Summary of Product Characteristics
TURBOVAS 10 & 20
(Rosuvastatin 10 mg and 20 mg film-coated tablets)

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1. Name of the medicinal product

Turbovas 10 and Turbovas 20 (Rosuvastatin Tablets 10 mg and 20 mg)

2. Qualitative and quantitative composition

Turbovas 10: each film-coated tablet contains rosuvastatin calcium equivalent to 10 mg of rosuvastatin.

Turbovas 20: each film-coated tablet contains rosuvastatin calcium equivalent to 20 mg of rosuvastatin.

Excipient with known effect:
Each tablet contains lactose.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet.

Orange-coloured, circular, biconvex film-coated tablet with ‘MICRO’ engraved on one surface and plain on the other.

4. Clinical particulars

4.1 Therapeutic indications

Treatment of hypercholesterolaemia

In adults, adolescents and children aged 6 years or older with primary hypercholesterolaemia (type IIa, including heterozygous familial hypercholesterolaemia) or mixed dyslipidaemia (type IIb), as an adjunct to diet when response to diet and other non-pharmacological treatment is inadequate; and in homozygous familial hypercholesterolaemia as an adjunct to diet and other lipid-lowering treatments or if such treatments are not appropriate.

Prevention of cardiovascular events

Prevention of major cardiovascular events in patients estimated to have a high risk for a first cardiovascular event, as an adjunct to correction of other risk factors.

4.2 Posology and method of administration

Before treatment, the patient should be placed on a standard cholesterol-lowering diet that should continue during treatment. The dose should be individualised according to the goal of therapy and the patient's response, using current consensus guidelines. Rosuvastatin may be given at any time of day, with or without food.

Treatment of hypercholesterolaemia

The recommended start dose is 5 or 10 mg once daily in both statin-naïve patients and those switched from another statin. The choice of start dose should take account of the individual

patient's cholesterol level, future cardiovascular risk and the potential risk of adverse reactions. A dose adjustment to the next dose level can be made after 4 weeks if necessary. Because of the increased reporting of adverse reactions with the 40 mg dose compared with lower doses, a final titration to the maximum 40 mg dose should be considered only in patients with severe hypercholesterolaemia at high cardiovascular risk who do not achieve their goal on 20 mg and in whom routine follow-up will be performed; specialist supervision is recommended when the 40 mg dose is initiated.

Prevention of cardiovascular events

The dose used in the cardiovascular risk-reduction study was 20 mg daily.

Elderly

A start dose of 5 mg is recommended in patients over 70 years; no other dose adjustment is necessary in relation to age.

Renal impairment

No dose adjustment is necessary in mild to moderate renal impairment; a 5 mg start dose is recommended in moderate impairment (creatinine clearance < 60 mL/min). Use is contraindicated in severe renal impairment for all doses, and the 40 mg dose is contraindicated in moderate impairment.

Hepatic impairment

Rosuvastatin is contraindicated in patients with active liver disease. Increased systemic exposure has been observed in patients with Child-Pugh scores of 8 and 9.

Race and genetic polymorphisms

Increased systemic exposure has been seen in Asian subjects; a 5 mg start dose is recommended and the 40 mg dose is contraindicated. A lower daily dose is recommended in patients known to have genetic polymorphisms associated with increased rosuvastatin exposure.

Paediatric population

Paediatric use should be supervised by specialists. In children aged 6–17 years with heterozygous familial hypercholesterolaemia the usual start dose is 5 mg daily (usual range 5–10 mg for ages 6–9 and 5–20 mg for ages 10–17). Rosuvastatin is not recommended in children under 6 years, and the 40 mg tablet is not suitable for paediatric patients.

4.3 Contraindications

- Hypersensitivity to rosuvastatin or to any of the excipients listed in section 6.1.
- Active liver disease, including unexplained persistent elevations of serum transaminases and any serum transaminase elevation exceeding 3 times the upper limit of normal.
- Severe renal impairment (creatinine clearance < 30 mL/min).
- Myopathy.
- Concomitant ciclosporin.
- Pregnancy, breast-feeding, and in women of childbearing potential not using appropriate contraceptive measures.

4.4 Special warnings and precautions for use

Renal effects

Proteinuria, mostly of tubular origin, has been observed, in most cases transient. An assessment of renal function should be considered during routine follow-up of patients treated with the 40 mg dose.

Musculoskeletal effects

Effects on skeletal muscle, e.g. myalgia, myopathy and, rarely, rhabdomyolysis, have been reported at all doses and in particular at doses above 20 mg. Creatine kinase should not be measured following strenuous exercise. Rosuvastatin should not be started in patients with predisposing factors for myopathy/rhabdomyolysis, and treatment should be discontinued if creatine kinase is markedly elevated (> 5 x ULN) or muscular symptoms are severe. Very rare cases of immune-mediated necrotising myopathy have been reported.

Liver effects

Liver function tests should be performed before and 3 months after initiation. Rosuvastatin should be used with caution in patients who consume excessive quantities of alcohol and/or have a history of liver disease.

Diabetes mellitus

Some evidence suggests that statins as a class raise blood glucose and may, in some patients at high risk of future diabetes, produce a level of hyperglycaemia where formal diabetes care is appropriate; this risk does not outweigh the benefit of statins in reducing vascular risk.

Interstitial lung disease

Exceptional cases of interstitial lung disease have been reported with some statins, especially with long-term therapy.

Lactose

This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Rosuvastatin is a substrate of transporter proteins (e.g. OATP1B1 and BCRP). The risk of myopathy, including rhabdomyolysis, is increased when rosuvastatin is co-administered with medicines that increase its plasma concentration through interactions with these transporters, such as ciclosporin (contraindicated) and certain protease inhibitors. Concomitant gemfibrozil, other fibrates and lipid-lowering doses of niacin increase the risk of myopathy. A dose reduction of rosuvastatin should be considered with regorafenib, certain antiviral combinations, fenofibrate and others. Rosuvastatin may increase the effect of vitamin-K antagonists (e.g. warfarin), raising the INR; antacids reduce rosuvastatin plasma concentrations if taken simultaneously.

4.6 Fertility, pregnancy and lactation

Rosuvastatin is contraindicated in pregnancy and breast-feeding. Women of childbearing potential should use appropriate contraceptive measures. As cholesterol and other products of cholesterol biosynthesis are essential for foetal development, the potential risk from inhibition of HMG-CoA reductase outweighs the advantage of treatment during pregnancy. If a patient becomes pregnant, treatment should be discontinued immediately.

4.7 Effects on ability to drive and use machines

Rosuvastatin has a negligible influence on the ability to drive and use machines. However, dizziness may occur during treatment.

4.8 Undesirable effects

The adverse reactions are generally mild and transient. They are listed below by System Organ Class and frequency, defined as: 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) and not known (cannot be estimated from the available data). The frequency of some reactions is dose-dependent.

System Organ Class	Frequency	Adverse reaction
Blood and lymphatic system disorders	Rare	Thrombocytopenia
Immune system disorders	Rare	Hypersensitivity reactions including angioedema

System Organ Class	Frequency	Adverse reaction
Endocrine disorders	Common	Diabetes mellitus
Psychiatric disorders	Not known	Depression
Nervous system disorders	Common	Headache, dizziness
	Very rare	Polyneuropathy, memory loss
	Not known	Peripheral neuropathy, sleep disturbances (including insomnia and nightmares)
Respiratory, thoracic and mediastinal disorders	Not known	Cough, dyspnoea
Gastrointestinal disorders	Common	Constipation, nausea, abdominal pain
	Rare	Pancreatitis
	Not known	Diarrhoea
Hepatobiliary disorders	Rare	Increased hepatic transaminases
	Very rare	Jaundice, hepatitis
Skin and subcutaneous tissue disorders	Uncommon	Pruritus, rash, urticaria
	Not known	Stevens-Johnson syndrome, erythema multiforme
Musculoskeletal and connective tissue disorders	Common	Myalgia
	Rare	Myopathy (including myositis), rhabdomyolysis
	Very rare	Arthralgia
	Not known	Immune-mediated necrotising myopathy, tendon disorders (sometimes complicated by rupture)
Renal and urinary disorders	Very rare	Haematuria
Reproductive system and breast disorders	Very rare	Gynaecomastia
General disorders and administration site conditions	Common	Asthenia
	Uncommon	Oedema
	Not known	Peripheral oedema

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 to the National Regulatory Authority.

4.9 Overdose

There is no specific treatment for overdose. In the event of overdose, the patient should be treated symptomatically with supportive measures instituted as required. Liver function and creatine kinase should be monitored. Haemodialysis is unlikely to be of benefit.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Lipid-modifying agents, HMG-CoA reductase inhibitors. ATC code: C10AA07.

Rosuvastatin is a selective and competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methylglutaryl coenzyme A to mevalonate, a precursor of cholesterol. Rosuvastatin increases the number of hepatic LDL receptors on the cell surface, enhancing uptake and catabolism of LDL, and inhibits hepatic synthesis of VLDL, thereby reducing total LDL and VLDL particles. It reduces LDL-cholesterol, total cholesterol and triglycerides, and increases HDL-cholesterol.

5.2 Pharmacokinetic properties

Peak plasma concentrations of rosuvastatin are reached approximately 5 hours after oral dosing; absolute bioavailability is approximately 20%. Rosuvastatin is extensively taken up by the liver, the primary site of cholesterol synthesis and LDL clearance, and is about 90% bound to plasma proteins, mainly albumin. It undergoes limited metabolism (approximately 10%), principally by CYP2C9. About 90% of a dose is excreted unchanged in the faeces, with the remainder in the urine; the plasma elimination half-life is approximately 19 hours.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, genotoxicity and carcinogenic potential. Effects seen in animal studies of reproductive toxicity occurred at exposures indicating little relevance to clinical use; as with other HMG-CoA reductase inhibitors, effects on the foetus/pup were observed at maternally toxic doses.

6. Pharmaceutical particulars

6.1 List of excipients

- Tribasic calcium phosphate
- Microcrystalline cellulose
- Lactose
- Crospovidone (Type B)
- Magnesium stearate
- Film-coating (containing titanium dioxide and iron oxide colourant)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store below 30°C. Keep out of the reach and sight of children.

6.5 Nature and contents of container

Alu-Alu blister pack of 10 tablets, presented in a printed carton together with the package insert.

6.6 Special precautions for disposal and other handling

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

7. Marketing Authorisation Holder

Micro Labs Ltd, 31 Race Course Road, Bangalore-560 001, India.

8. Marketing Authorisation Number

H2014/CTD1933/497

9. Date of first authorisation / renewal of the authorisation

10. Date of revision of the text