurred vision; cardiac awareness; headache and/or pounding in the ears.
Rare - Fainting; increased dizziness; slow pulse.

Other side effects may occur that usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. However, check with your doctor if any of the following side effects continue or are bothersome.

More common – Burning, itching or prickling of the scalp; chills; goosebumps; urinary frequency, retention, or urgency; heartburn and stomatitis.

Less common - Anxiety or nervousness; confusion; dry mouth; flushing; headache or feeling of pressure in the head; skin rash.

Rare - Backache; canker sores; dizziness; drowsiness; dry skin; leg cramps; pain or sensitivity of skin to touch; stomach problems such as gas, heartburn, or nausea; trouble in sleeping; trouble seeing; weakness; restlessness; excitability; irritability; reflex bradycardia; tachycardia; abdominal pain; vomiting; diarrhoea; hepatic function abnormal and raised liver enzymes.

Other side effects not listed above may also occur in some patients. If you notice any other effects, check with your doctor.

How should you keep GUTRON Tablets?
Do not use GUTRON Tablets after the expiry date printed on the pack.
Store at room temperature and out of the reach of children - preferably in a locked cupboard or medicine cabinet.
Remember - this medicine has been prescribed just for you. Do not give this medicine to anyone else - it may not be suitable for them, even if their symptoms seem the same as yours.

How can I obtain more information about GUTRON?
In this short leaflet we can give you only the most important patient information about GUTRON. If you would like to know more, ask your doctor or pharmacist.