COMPOSITION*: Triveram 10mg/5mg/5mg, 20mg/5mg/5mg, 20mg/10mg/5mg, 20mg/10mg/10mg , 40mg/10mg/10mg film-coated tablets contain 10 mg atorvastatin (ator)/5 mg perindopril arginine (per)/5 mg amloidipine (amlo), 20 mg ator/5 mg per/5 mg amlo, 20 mg ator/10 mg per/5 mg amlo, 20 mg ator/10 mg per/10 mg amlo. Contains lactose as excipient. INDICATIONS*: Substitution therapy for treatment of essential hypertension and/or stable coronary artery disease, in association with primary hypercholesterolaemia or mixed hyperlipidaemia, in adult patients adequately controlled with atorvastatin, perindopril and amloidipine given concurrently at the same dose level. DOSAGE AND ADMINISTRATION*: One tablet once daily before a meal in the morning. Triveram is not suitable for initial therapy. If a change of posology is required, the dose could be modified or individual titration with free combination may be considered. Elderly and patients with renal failure: frequent monitoring of creatinin and potassium. Clcr < 60 ml/min: not suitable. Hepatic impairment: should be used with caution. Triveram is contraindicated in patients with active liver disease. Children and adolescents: should not be used. CONTRAINDICATIONS*: Hypersensitivity to the active substances or to any other ACE inhibitor or dihydropyridine derivatives or statin or to any of the excipients, active liver disease or unexplained persistent elevations of serum transaminases exceeding 3 times the upper limit of normal, during pregnancy, while breast-feeding and in women of child-bearing potential not using appropriate contraceptive measures (see section PREGNANCY* and BREASTFEEDING*), severe hypotension, shock (including cardiogenic shock), obstruction of the outflow tract of the left ventricle (e.g., hypertrophic obstructive cardiomyopathy and high grade aortic stenosis), haemodynamically unstable heart failure after acute myocardial infarction, history of angioedema (Quincke’s oedema) associated with previous ACE inhibitor therapy, hereditary or idiopathic angioedema, concomitant use with aliskiren-containing products in patients with diabetes mellitus or renal impairment (GFR < 60 mL/min/1.73m²) (see section INTERACTIONS*). WARNINGS*: Special warnings and precautions for use. Liver effects: liver function tests should be performed periodically and in case of transaminase levels increased, the patient should be monitored until resolution. Stop treatment if jaundice or marked elevations of hepatic enzymes (serum transaminases exceeding 3 times the upper limit of normal) and in patients with active liver disease. Use with caution in patients with hepatic impairment, who consume alcohol and/or have history of liver disease. Skeletal muscle effects: stop treatment if elevation of CK levels > 10 x ULN or muscular symptoms with elevation of CK level > 5 x ULN occur, or if rhabdomyolysis is suspected. Caution should be exercised when Triveram is used with certain medicinal products that may increase the plasma concentration of atorvastatin and then the risk of rhabdomyolysis such as potent inhibitors of CYP3A4 or transport proteins (e.g. ciclosporine, ketoconazole, ritonavir…). Interstitial lung disease: treatment should be discontinued. Diabetes Mellitus: In diabetic patients, glycaemic control should be closely monitored during first month of treatment. Patients with cardiac failure: use with caution. Hypotension: monitor blood pressure, renal function and potassium in patients at high risk of symptomatic hypotension (volume depleted or who have severe renin-dependent hypertension) or with symptomatic heart failure (without our renal insufficiency), or with ischaemic heart or cerebrovascular disease. A transient hypotensive response is not a contraindication to further doses once the blood pressure has increased after volume expansion. Aortic and mitral valve stenosis/hypertrophic cardiomyopathy: use with caution and see CONTRAINDICATIONS. Kidney transplantation: no experience in case of recent transplantation. Renal impairment: monitor potassium and creatinine; individual dose titration with the monocomponents recommended if Clcr < 60 ml/min. In patients with renal artery stenosis, blood urea and creatinine may increase; with renovascular hypertension, risk of severe hypotension and renal insufficiency. Amlodipine may be used at normal doses in patients with renal failure. Haemodialysis patients: use with caution. Hyperkalaemia: stop treatment and monitor until complete resolution of symptoms. Angioedema associated with laryngeal oedema may be fatal. Anaphylactoid reactions during low-density lipoproteins (LDL) apheresis: rarely, patients have experienced life-threatening anaphylactoid reactions, temporarily withhold treatment prior to exams. Anaphylactoid reactions during desensitisation: temporarily withhold treatment prior to exams. These reactions reappeared upon inadvertent rechallenge. Neutropenia/agranulocytosis/thrombocytopenia/anaemia: extreme caution in patients with collagen vascular disease, immunosuppressant therapy, treated with allopurinol or procainamide, periodic monitor of white blood cell counts advised. Race: perindopril may be less effective and cause a higher rate of angioedema than in non-black. Cough: resolves after discontinuation. Surgery/Aesthesia: stop treatment one day prior to surgery. Hyperkalaemia: frequent monitoring of blood potassium if renal insufficiency, worsening of renal function, age (>70 years), diabetes mellitus, dehydration, acute cardiac decompensation, metabolic acidosis, and concomitant use of potassium-sparing diuretics and potassium salts or supplements. Combination with lithium: not recommended. Dual blockade of the renin-angiotensin-aldosterone system (RAAS): concomitant use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren increases the risk of hypotension, hyperkalaemia and decreased renal function (including acute renal failure). Dual blockade of RAAS is therefore not recommended. ACE-inhibitors and angiotensin II receptor blockers should not be used concomitantly in patients with diabetic nephropathy. Galactose intolerance/glucose-galactose malabsorption/Lapp lactase deficiency: should not be taken. INTERACTIONS*: Contraindicated: Aliskiren. Not recommended: CYP3A4 inhibitors, concomitant therapy with ACE inhibitor and angiotensin-receptor blocker, estramustine, lithium, potassium-sparing diuretics (e.g. triamterene,amiloride, eplerenone, spironolactone), potassium salts, danthrolene (infusion), grapefruit or grapefruit juice. Precautions: CYP3A4 inducers, digoxin, ezetimibe, fasicid acid, gemfibrozil / fibric acid derivatives, transport protein inhibitors, warfarin, antidiabetic agents (insulins, oral hypoglycaemic agents), baelcon, non-steroidal anti-inflammatory medicinal products (NSAIDs) (including aspirin ≥ 3 g/day), colchicine,olestipol, oral contraceptives, glitpins (linaglaptin, saxagliptin, sitagliptin, vildagliptin), sympatohimimetics, tricyclic antidepressants/antipsychotics/anesthetics, gold, digoxin, atorvastatin, warfarin or cyclosporine, antihypertensive agents and vasodilators. PREGNANCY AND BREASTFEEDING*: Triveram is contraindicated during pregnancy and lactation. FERTILITY*: Reversible biochemical changes of spermatozoa in some patients treated by calcium channel blockers. DRIVE AND USE MACHINES*: May be impaired if dizziness, headache, fatigue, weariness or nausea. Caution is recommended especially at the start of treatment. UNDESIRABLE EFFECTS*: Common: nasopharyngitis, allergic reactions, hyperglycaemia, somnolence, dizziness, headache, dysgeusia, paraesthesia, vertigo, visual disturbances, tinnitus, palpitations, hypotension (and effects related to hypotension), flushing, pharyngolaryngeal pain, epistaxis , cough , dyspnhea, nausea, vomiting, abdominal pain upper and lower, dyspepsia, diarrhoea, constipation, flatulence, rash, pruritus, joint swelling, ankle swelling, pain in extremity, arthralgia, muscle spasms, myalgia, muscle cramps, back pain, asthenia, fatigue, oedema peripheral, liver function test abnormal, blood creatine kinase increased. Uncommon: Rhinitis, eosinophilia, hypoglycaemia, hyponatraemia, hyperkalaemia reversible on discontinuation, anoxemia, insomnia, mood swings, sleep disorder, depression, nightmares, tremor, syncope, hypoesthesia, amnesia, vision blurred, tachycardia, vasculitis, bronchospasm, dry mouth, pancreatitis, altered bowel habits (including diarrhoea and
constipation), eructation, hepatitis either cytolytic or cholestatic, urticaria, purpura, skin discolouration, hyperhidrosis, exantheme, alopecia, angioedema, pemphigoid, photosensitivity reactions, neck pain, muscle fatigue, micturition disorder, nocturia, increased urinary frequency, renal insufficiency, impotence/erectile dysfunction, gynaecomastia, chest pain, pain, malaise, pyrexia, blood urea increased, blood creatinine increased, weight increase, white blood cells urine positive, weight decrease, fall. Rare: Thrombocytopenia, confusion, peripheral neuropathy, cholestasis, stevens-johnson syndrome, toxic epidermal necrolysis, erythema multiforme, myopathy, myositis, rhabdomyolysis, tendonopathy sometimes complicated by rupture, hepatic enzymes increased, blood bilirubin increased. Very rare: Leucopenia/neutropenia, agranulocytosis or pancytopenia, haemolytic anaemia in patients with a congenital deficiency of g-6pdh, haemoglobin decreased and haematocrit decreased, anaphylaxis, hypertonia, hearing loss, myocardial infarction secondary to excessive hypotension in high-risk patients, angina pectoris, arrhythmia, stroke possible secondary to excessive hypotension in high-risk patients, eosinophilic pneumonia, gastritis, gingival hyperplasia, jaundice, hepatic failure, exfoliative dermatitis, acute renal failure. Not known: immune-mediated necrotizing myopathy. OVERDOSE*: Amlodipine is a calcium ion influx inhibitor of the dihydropyridine group (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle. **PROPERTIES**: Amlodipine is a calcium ion influx inhibitor of the dihydropyridine group (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle. **PRESENTATION**: Box of 30, 90 (3 tablet containers of 30) or 100 film-coated tablets OF Triveram 10mg/5mg/5mg, 20mg/5mg/5mg, 20mg/10mg/5mg, 20mg/10mg/10mg, 40mg/10mg/10mg. LABORATOIRES SERVIER, 50 rue Carnot, 92284 Suresnes cedex France. www.servier.com For complete information, please refer to the Summary of Product Characteristics for your country.