For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

MIDORISE

1. Generic Name

Midodrine Hydrochloride Tablets U.S.P.

2. Qualitative and quantitative Composition:

MIDORISE 2.5

Each uncoated tablet contains:

Midodrine Hydrochloride U.S.P. ……. 2.5 mg

Excipients …… q.s

The List of Excipients used are Colloidal Silicon Dioxide, Croscarmellose Sodium, Microcrystalline Cellulose, Magnesium stearate, Povidone and Starch.

MIDORISE 5

Each uncoated tablet contains:

Midodrine Hydrochloride U.S.P. ……. 5 mg

Excipients …… q.s

Colour: Ponceau 4R Lake

The List of Excipients used are Colloidal Silicon Dioxide, Ponceau 4R Lake, Croscarmellose Sodium, Microcrystalline Cellulose, Magnesium stearate and Povidone and Starch.

MIDORISE 10

Each uncoated tablet contains:

Midodrine Hydrochloride U.S.P. ……. 10 mg

Excipients ……..... q.s

Colour: Sunset Yellow FCF Lake

The excipients used are Microcrystalline Cellulose, Starch, Sunset Yellow Lake, Polyvinyl Pyrrolidone, Croscarmellose Sodium, Colloidal Silicon Dioxide and Magnesium Stearate.

3. Dosage form and strength

Dosage form: Uncoated Tablet

Strength: 2.5 mg, 5 mg, and 10 mg

4. Clinical particulars

4.1. Therapeutic indication

It is indicated for the treatment of symptomatic orthostatic hypotension.

4.2. Posology and method of administration

Posology

Initial dose

2.5 mg three times a day (Midodrine hydrochloride 2.5 mg tablets are also available). Depending on the results of supine and standing blood pressure recordings, this dose may be increased weekly up to a dose of 10 mg three times a day. This is the usual maintenance dosage.

A careful evaluation of the response to treatment and of the overall balance of the expected benefits and risks needs to be undertaken before any dose increase and advice to continue therapy for long periods.

The last daily dose should be taken at least 4 hours before bedtime in order to prevent supine hypertension.

Midodrine hydrochloride 10 mg tablets may be taken with food.

Paediatric population

The safety and efficacy of midodrine hydrochloride in children have not been established. No data are available.

Elderly population

There is limited data on dosing in the elderly and there are no specific studies which have focused on a possible dose reduction in the elderly population. Cautious dose titration is recommended.

Patients with renal impairment

There are no specific studies that have focused on a possible dose reduction in patients with renal impairment. Typically, midodrine hydrochloride is contraindicated in patients with acute renal impairment and severe renal impairment.

Patients with hepatic impairment

There are no specific studies in this patient population.

Method of administration

For oral use.

4.3. Contraindications

- Severe organic heart disease (e.g. bradycardia, heart attack, congestive heart failure, cardiac conduction disturbances or aortic aneurysm).
- Hypertension
- Serious obliterative blood vessel disease, cerebrovascular occlusions and vessel spasms
- Acute kidney disease
- Severe renal impairment (creatinine clearance of less than 30 ml/min)
- Serious prostate disorder
- Urinary retention
- Proliferative diabetic retinopathy
- Pheochromocytoma
- Hyperthyroidism
- Narrow angle glaucoma
- Hypersensitivity to the active substance or to any of the excipients

4.4. Special warnings and precautions for use

Severe orthostatic hypotension with supine hypertension

Regular monitoring of supine and standing blood pressure is necessary due to the risk of hypertension in the supine position, e.g. at night. Patients should be told to report symptoms of supine hypertension immediately such as chest pain, palpitations, shortness of breath, headache, and blurred vision, and should be monitored for these side effects by the treating physician. Supine hypertension may often be controlled by an adjustment to the dose. If supine hypertension occurs, which is not overcome by reducing the dose, treatment with midodrine hydrochloride must be stopped.

The time of administration of the drug is important in this context. Avoid administration in the late evening. The last daily dose should be taken at least 4 hours before bedtime in order to prevent supine hypertension. The risk of supine hypertension occurring during the night can be reduced by elevating the head.

Severe disturbances of the autonomic nervous system

In patients suffering from a severe disturbance of the autonomic nervous system, administration of midodrine hydrochloride may lead to a further reduction of blood pressure when standing. If this occurs, further treatment with midodrine hydrochloride should be stopped.

Atherosclerotic disease

Caution must be observed in patients with atherosclerotic disease especially with symptoms of intestinal angina or claudication of the legs.

Prostate disorders

Caution is advised in patients with prostate disorders. Use of the drug may cause urinary retention.

Renal and hepatic function

This medicinal product is contraindicated in patients with acute renal impairment or severe renal impairment. Treatment with midodrine hydrochloride has not been studied in patients with hepatic impairment. It is therefore recommended to evaluate the renal and hepatic parameters before starting treatment with midodrine hydrochloride and on a regular basis.

Heart rate

Slowing of the heart rate may occur after midodrine hydrochloride administration, due to vagal reflex. Caution is advised when midodrine hydrochloride is used concomitantly with cardiac glycosides (such as digitalis preparations) and other agents that directly or indirectly reduce heart rate. Patients should be monitored for signs or symptoms suggesting bradycardia.

4.5. Drugs interactions

Sympathomimetics and other vasopressor agents

Concomitant treatment with sympathomimetics and other vasoconstrictive substances such as reserpine, guanethidine, tricyclic antidepressants, antihistamines, thyroid hormones and MAO-inhibitors, including treatments that are available without prescription, should be avoided as a pronounced increase in blood pressure may occur.

Alpha-adrenergic antagonists

As with other specific α-adrenergic agonists, the effect of midodrine hydrochloride is blocked by α-adrenergic antagonists such as prazosin and phentolamine.

Heart rate reducing drugs

Monitoring is recommended if midodrine hydrochloride is combined with other drugs that directly or indirectly reduce the heart rate.

Glycosides

Simultaneous use of digitalis preparations is not recommended, as the heart rate reducing effect may be potentiated by midodrine hydrochloride and heart block may occur.

Corticosteroid preparations

Midodrine hydrochloride may potentiate or enhance the hypertensive effects of corticosteroid preparations. Patients being treated with midodrine hydrochloride in combination with mineralocorticoids or glucocorticoids (e.g. fludrocortisone) may be at increased risk of glaucoma/increased intraocular pressure and should be carefully monitored.

Potential pharmacokinetic interactions

The potential for pharmacokinetic interaction is limited as the metabolic pathways do not involve cytochrome P450 enzymes. However, decreased clearance of medicinal products metabolised by CYP2D6 (e.g. promethazine) has been reported.

Potential effect of other drugs on midodrine

No studies to evaluate the effect of other drugs on the pharmacokinetics of midodrine or the active metabolite desglymidodrine have been conducted. In vitro data indicate that desglymidodrine is a substrate of CYP2D6. Concomitant administration of drugs that inhibit this enzyme (e.g. quinidine, paroxetine, fluoxetine and bupropion) may cause increased plasma levels of desglymidodrine with a potential risk of increased adverse events.

Potential effect of midodrine on other drugs

Midodrine is an inhibitor of CYP2D6 and may affect the metabolism of other drugs. This may be of clinical relevance for active substances that are mainly metabolized by CYP2D6, e.g. tricyclic antidepressants, beta blockers, selective serotonin reuptake inhibitors (SSRI), antiarrhythmics (including class 1A, 1B and 1C) and monoamine oxidase inhibitors (MAO inhibitors) type B, especially if the active substance also has a narrow therapeutic index.

Falsely elevated plasma metanephrine

Patients taking midodrine may have falsely elevated plasma metanephrine as a result of analytical interference when measured by HILIC-based HPLC-MS/MS. This potential for interference should be considered in cases where patients taking midodrine require biochemical investigation for potential phaeochromocytomas and paragangliomas.

4.6. Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

There are no data from the use of midodrine hydrochloride in pregnant women. Studies in animals have shown reproductive toxicity at maternally toxic doses.

Midodrine hydrochloride 10 mg tablets are not recommended during pregnancy and in women of childbearing potential not using contraception.

Breast-feeding

It is unknown whether midodrine hydrochloride and its metabolites are excreted in human milk.

A risk to newborns/infants cannot be excluded. Midodrine hydrochloride 10 mg tablets should not be used during breast-feeding.

Fertility

Animal studies are insufficient with respect to the assessment of fertility.

4.7. Effects on ability to drive and use machines

Midodrine hydrochloride 10 mg tablets have negligible influence on the ability to drive and use machines.

However, patients who experience dizziness or light-headedness should refrain from driving or operating machinery.

4.8. Undesirable effects

Summary of the safety profile

The most frequent and very common adverse reactions related to midodrine hydrochloride therapy are piloerection, pruritus of the scalp and dysuria.

Table: List of adverse reactions

Organ Class	**Very Common (> 1/10)**	**Common (> 1/100, < 1/10)**	**Uncommon (> 1/1,000, < 1/100)**	**Rare (> 1/10,000, < 1/1,000)**	**Frequency not known (cannot be estimated from available data)**
Psychiatric disorders			Sleep disorders Insomnia		Anxiety Confusional state
Nervous system disorders		Paraesthesia Paraesthesia of the scalp Headache	Restlessness Excitability Irritability		
Cardiac disorders			Reflex bradycardia	Tachycardia Palpitations	
Vascular disorders		Supine hypertension (dose dependent effect)			
Gastrointestinal disorders		Nausea Dyspepsia Stomatitis			Abdominal pain Vomiting Diarrhoea
Hepatobiliary disorders				Abnormal hepatic function Raised liver enzymes	

Organ Class	Very Common (> 1/10)	Common (> 1/100, < 1/10)	Uncommon (> 1/1,000, < 1/100)	Rare (> 1/10,000, < 1/1,000)	Frequency not known (cannot be estimated from available data)
Skin and subcutaneous tissue disorders	Piloerection (goose bumps) Pruritus of the scalp	Pruritus Chills Flushing Rash			
Renal and Urinary disorders	Dysuria	Urinary retention	Urinary urgency		

Reporting of 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. Report suspected adverse reactions via any point of contact available at www.torrentpharma.com or at email: pv@torrentpharma.com or call on 1800-120-3001.

4.9. Overdose

The symptoms of overdose are the same as experienced with side effects. The following in particular may occur: hypertension, piloerection (goose bumps) and feeling cold, bradycardia (reflex bradycardia) and urinary retention.

Treatment:

In addition to the main general "life support" measures, induced vomiting, and the administration of an α-sympatholytic agent (e.g. nitroprusside, phentolamine, nitro-glycerine) is recommended, based on the pharmacology of the drug.

Bradycardia and bradycardic conduction disturbances can be blocked by atropine.

The active metabolite desglymidodrine is dialysable.

5. Pharmacological properties

5.1. Mechanism of Action

Midodrine hydrochloride is the rapidly absorbed pro-drug of the pharmacologically active constituent desglymidodrine. Desglymidodrine is a sympathomimetic agent with a direct and selective effect on the peripheral α 1-adrenergic receptors.

5.2. Pharmacodynamic properties

This α 1 stimulative effect induces vasoconstriction of the venous system (causing a reduction in venous pooling). The α 1-adrenergic effects of desglymidodrine are almost wholly attributable to the (-) enantiomer of desglymidodrine. After taking midodrine hydrochloride, which is a racemic mixture, (+) desglymidodrine is also present, though this contributes almost nothing to the desired effect.

Desglymidodrine increases the peripheral arterial resistance, resulting in an increase in arterial blood pressure.

Only limited data is available on the long-term effects of taking midodrine hydrochloride.

Stimulation of the α-adrenergic receptors of the bladder and the ureter increases the sphincter muscle tone.

Desglymidodrine has no β-adrenergic effects.

5.3. Pharmacokinetic properties

Absorption

After oral administration, midodrine hydrochloride is rapidly absorbed. Peak plasma concentrations are reached after approximately 30 minutes, and the plasma concentration of the active metabolite, desglymidodrine, peaks after approximately 1 hour.

AUC and C_{max} increase proportionally to the dose across a dosage range of 2.5 – 22.5 mg. Administration with food increases the AUC by approximately 25%, and the C_{max} decreases by approximately 30%. The pharmacokinetics of desglymidodrine are not affected.

Distribution

Neither midodrine hydrochloride nordesgylmidodrine are bound to plasma proteins to any significant extent (less than 30%). Desglymidodrine diffuses poorly across the blood-brain barrier. Diffusion across the placenta has been reported. It is not known whether this drug is excreted in human milk.

Metabolism

Midodrine hydrochloride is partially hydrolysed before absorption (in the intestines), and partially after absorption (in plasma) by the separation of glycine, herewith generating the active metabolite, desglymidodrine. The elimination of desglymidodrine is primarily caused by an oxidating metabolism, followed by (partial) conjugation.

Excretion

Midodrine hydrochloride (8%), desglymidodrine (40%), and their degradation products (55%) are excreted in the urine by more than 90% within 24 hours in conjugated or non-conjugated forms. The plasma elimination half-life for midodrine hydrochloride is approximately 30 minutes and is approximately 3 hours for desglymidodrine. Elimination of the active (-) enantiomer of desglymidodrine is slower than the elimination of the inactive (+) enantiomer.

6. Nonclinical properties

6.1. Animal Toxicology or Pharmacology

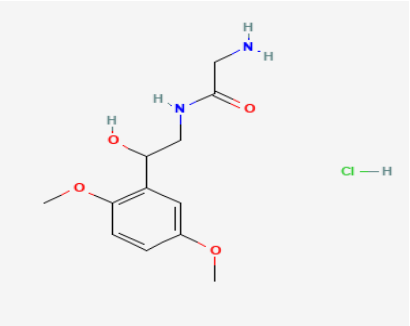
Safety Pharmacology studies and repeat-dose toxicity studies with animals did not show any indications of a safety risk for humans at therapeutic doses. Studies in the rat and rabbit show that at maternally toxic doses, midodrine hydrochloride is embryotoxic. There is no evidence of teratogenicity.

Midodrine hydrochloride is not genotoxic and after long term studies in rats (104 weeks) and mice (78 weeks), there was no evidence that midodrine hydrochloride was carcinogenic at doses of up to 10 mg/kg/day and up to 15 mg/kg/day, respectively, compared to a maximum patient daily dose of 30 mg (~0.5 mg/kg/day).

7. Description

MIDODRINE HYDROCHLORIDE

Midodrine Hydrochloride is 2-amino-N-[2-(2,5-dimethoxyphenyl)-2-hydroxyethyl] acetamide, hydrochloride. The empirical formula is $C_{12}H_{19}ClN_2O_4$, and its molecular weight is 290.74 g/mol. Its structural formula is:



Midorise 2.5 mg

Midodrine Hydrochloride Tablets are white to off white, round, flat, one side scored, other side plain and uncoated tablets.

The List of Excipients used are Colloidal Silicon Dioxide, Croscarmellose Sodium, Microcrystalline Cellulose, Magnesium stearate, Povidone and Starch.

Midorise 5 mg

Midodrine Hydrochloride Tablets are Pink coloured, round, flat, one side scored, plain on other side and uncoated tablets.

The List of Excipients used are Colloidal Silicon Dioxide, Ponceau 4R Lake, Croscarmellose Sodium, Microcrystalline Cellulose, Magnesium stearate, Povidone and Starch.

Midorise 10 mg

Midodrine Hydrochloride Tablets are Light Orange coloured, round, flat, one side scored, other side plain and uncoated tablets.

The excipients used are Microcrystalline Cellulose, Starch, Sunset Yellow Lake, Polyvinyl Pyrrolidone, Croscarmellose Sodium, Colloidal Silicon Dioxide and Magnesium Stearate.

8.1. Incompatibilities

Not applicable

8.2. Shelf-life

Do not use later than date of expiry.

8.3. Packaging information

MIDORISE 2.5 is available in pack of 20 tablets.

MIDORISE 5 & 10 is available in pack of 10 tablets

8.4. Storage and handing instructions

Store Protected from light & moisture, at a temperature not exceeding 25^{o}C.

Keep all medicines out of reach of children.

With the condition:- To be sold by retail on the prescription of cardiologist only.

8. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant

- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

9. Details of manufacturer

Pure & Cure Healthcare Pvt. Ltd.(A subsidiary of Akums Drugs & Pharmaceuticals Ltd.)
Plot No. 26A, 27-30, sector -8A, I.I.E.,
SIDCUL, Ranipur, Haridwar-249 403, Uttarakhand.

10. Details of permission or licence number with date

Midorise 2.5 mg

Mfg. Lic. No. is 31/UA/2013, issue on 04.06.2020.

Midorise 5 mg

Mfg. Lic. No. is 31/UA/2013, issue on 27.10.2020

Midorise 10 mg

Mfg. Lic. No. is 31/UA/2013, issue on 03.08.2022.

11. Date of revision

MAY 2026

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/MIDORISE 2.5, 5, and 10 mg/MAY 2026/02/PI