Trivendia MR Tablets

(Trimetazidine dihydrochloride)

Composition

Trivendia-MRTablet

Each film-coated modified-release tablet contains trimetazidine dihydrochloride..... 35 mg

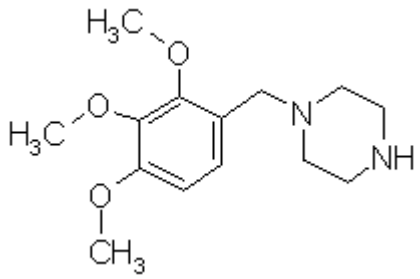
Dosage Form

Modified-release Tablet

Description

Trimetazidine is a drug for angina pectoris sold under the brand name Trivendia- MR. Trimetazidine is described as the first cytoprotective anti-ischemic agent developed and marketed by MESPA Health Care Pvt. Ltd. Trimetazidine is an anti-ischemic (anti-anginal) metabolic agent, which improves myocardial glucose utilization through inhibition of long-chain 3-ketoacyl CoA thiolase activity, which results in a reduction in fatty acid oxidation and a stimulation of glucose oxidation. High fatty acid oxidation rates are detrimental during ischemia due to an inhibition of glucose oxidation leading to uncoupling of glycolysis and an increase in proton production, which has the potential to accelerate sodium and calcium overload in the heart, which leads to an exacerbation of ischemic injury and decreased cardiac efficiency during reperfusion.

Chemical Structure



Chemical Formula- $C_{14}H_{22}N_2O_3$
IUPAC Name- 1-[(2,3,4-trimethoxyphenyl)methyl]piperazine

Pharmacology

Pharmacodynamics

By preserving energy metabolism in cells exposed to hypoxia or ischemia, trimetazidine prevents a decrease in intracellular adhenosine triphosphate (ATP) levels, thereby ensuring the proper functioning of ionic pumps and transmembrane sodium-potassium flow whilst maintaining cellular homeostasis.

Trimetazidine inhibits beta-oxidation of fatty acids by blocking long-chain 3-ketoacyl-CoA thiolase, which enhances glucose oxidation. In an ischemic cell, energy obtained during glucose

oxidation requires less oxygen consumption than in the beta-oxidation process. Potentiation of glucose oxidation optimizes cellular energy processes, thereby maintaining proper energy metabolism during ischemia.

In patients with ischemic heart disease, trimetazidine acts as a metabolic agent, preserving the myocardial high-energy phosphate intracellular levels. Anti-ischemic effects are achieved without concomitant hemodynamic effects.

Pharmacokinetics

By oral route, maximum concentration is observed, on average, five hours after taking the tablet. Over 24 hours, the plasma concentration is maintained at concentrations greater than or equal to 75% of the maximum concentration for 11 hours.

Steady state is reached by the 60^{th} hour, at the latest.

- ✓ The pharmacokinetic properties of trimetazidine 35 mg are not influenced by meals
- ✓ The apparent distribution volume is 4.8 l/kg, trimetazidine protein binding is low: its value measured *in vitro* is 16%.
- ✓ Trimetazidine is eliminated primarily in the urine, mainly in the unaltered form
- ✓ The elimination half-life of trimetazidine 35 mg is, on average, seven hours in young healthy volunteers, and 12 hours in subjects over the age of 65
- ✓ Total clearance of trimetazidine is the result of major renal clearance, which is directly correlated to creatinine clearance and, to a lesser extent, to hepatic clearance, which reduces with age
- ✓ A specific clinical study, performed in an elderly population, at a dosage of 2 tablets per day taken in 2 doses, analyzed by a kinetic population method, showed an increase in plasma exposure

Indications

Trivendia MR is indicated in adults as add-on therapy for the symptomatic treatment of patients with stable angina pectoris who are inadequately controlled by or intolerant to first-line antianginal therapies.

Dosage and Administration

The dose is one tablet of Trivendia-MR twice daily i.e., one in the morning and one in the evening during meals.
The benefit of the treatment should be assessed after three months and trimetazidine should be discontinued if there is no treatment response.

Special Population

Patients with Renal Impairment In patients with moderate renal impairment (creatinine clearance 30-60 ml/min), the recommended dose is one tablet of Trivendia-MR in the morning during breakfast.

Elderly Patients

Elderly patients may have increased trimetazidine exposure due to age-related decrease in renal function. In patients with moderate renal impairment (creatinine clearance 30-60 ml/min), the recommended dose is one tablet of Trivendia-MR in the morning during breakfast.
Dose titration in elderly patients should be exercised with caution.

Pediatric Population
The safety and efficacy of trimetazidine in children aged below 18 years have not been established. No data are available.

Contraindications

- ✓ Hypersensitivity to the active substance or to any of the excipients
- ✓ Parkinson disease, parkinsonian symptoms, tremors, restless leg syndrome, and other related movement disorders,
- ✓ Severe renal impairment (creatinine clearance

Warnings and Precautions

Drug Interactions
Trimetazidine may increase the vasodilatory activities of Isosorbide mononitrate.

The risk or severity of adverse effects can be increased when Metoclopramide is combined with Trimetazidine.

The therapeutic efficacy of Trimetazidine can be decreased when used in combination with Patent Blue.

Food Interactions

Not Available

Ischemic Heart Disease

This medicine is not a curative treatment for angina attacks, nor is it indicated as an initial treatment for unstable angina or myocardial infarction, nor in the pre-hospital phase or during the first days of hospitalization.

Coronaropathy

In the event of an angina attack, the coronaropathy should be reevaluated and an adaption of the treatment considered (medicinal treatment and possibly revascularization).

Neurological Symptoms

Trimetazidine can cause or worsen parkinsonian symptoms (tremor, akinesia, hypertonia), which should be regularly investigated, especially in elderly patients. In doubtful cases, patients should be referred to a neurologist for appropriate investigations.

The occurrence of movement disorders such as parkinsonian symptoms, restless leg syndrome, tremors, gait instability should lead to definitive withdrawal of trimetazidine.

These cases have a low prevalence and are usually reversible after treatment discontinuation. The majority of the patients recovered within 4 months after trimetazidine withdrawal. If parkinsonian symptoms persist more than 4 months after drug discontinuation, a neurologist opinion should be sought.

Falls may occur, related to gait instability or hypotension, in particular in patients taking antihypertensive treatment.

Renal Impairment

Caution should be exercised when prescribing trimetazidine to patients with moderate renal impairment as increased exposure of the drug is expected.

Pregnancy

There are no data from the use of trimetazidine in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Trivendia-MR during pregnancy.

Lactation

It is unknown whether trimetazidine is excreted in human milk. A risk to the newborns/infants cannot be excluded. Thus, Trivendia-MR should not be used during breast-feeding.

Pediatric Use

The safety and efficacy of trimetazidine in children aged below 18 years have not been established. No data are available.

Geriatric Use

Caution should be exercised when prescribing trimetazidine to elderly patients older than 75 years old as increased exposure of the drug is expected.

Undesirable Effects

Adverse reactions, defined as adverse events considered at least possibly related to trimetazidine treatment are listed below using the following convention frequency: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

System Organ Class	Frequency	Preferred Term
Nervous system disorders	Common	Dizziness, headache
	Not known	Parkinsonian symptoms (tremor, , akinesia, hypertonia), gait instability, restless leg syndrome, other related movement disorders, usually reversible after treatment discontinuation
	Not known	Sleep disorders (insomnia, drowsiness)
Cardiac disorders	Rare	Palpitations, extrasystoles, tachycardia
Vascular disorders	Rare	Arterial Hypotension , Orthostatic hypotension that may be associated with malaise, dizziness or fall, in particular in patients taking antihypertensive treatment, flushing
Gastrointestinal disorders	Common	Abdominal pain, diarrhea, dyspepsia, nausea and vomiting
	Not known	Constipation
Skin and subcutaneous tissue disorders	Common	Rash, pruritus, urticaria.
	Not known	Acute generalized exanthematus pustulosis (AGEP), angioedema

General disorders and administration conditions	Common	Asthenia
Blood and lymphatic, system disorders	Not known	Agranulocytosis
		Thrombocytopenia
		Thrombocytopenic purpura
Hepatobiliary disorders	Not known	Hepatitis

Overdosage

Not applicable.

Packaging Information

Trivendia-MR : Blister pack of 10 tablets and one box contains 10 strips.