

**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE MEDICINAL PRODUCT

<Invented name>® 40 mg, prolonged-release hard capsule.

<Invented name>® 80 mg, prolonged-release hard capsule.

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

<Invented name>® 40 mg, prolonged-release hard capsule

One prolonged-release hard capsule contains 40 mg of trimetazidine dihydrochloride

<Invented name>® 80 mg, prolonged-release hard capsule.

One prolonged-release hard capsule contains 80 mg of trimetazidine dihydrochloride

Excipient with known effect:

<Invented name>® 40 mg, prolonged-release hard capsule

Sucrose: 16.87 mg per capsule

<Invented name>® 80 mg, prolonged-release hard capsule.

Sucrose 33.75mg per capsule

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Prolonged-release hard capsules.

<Invented name>® 40 mg, prolonged-release hard capsule.

Hard capsule with a white body and an white cap with a printed grey Servier logo  and “40” on it.

<Invented name>® 80 mg, prolonged-release hard capsule.

Hard capsule with a white body and an orange red cap with a printed white Servier logo  and “80” on it.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

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.

### 4.2 Posology and method of administration

#### Posology

The dose is one capsule of 80mg of trimetazidine once daily during breakfast.

The benefit of the treatment should be assessed after three months and trimetazidine should be discontinued if there is no treatment response.

#### Special populations

##### *Patients with renal impairment*

In patients with moderate renal impairment (creatinine clearance [30-60] ml/min) (see sections 4.4 and 5.2), the recommended dose is reduced by half *ie*, <1 capsule of 40mg> <1 tablet of 35mg> in the morning during breakfast.

Commented [BEI\_CB1]: 2 propositions en fonction de l'enregistrement ou non de la forme 40 mg.

#### *Elderly patients*

Elderly patients may have increased trimetazidine exposure due to age-related decrease in renal function (see section 5.2). In patients with moderate renal impairment (creatinine clearance [30-60] ml/min), the recommended dose is reduced by half *ie* <1 capsule of 40mg> <1 tablet of 35mg> in the morning during breakfast. Dose titration in elderly patients should be exercised with caution (see section 4.4).

Commented [BEI\_CB2]: 2 propositions en fonction de l'enregistrement ou non de la forme 40 mg

#### *Paediatric population:*

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

#### Method of administration

Capsule must be taken orally without opening it, once daily *i.e.* one in the morning during breakfast

### **4.3 Contraindications**

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Parkinson disease, parkinsonian symptoms, tremors, restlessleg syndrome, and other related movement disorders,
- Severe renal impairment (creatinine clearance < 30ml/min).

### **4.4 Special warnings and precautions for use**

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 hospitalisation.

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

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, restlessleg syndrome, tremors, gait instability should lead to definitive withdrawal of trimetazidine.

These cases have a low incidence 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 (see section 4.8).

Caution should be exercised when prescribing trimetazidine to patients in whom an increased exposure is expected:

- moderate renal impairment (see sections 4.2 and 5.2),
- elderly patients older than 75 years old (see section 4.2)

This drug contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

### **4.5 Interaction with other medicinal products and other forms of interaction**

No drug interactions have been identified.

### **4.6 Fertility, pregnancy and lactation**

**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 (see section 5.3.) As a precautionary measure, it is preferable to avoid the use of trimetazidine during pregnancy.

**Breastfeeding:**

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

**Fertility**

Reproductive toxicity studies have shown no effect on fertility in female and male rats (see section 5.3)

**4.7 Effects on ability to drive and use machines**

Trimetazidine does not have haemodynamic effects in clinical studies, however cases of dizziness and drowsiness have been observed in post-marketing experience (see section 4.8), which may affect ability to drive and use machines.

**4.8 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 ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  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, restlessleg syndrome, other related movement disorders, usually reversible after treatment discontinuation
	Not known	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, diarrhoea, 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

Reporting of suspected 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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system

#### 4.9 Overdose

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

### 5. PHARMACOLOGICAL PROPERTIES

#### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other cardiovascular antianginal drug, ATC code: C01EB15

##### Mechanism of action

By preserving energy metabolism in cells exposed to hypoxia or ischaemia, trimetazidine prevents a decrease in intracellular 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 ischaemic 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 ischaemia.

##### Pharmacodynamic effects

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

##### Clinical efficacy and safety

Clinical studies on trimetazidine have demonstrated its efficacy and safety in the treatment of patients with chronic angina, either alone or when the benefit from other antianginal medicinal products was insufficient.

In a 426-patients randomized, double blind, placebo-controlled study (TRIMPOL-II), trimetazidine (60mg/day) added to metoprolol 100mg daily (50 mg b.i.d) for 12 weeks significantly improved statistically exercise tests parameters and clinical symptoms as compared to placebo: total exercise duration +20.1s,  $p=0.023$ , total workload +0.54 METs,  $p=0.001$ , time to 1-mm ST-segment depression +33.4s,  $p=0.003$ , time to onset of angina +33.9s,  $p<0.001$ , angina attacks/week -0.73,  $p=0.014$  and short acting nitrates consumption/week, -0.63,  $p=0.032$ , without hemodynamic changes.

In a 223 patients randomized, double blind, placebo-controlled study (Sellier), one 35 mg trimetazidine modified release tablet (b.i.d.) added to 50 mg atenolol (o.d.) for 8 weeks produced a significant increase (+34.4s,  $p=0.03$ ) in the time to 1-mm ST-segment depression in exercise tests, in a sub-group of patients ( $n=173$ ), when compared to placebo, 12 hours after taking the drug. A significant difference was also evidenced for the time to onset of angina pectoris ( $p=0.049$ ). No significant difference between groups could be found for the other secondary endpoints (total exercise duration, total workload and clinical endpoints).

In a 1962 patients three-month randomised, double-blinded study (Vasco study) on top of atenolol 50 mg/d, two dosages of trimetazidine (70 mg/d and 140 mg/d) were tested versus placebo. In the overall population, including both asymptomatic and symptomatic patients, trimetazidine failed to

demonstrate a benefit on both ergometric (total exercise duration, time to onset of 1mm ST and time to onset angina) and clinical endpoints. However, in the subgroup of symptomatic patients (n= 1574) trimetazidine (140 mg) significantly improved total exercise duration (+23.8 s versus +13.1 s placebo; p=0.001) and time to onset of angina (+46.3 s versus +32.5 s placebo; p=0.005).

In a 165 patients three-month randomised, double-blind acceptability study on top of both routine antianginal therapies and secondary prevention therapy, the safety profile of trimetazidine 80 mg once daily was shown to be similar to that of trimetazidine MR 35 mg bid. No unexpected adverse event was reported and the study showed no concern regarding the once daily intake of trimetazidine 80 mg.

## 5.2 Pharmacokinetic properties

### Absorption

After oral administration of trimetazidine 80mg capsule, trimetazidine PK profile is flat with a peak of trimetazidine concentration reached around 14 hours after drug intake. Over dosing interval i.e. 24 hours the plasma concentration remains for 15 hours at levels above or equal to 75% of the maximum concentration. Steady state is reached by the third dose intake (3 days). Food intake has no effect on trimetazidine PK after administration of the 80mg formulation.

### Distribution

The volume of distribution is 4.8 l/kg; protein binding is low (16%).

### Elimination

Trimetazidine is primarily eliminated in the urine, mainly as unchanged form. The elimination half-life is on average 7 hours in healthy young volunteers and 12 hours in elderly (more than 65 years). Total clearance of trimetazidine mainly consists of renal clearance which is directly correlated to creatinine clearance and, to a lesser extent, of liver clearance which is reduced with age.

### Special populations

*Elderly:* The elderly may have increased trimetazidine exposure due to age-related decrease in renal function. A dedicated pharmacokinetic study performed in elderly 75-84 years or very elderly ( $\geq 85$  years) participants showed that moderate renal impairment (creatinine clearance between 30 and 60 ml/min) increased respectively by 1.0 and 1.3 fold the Trimetazidine exposure in comparison to younger participants (30-65 years) with moderate renal impairment.

A specific clinical study carried out in an elderly population (older than 75 years old) using a dosage of 2 tablets of trimetazidine MR 35mg per day taken in 2 doses, analysed by a kinetic population method, showed on average a 2-fold increase in plasma exposure in patients with severe renal impairment (creatinine clearance below 30ml/min) as compared to those with a creatinine clearance above 60 ml/min.

No safety concern was observed in the elderly population as compared to the general population.

*Renal impairment:* Trimetazidine exposure is increased on average by 1.7-fold in patients with moderate renal impairment (creatinine clearance between 30 and 60 ml/min), and on average by 3.1-fold in patients with severe renal impairment (creatinine clearance below 30ml/min) as compared to healthy volunteers, with normal renal function.

No safety concern was observed in this population as compared to the general population.

*Paediatrics:* The pharmacokinetics of trimetazidine has not been studied in the paediatric population (<18 years old).

## 5.3 Preclinical safety data

Chronic toxicity studies conducted by the oral route in dogs (5 to 40 mg.kg<sup>-1</sup>.d<sup>-1</sup>) and rats (5 to 200 mg.kg<sup>-1</sup>.d<sup>-1</sup>), showed a good safety profile.

Neither embryo-foetotoxic effect nor teratogenicity were detected in mice and in rabbits. A general study on reproduction and embryogenesis in 3 generations of rats showed no anomalies. The genotoxic potential was thoroughly assessed with in vitro studies including the evaluation of the mutagenic and clastogenic potential and one in vivo study. All tests were negative.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

#### Capsule content:

Sugar sphere containing sucrose and maiz starch  
Hypromellose  
Ethylcellulose  
Tributyl acetylacrylate  
Talc  
Magnesium stearate

<Invented name>® 40 mg, prolonged-release hard capsule

#### Capsule shell:

Gelatin  
Titanium dioxide (E171),

#### Printing Ink

Shellac (E904)  
Titanium dioxide (E171)  
Iron oxide black (E172)  
Potassium hydroxide (E525)  
Propylene Glycol (E1520)  
Ammonium hydroxide 28% (E527)

<Invented name>® 80 mg, prolonged-release hard capsule

#### Capsule shell:

Gelatin  
Titanium dioxide (E171),  
Red iron oxide (E172),

#### Printing Ink

Shellac-Glaze (E904)  
Titanium dioxide (E171)  
Simethicone  
Propylene Glycol (E1520)  
Ammonium hydroxide 28% (E527)

### 6.2 Incompatibilities

Not Applicable

### 6.3 Shelf life (to be adapted locally)

2 years

### 6.4 Special precautions for storage (to be adapted locally)

This medicinal product does not require any special storage conditions

#### 6.5 Nature and contents of container (to be adapted locally)

Cartons of <30, 60 and 90> hard capsules in blister consisting of a foil of polyamide -aluminium - PVC and a foil of aluminium.

Commented [BEI\_CB3]: To be adapted locally

Not all of these pack sizes may be marketed

#### 6.6 Special precautions for disposal

No special requirements for disposal

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

#### 7. MARKETING AUTHORISATION HOLDER

Les Laboratoires Servier  
50 rue Carnot  
92284 Suresnes cedex  
France

#### 8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

#### 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD month YYYY}

Date of latest renewal: {DD month YYYY}

[To be completed nationally]

#### 10. DATE OF REVISION OF THE TEXT

{MM/YYYY}

{DD/MM/YYYY}

{DD month YYYY}

[To be completed nationally]

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**CARTON**

**1. NAME OF THE MEDICINAL PRODUCT**

<Invented name>® 40 mg, prolonged-release hard capsule

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

40 mg Trimetazidine dihydrochloride per prolonged-release hard capsules

**3. LIST OF EXCIPIENTS**

Contains sucrose  
See leaflet for further information

**4. PHARMACEUTICAL FORM AND CONTENTS**

30 prolonged-release hard capsules  
60 prolonged-release hard capsules  
90 prolonged-release hard capsules

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Oral use  
Read the package leaflet before use.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY**

**8. EXPIRY DATE**

**9. SPECIAL STORAGE CONDITIONS**

[To be completed nationally]

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Les Laboratoires Servier  
50 rue Carnot  
92284 Suresnes cedex  
France

**12. MARKETING AUTHORISATION NUMBER(S)**

[To be completed nationally]

**13. BATCH NUMBER**

**14. GENERAL CLASSIFICATION FOR SUPPLY**

[To be completed nationally]

**15. INSTRUCTIONS ON USE**

[To be completed nationally]

**16. INFORMATION IN BRAILLE**

[To be completed nationally]

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING**

**CARTON**

**1. NAME OF THE MEDICINAL PRODUCT**

<Invented name>® 80 mg, prolonged-release hard capsule

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

80 mg Trimetazidine dihydrochloride per prolonged-release hard capsules

**3. LIST OF EXCIPIENTS**

Contains sucrose  
See leaflet for further information

**4. PHARMACEUTICAL FORM AND CONTENTS**

30 prolonged-release hard capsules  
60 prolonged-release hard capsules  
90 prolonged-release hard capsules

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Oral use  
Read the package leaflet before use.

**6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN**

Keep out of the sight and reach of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY**

**8. EXPIRY DATE**

**9. SPECIAL STORAGE CONDITIONS**

[To be completed nationally]

**10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**

**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Les Laboratoires Servier  
50 rue Carnot  
92284 Suresnes cedex  
France

**12. MARKETING AUTHORISATION NUMBER(S)**

[To be completed nationally]

**13. BATCH NUMBER**

**14. GENERAL CLASSIFICATION FOR SUPPLY**

[To be completed nationally]

**15. INSTRUCTIONS ON USE**

[To be completed nationally]

**16. INFORMATION IN BRAILLE**

[To be completed nationally]

**MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS**

**BLISTER**

**1. NAME OF THE MEDICINAL PRODUCT**

<Invented name>® 40 mg, prolonged-release hard capsule  
Trimetazidine dihydrochloride

**2. NAME OF THE MARKETING AUTHORISATION HOLDER**

Les Laboratoires Servier

**3. EXPIRY DATE**

**4. BATCH NUMBER**

**5. OTHER**

**MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS**

**BLISTER**

**1. NAME OF THE MEDICINAL PRODUCT**

<Invented name>® 80 mg, prolonged-release hard capsule

Trimetazidine dihydrochloride

**2. NAME OF THE MARKETING AUTHORISATION HOLDER**

Les Laboratoires Servier

**3. EXPIRY DATE**

**4. BATCH NUMBER**

**5. OTHER**

**B. PACKAGE LEAFLET**

## Package leaflet: Information for the patient

<Invented name>® 40 mg, prolonged-release hard capsule>

<Invented name>® 80 mg, prolonged-release hard capsule>

Trimetazidine dihydrochloride

**Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

### **What is in this leaflet:**

1. What <invented name> is and what it is used for
2. What you need to know before you take <invented name>
3. How to take <invented name>
4. Possible side effects
5. How to store <invented name>
6. Contents of the pack and other information

### **1. What <invented name> is and what it is used for**

This medicine is intended for use in adult patient, in combination with other medicines to treat angina pectoris (chest pain caused by coronary disease).

### **2. What you need to know before you take <invented name>**

#### **Do not take <invented name>**

- if you are allergic to trimetazidine or any of the other ingredients of this medicine (listed in section 6),
- if you have a Parkinson disease: disease of the brain affecting movement (trembling, rigid posture, slow movements and a shuffling, unbalanced walk),
- if you have severe kidney problems.

#### **Warnings and precautions**

Talk to your doctor or pharmacist before taking <invented name>

This drug is not a curative treatment for angina attacks, nor an initial treatment for unstable angina pectoris. It is not a treatment for myocardial infarction.

In the event of an angina attack, inform your doctor. Tests may be required and your treatment may possibly be modified.

This medicine can cause or worsen symptoms such as trembling, rigid posture, slow movements and a shuffling, unbalanced walk, especially in elderly patients, which should be investigated and reported to your doctor who could reassess the treatment.

Falls may occur following a drop in blood pressure or a loss of balance (see description of side effects).

#### **Children and adolescents**

<invented name> is not recommended in children aged below 18 years.

**Other medicines and <invented name>**

No drug interaction has been identified.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

**<invented name> with food and drink**

<invented name> can be taken with food and drink.

**Pregnancy and breast-feeding**

It is preferable not to take this medicine during pregnancy. If you discover that you are pregnant whilst taking this medicine, consult your doctor as he alone can judge the necessity of continuing your treatment.

In the absence of data on excretion in breast milk, you should not take <invented name> during breastfeeding.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

**Driving and using machines**

This medicine may make you feel dizzy and drowsy that may affect your ability to drive or use machinery.

**<invented name> contains sucrose**

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

**3. How to take <invented name>**

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose of <invented name> is one capsule to be taken once a day during breakfast.

If you have kidney problems or if you are older than 75 years old, your doctor may adjust the recommended dose.

<Invented name> is for oral use. The capsules are to be swallowed, without opening them, with a glass of water at breakfast.

**If you take more <invented name> than you should:**

If you may have taken more capsules than you should, consult a doctor or a pharmacist immediately.

**If you forget to take <invented name>:**

If you forget to take a dose of your medicine, take the next dose at the usual time. Do not take a double dose to make up for a forgotten dose.

**If you stop taking <invented name>:**

Your doctor will tell you how long the treatment will last. You should discuss with your doctor before stopping this medicinal product.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

**4. Possible side effects**

Like all medicines, this medicine can cause side effects, although not everybody gets them.

**Common: (may affect up to 1 in 10 people)**

Dizziness, headache, abdominal pain, diarrhoea, indigestion, feeling sick, vomiting, rash, itching, hives and feeling of weakness.

**Rare (may affect up to 1 in 1000 people)**

Fast or irregular heartbeats (also called palpitations), extra heartbeats, faster heartbeat, fall in blood pressure on standing-up which causes dizziness, light headedness or fainting, malaise (generally feeling unwell) or fall, flushing.

**Frequency unknown:**

- Extrapyramidal symptoms (unusual movements, including trembling and shaking of the hands and fingers, twisting movements of the body, shuffling walk and stiffness of the arms and legs), usually reversible after treatment discontinuation.
- Sleep disorders (difficulty in sleeping, drowsiness), constipation, serious generalised red skin rash with blistering, swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing.
- Spinning sensation (vertigo).
- Severe reduction in number of white blood cells which makes infections more likely, reduction in blood platelets, which increases risk of bleeding or bruising.
- A liver disease (nausea, vomiting, loss of appetite, feeling generally unwell, fever, itching, yellowing of the skin and eyes, light coloured bowel motions, dark coloured urine).

If you get any side effects, talk to your doctor or pharmacist. This includes any side effects not listed in this leaflet.

**5. How to store <invented name>**

[To be completed nationally]

Keep this medicine out of the sight and reach of children

Do not take this medicine after the expiry date which is stated on the carton and blister after 'EXP'. The expiry date refers to the last day of that month.

**This medicine does not require any special storage conditions**

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

**6. Contents of the pack and other information**

**What <invented name>40 mg, prolonged-release hard capsule> contains**

The active substance is trimetazidine (as dihydrochloride)  
One prolonged-release hard capsule contains 40 mg of trimetazidine dihydrochloride

The other ingredients are:

**Capsule content:**

Sugar sphere containing sucrose and maize starch  
Hypromellose  
Ethylcellulose  
Tributyl acetylcitrate  
Talc  
Magnesium stearate

**Capsule shell:**

Gelatin  
Titanium dioxide (E171),

**Printing Ink**

Shellac (E904)  
Titanium dioxide (E171)  
Iron oxide black (E172)  
Potassium hydroxide (E525)  
Propylene Glycol (E1520)  
Ammonium hydroxide 28% (E527)

**What <invented name>80 mg, prolonged-release hard capsule> contains**

The active substance is trimetazidine (as dihydrochloride)  
One prolonged-release hard capsule contains 80 mg of trimetazidine dihydrochloride.

The other ingredients are:

**Capsule content:**

Sugar sphere containing sucrose and maize starch  
Hypromellose  
Ethylcellulose  
Tributyl acetylcitrate  
Talc  
Magnesium stearate

**Capsule shell:**

Gelatin  
Titanium dioxide (E171),  
Red iron oxide (E172),

**Printing Ink**

Shellac (E904)  
Titanium dioxide (E171)  
Simethicone  
Propylene Glycol (E1520)  
Ammonium hydroxide 28% (E527)

**What <invented name> looks like and contents of the pack**

<invented name>40 mg, prolonged-release hard capsule  
<invented name> prolonged-release hard capsules are with a white body and a white cap with a printed on grey Servier logo  and "40" on it.

<invented name>80 mg, prolonged-release hard capsule  
<invented name> prolonged-release hard capsules are with a white body and an orange red cap with a printed on white Servier logo  and "80" on it.

The capsules are available in polyamide-aluminium-PVC/Aluminium blisters in cartons containing X prolonged release hard capsules. Not all packs sizes may be marketed.

**Marketing Authorisation Holder and Manufacturer:**

**Marketing Authorisation Holder**

Les Laboratoires Servier  
50 rue Carnot  
92284 Suresnes cedex  
France

**Manufacturer**

EGIS Pharmaceuticals PLC  
H-9900 Kőrmend, Mátyás király u.65

**Hungary**

Or  
EGIS Pharmaceuticals PLC  
H-1165 Budapest, Bökényföld ut 118-120  
Hungary

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

**This leaflet was last revised in {MM/YYYY}**

[To be completed nationally]

Detailed information on this medicine is available on the web site of {MA/ Agency}