TRIMETAZIDINE

VASTAREL® MR

35 mg Modified release tablet
ANTI-ANGINA

Description: Modified-release, pink film-coated lenticular tablet.

Formulation: Each modified release film-coated tablet contains Trimetazidine dihydrochloride 35 mg.

Pharmacodynamic Properties: 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.

Pharmacokinetic Properties: After oral administration, maximum concentration is found, on average, 5 hours after taking the tablet. Over 24 hours the plasma concentration remains at levels above or equal to 75% of the maximum concentration for 11 hours. Steady state is reached by the 60th hour, at the latest. The pharmacokinetic characteristics of Trimetazidine (Vastarel MR) are not influenced by meals. The apparent distribution volume is 4.8 L/kg; protein binding is low: in vitro measurements give value of 16%. Trimetazidine (Vastarel MR) is eliminated primarily in the urine, mainly in the unchanged form. The elimination half-life of Trimetazidine (Vastarel MR) is an average of 7 hours in healthy young volunteers and 12 hours in subjects aged more than 65 years. Total clearance of trimetazidine is the result of major renal clearance which is directly correlated to creatinine clearance and, to a lesser extent, to liver clearance which is reduced with age.

Indication:
Trimetazidine 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.

Contraindications:
- Hypersensitivity to Trimetazidine or to any of the other ingredients of Trimetazidine (Vastarel MR).
- Parkinson disease, parkinsonian symptoms, tremors, restless leg syndrome, and other related movement disorders.
- Severe renal impairment (creatinine clearance <30ml/min).

Special Warnings & Precautions:
This medicinal product is not a curative treatment for angina attacks, nor an initial treatment for unstable angina pectoris or myocardial infarction, nor in the pre-hospital phase or during the first days of hospitalization.

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

This medicinal product can aggravate or cause symptoms similar to those of Parkinson's disease (tremor, difficulty in making movements, rigidity of limbs), which should be investigated and reported to the doctor, 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 (Vastarel MR).

These cases have a low incidence and are usually reversible after treatment discontinuation. The majority of the patients recovered within 4 months after Trimetazidine (Vastarel MR) withdrawal. If parkinsonian symptoms persist more than 4 months after drug discontinuation, a neurologist's opinion should be sought.

Falls may occur following a drop in blood pressure or a loss of balance, in particular in patients taking antihypertensive treatment (see description of side effects).
Caution should be exercised in patients with moderate renal impairment and elderly (>75 years old).

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 Trimetazidine (Vastarel MR) during pregnancy.

Breastfeeding: It is unknown whether trimetazidine/metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded. Trimetazidine (Vastarel MR) should not be used during breastfeeding.

Children and adolescents: Trimetazidine (Vastarel MR) must not be administered to children aged below 18 years.

Driving and using machines: Trimetazidine (Vastarel MR) does not have hemodynamic effects in clinical studies, however cases of dizziness and drowsiness have been observed in post-marketing experience, which may affect ability to drive and use machines.

Drug Interaction: No drug interaction has been reported.

Adverse Drug Reaction:
As with all medicines, Trimetazidine (Vastarel MR) is likely to have side effects, although not everyone may be prone to them. The table below includes the adverse reactions from spontaneous notifications and scientific literature.
Very common (≥1/10); common (≥1/100,<1/10); uncommon (≥1/1000, <1/100); rare (≥1/10000, <1/1000); very rare (<1/10000); 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 Sleep disorders (insomnia, drowsiness)
Ear and labyrinth disorders	Not known	Vertigo
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 site conditions	Common	Asthenia
Blood and lymphatic system disorders	Not known	Agranulocytosis Thrombocytopenia Thrombocytopenic purpura
Hepatobiliary disorders	Not known	Hepatitis

Reporting of Adverse Drug Reaction:
For suspected adverse drug reaction, report to the FDA at ***www.fda.gov.ph***
Seek medical attention immediately at the first sign of any adverse drug reaction.

Dosage and Administration:
Oral route.
One tablet twice daily, that is once in the morning and once 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.

Patients with renal impairment
In patients with moderate renal impairment (creatinine clearance 30-60 ml/min), the recommended dose is one 35 mg tablet 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 35 mg in the morning during breakfast. Dose titration in elderly patients should be exercised with caution.

Pediatric population
The safety and efficacy of Trimetazidine (Vastarel MR) in children aged below 18 years have not been established. No data are available.

Overdose and Treatment:
Limited information is available on trimetazidine overdose. Treatment should be symptomatic.

Missed dose:
Resume treatment normally. Do not take a double dose to compensate for the single dose that you forgot to take.

Presentation:
Blister pack x 15's (box of 60's).

Storage Conditions:
Keep out of reach and sight of children.
Do not use after the expiry date indicated on the box.
Store at temperatures not exceeding 30oC.

Caution: Food, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

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Les Laboratoires Servier - France

Manufactured by:
Les Laboratoires Servier Industrie
905, route de Saran
45520 Gidy, France

Imported by: Servier Philippines, Inc.
Unit AD, 11F, 8 Rockwell, Hidalgo Drive
Rockwell Center, Brgy. Poblacion
Makati, Metro Manila

Distributed by:
Zuellig Pharma Corporation
Km. 14 West Service Road,
South Super Highway cor. Edison Ave.,
Sun Valley, Parañaque City

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