# SUMMARY OF PRODUCT CHARACTERISTICS
**ROSHAL 20 (Rosuvastatin Tablets 20 mg)**

## 1. NAME OF THE MEDICINAL PRODUCT

ROSHAL 20 (Rosuvastatin Tablets 20 mg)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains rosuvastatin calcium BP equivalent to rosuvastatin 20 mg.

**Excipients with known effect:**

This product contains lactose. For warnings, see section 4.4.

This product contains azo colouring agents: allura red AC (E129) and sunset yellow FCF (E120). For warnings, see section 4.4.

For a full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Film-coated tablet.

Red film-coated tablet.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

**Treatment of hypercholesterolaemia**

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 treatments (e.g. exercise, weight reduction) is inadequate.

Adults, adolescents and children aged 6 years or older with homozygous familial hypercholesterolaemia as an adjunct to diet and other lipid-lowering treatments (e.g. LDL apheresis) or if such treatments are not appropriate.

**Prevention of cardiovascular events**

Prevention of major cardiovascular events in patients who are 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

**General**

Before treatment initiation, 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 patient response, using current consensus guidelines. Rosuvastatin may be given at any time of day, with or without food.

**Adults — treatment of hypercholesterolaemia**

The recommended starting dose is 5 mg or 20 mg orally once daily in both statin-naïve patients and patients switched from another HMG-CoA reductase inhibitor. The choice of starting dose should take into account the individual patient's cholesterol level and future cardiovascular risk as well as the potential risk for adverse reactions. A dose adjustment to the next dose level can be made after 4 weeks if necessary. Due to an increased reporting rate of adverse reactions with the 40 mg dose compared to lower doses, a final titration to the maximum dose of 40 mg should only be considered in patients with severe hypercholesterolaemia at high cardiovascular risk who do not achieve their treatment goal on 20 mg, and in whom routine follow-up will be performed. Specialist supervision is recommended when the 40 mg dose is initiated.

**Adults — prevention of cardiovascular events**

In the cardiovascular events risk reduction study, the dose used was 20 mg once daily.

**Paediatric population (6 to 17 years)**

Paediatric use should only be carried out by specialists.

Heterozygous familial hypercholesterolaemia — children 6 to 9 years: usual dose range 5–20 mg once daily; children 10 to 17 years: usual dose range 5–20 mg once daily. Titration should be conducted according to individual response and tolerability, as recommended by paediatric treatment guidelines. The 40 mg tablet is not suitable for use in paediatric patients.

Homozygous familial hypercholesterolaemia — children 6 to 17 years: recommended maximum dose 20 mg once daily. A starting dose of 5–20 mg once daily depending on age, weight and prior statin use is advised. There is limited experience with doses other than 20 mg in this population.

Children younger than 6 years: safety and efficacy have not been established. Rosuvastatin is not recommended for use in children younger than 6 years.

**Elderly (>70 years)**

A starting dose of 5 mg is recommended. No other dose adjustment is necessary in relation to age.

**Renal impairment**

No dose adjustment is necessary in patients with mild to moderate renal impairment. The recommended starting dose is 5 mg in patients with moderate renal impairment (creatinine clearance <60 ml/min). The 40 mg dose is contraindicated in patients with moderate renal impairment. Use in patients with severe renal impairment is contraindicated for all doses.

**Hepatic impairment**

There was no increase in systemic exposure in subjects with Child-Pugh scores of 7 or below. Increased systemic exposure has been observed in subjects with Child-Pugh scores of 8 and 9; renal function assessment should be considered in these patients. Rosuvastatin is contraindicated in patients with active liver disease.

**Race**

Increased systemic exposure has been seen in Asian subjects. The recommended starting dose is 5 mg for patients of Asian ancestry.

**Genetic polymorphisms**

Specific types of genetic polymorphisms (SLCO1B1 c.521CC; ABCG2 c.421AA) can lead to increased rosuvastatin exposure. A lower daily dose of rosuvastatin is recommended for patients known to have such polymorphisms.

**Patients with pre-disposing factors to myopathy/rhabdomyolysis**

The recommended starting dose is 5 mg in patients with pre-disposing factors to myopathy (see section 4.4).

**Concomitant therapy**

Rosuvastatin is a substrate of various transporter proteins. The risk of myopathy is increased when rosuvastatin is administered concomitantly with certain medicinal products that may increase its plasma concentration. Whenever possible, alternative medications should be considered, and doses of rosuvastatin should be adjusted appropriately (see sections 4.3 and 4.5).

**Method of administration**

Oral, with or without food, at any time of day.

## 4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Active liver disease, including unexplained persistent elevations of serum transaminases or any serum transaminase elevation exceeding 3 times the upper limit of normal (ULN).
- Severe renal impairment (creatinine clearance <30 ml/min).
- Myopathy.
- Concomitant use with sofosbuvir/velpatasvir/voxilaprevir.
- Concomitant use with ciclosporin.
- Pregnancy, lactation, and in women of childbearing potential not using appropriate contraceptive measures.
- The 40 mg dose is additionally contraindicated in: moderate renal impairment (CrCl <60 ml/min); hypothyroidism; personal or family history of hereditary muscular disorders; previous history of muscular toxicity with another HMG-CoA reductase inhibitor or fibrate; alcohol abuse; situations where increased plasma levels may occur; Asian patients; concomitant use of fibrates.

## 4.4 Special warnings and precautions for use

**Renal effects**

Proteinuria, detected by dipstick testing and mostly tubular in origin, has been observed at higher doses (particularly 40 mg). Proteinuria has not been shown to be predictive of acute or progressive renal disease. An assessment of renal function should be considered during routine follow-up of patients treated with 40 mg.

**Skeletal muscle effects**

Effects on skeletal muscle (myalgia, myopathy and, rarely, rhabdomyolysis) have been reported at all doses and particularly at doses >20 mg. Very rare cases of rhabdomyolysis have been reported with ezetimibe in combination with HMG-CoA reductase inhibitors; caution should be exercised with their combined use.

Pre-disposing factors for myopathy/rhabdomyolysis include: renal impairment; hypothyroidism; personal or family history of hereditary muscular disorders; previous history of muscular toxicity with another HMG-CoA reductase inhibitor or fibrate; alcohol abuse; age >70 years; situations where an increase in plasma levels may occur; concomitant use of fibrates.

Creatine kinase (CK) should not be measured following strenuous exercise or in the presence of a plausible alternative cause of CK increase. If CK levels are significantly elevated at baseline (>5xULN), treatment should not be started. During treatment, patients should be asked to report unexplained muscle pain, weakness or cramps. Therapy should be discontinued if CK levels are markedly elevated (>5xULN) or if muscular symptoms are severe and cause daily discomfort.

Rosuvastatin must not be co-administered with systemic formulations of fusidic acid or within 7 days of stopping fusidic acid treatment. If systemic fusidic acid is considered essential, statin treatment should be discontinued for the duration of treatment. There have been reports of rhabdomyolysis (including some fatalities) with the fusidic acid/statin combination.

Immune-mediated necrotising myopathy (IMNM), characterised by proximal muscle weakness and elevated serum CK persisting despite discontinuation of statin treatment, has been reported very rarely.

**Liver effects**

Liver function tests should be carried out prior to, and 3 months following, initiation of treatment. Rosuvastatin should be discontinued or the dose reduced if serum transaminases exceed 3 times the ULN. The reporting rate for serious hepatic events is higher at the 40 mg dose. Rosuvastatin should be used with caution in patients who consume excessive quantities of alcohol and/or have a history of liver disease. Secondary hypercholesterolaemia caused by hypothyroidism or nephrotic syndrome should be treated prior to initiating rosuvastatin.

**Race**

Pharmacokinetic studies show an approximately 2-fold elevation in median AUC and Cmax in Asian subjects compared with Caucasians.

**Protease inhibitors**

Increased systemic exposure to rosuvastatin has been observed with various protease inhibitors in combination with ritonavir. Concomitant use with certain protease inhibitors is not recommended unless the dose of rosuvastatin is adjusted.

**Interstitial lung disease**

Exceptional cases of interstitial lung disease have been reported with some statins, especially with long-term therapy. If interstitial lung disease is suspected, statin therapy should be discontinued.

**Diabetes mellitus**

Some evidence suggests that statins as a class raise blood glucose and, in some patients at high risk of future diabetes, may produce a level of hyperglycaemia where formal diabetes care is appropriate. This risk is outweighed by the reduction in vascular risk with statins and should not be a reason for stopping treatment. Patients at risk should be monitored clinically and biochemically.

**Severe cutaneous adverse reactions**

Severe cutaneous adverse reactions including Stevens-Johnson syndrome (SJS) and drug reaction with eosinophilia and systemic symptoms (DRESS), which could be life-threatening or fatal, have been reported with rosuvastatin. Patients should be advised of the signs and symptoms of severe skin reactions and closely monitored. If signs or symptoms suggestive of SJS or DRESS appear, rosuvastatin should be discontinued immediately and must not be restarted.

**Lactose content**

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

**Azo colouring agents**

This product contains allura red AC (E129) and sunset yellow FCF (E120), which may cause allergic reactions.

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

**Effect of co-administered medicinal products on rosuvastatin**

**Transporter protein inhibitors (OATP1B1, BCRP):**

Concomitant administration of rosuvastatin with medicinal products that are inhibitors of these transporter proteins may result in increased rosuvastatin plasma concentrations and an increased risk of myopathy. See Table 1 for dose adjustment recommendations.

**Ciclosporin:**

During concomitant treatment, rosuvastatin AUC values were on average 7 times higher than in healthy volunteers. Rosuvastatin is contraindicated with concomitant ciclosporin.

**Protease inhibitors:**

Concomitant protease inhibitor use may strongly increase rosuvastatin exposure (e.g. atazanavir/ritonavir 300/200 mg resulted in approximately 3-fold AUC and 5–7-fold Cmax increase). See Table 1 for specific combinations and dose adjustments.

**Gemfibrozil:**

Concomitant use resulted in a 2-fold increase in rosuvastatin Cmax and AUC. Gemfibrozil and other fibrates increase the risk of myopathy when given concomitantly with statins. The 40 mg dose is contraindicated with concomitant fibrate use.

**Fusidic acid:**

Interaction studies have not been conducted but risk of myopathy including rhabdomyolysis (including some fatalities) has been reported. Concomitant systemic fusidic acid is contraindicated (see section 4.4).

**Antacids:**

Simultaneous dosing with aluminium/magnesium hydroxide antacid resulted in approximately 50% decrease in rosuvastatin plasma concentration. This effect was mitigated when the antacid was dosed 2 hours after rosuvastatin.

**Erythromycin:**

Concomitant use resulted in a 20% decrease in AUC and a 30% decrease in Cmax of rosuvastatin, probably due to increased gut motility.

**Effect of rosuvastatin on co-administered medicinal products**

**Vitamin K antagonists (warfarin):**

Initiation or dose up-titration of rosuvastatin in patients on vitamin K antagonists may result in an increase in INR. Discontinuation or dose down-titration may result in a decrease in INR. Appropriate monitoring of INR is desirable in such situations.

**Oral contraceptives / HRT:**

Concomitant use resulted in an increase in ethinyl estradiol AUC of 26% and norgestrel AUC of 34%. These increased plasma levels should be considered when selecting oral contraceptive doses.

**Ticagrelor:**

Ticagrelor can cause renal insufficiency and may affect renal excretion of rosuvastatin, increasing the risk for rosuvastatin accumulation. Renal function and CK monitoring is recommended when used concomitantly.

**Cytochrome P450 enzymes**

Rosuvastatin is neither an inhibitor nor an inducer of cytochrome P450 isoenzymes and is a poor substrate for these isoenzymes. No clinically relevant interactions have been observed with fluconazole (CYP2C9/3A4 inhibitor) or ketoconazole (CYP2A6/3A4 inhibitor).

**Table 1 — Effect of co-administered drugs on rosuvastatin AUC (selected key interactions)**

| Interacting drug regimen | Rosuvastatin dose | Change in AUC |
|---|---|---|
| Sofosbuvir/velpatasvir/voxilaprevir 400/200/200 mg + voxilaprevir 200 mg OD × 15 days | 20 mg single dose | 7.4-fold ↑ |
| Ciclosporin 75–200 mg BID, 6 months | 20 mg OD × 20 days | 7.1-fold ↑ |
| Darolutamide 600 mg BID × 5 days | 5 mg single dose | 5.2-fold ↑ |
| Atazanavir 300 mg/ritonavir 200 mg OD × 8 days | 20 mg single dose | 3.1-fold ↑ |
| Gemfibrozil 600 mg BID × 7 days | 80 mg single dose | 1.9-fold ↑ |
| Erythromycin 500 mg QID × 7 days | 80 mg single dose | 20% ↓ |

### 4.6 Fertility, pregnancy and lactation

Rosuvastatin is contraindicated during pregnancy and lactation, and in women of childbearing potential not using appropriate contraceptive measures.

Since 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 during use, treatment should be discontinued immediately. Rosuvastatin is excreted in the milk of rats; there are no data on excretion in human milk.

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

Studies to determine the effect on the ability to drive and use machines have not been conducted. However, based on its pharmacodynamic properties, rosuvastatin is unlikely to affect this ability. When driving vehicles or operating machines, it should be taken into account that dizziness may occur during treatment.

### 4.8 Undesirable effects

**Summary of the safety profile**

Adverse reactions seen with rosuvastatin are generally mild and transient. In controlled clinical trials, less than 4% of rosuvastatin-treated patients were withdrawn due to adverse reactions. Adverse reactions listed below are classified according to frequency and system organ class (SOC). Frequencies: 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.

| System Organ Class | Common | Uncommon | Rare | Very Rare / Not Known |
|---|---|---|---|---|
| Endocrine disorders | Diabetes mellitus[1] | | | |
| Psychiatric disorders | | | | Depression (not known) |
| Nervous system disorders | Headache, dizziness | | | Polyneuropathy, memory loss (very rare); peripheral neuropathy, sleep disturbances (not known) |
| Respiratory disorders | | | | Cough, dyspnoea (not known) |
| Gastrointestinal disorders | Constipation, nausea, abdominal pain | | Pancreatitis | Diarrhoea (not known) |
| Hepatobiliary disorders | | | Increased hepatic transaminases | Jaundice, hepatitis (very rare) |
| Skin disorders | | Pruritus, rash, urticaria | | SJS, DRESS (not known) |
| Musculoskeletal disorders | Myalgia | | Myopathy (including myositis), rhabdomyolysis, lupus-like syndrome, muscle rupture | Arthralgia (very rare); tendon disorders, IMNM (not known) |
| Renal and urinary disorders | | | | Haematuria (very rare) |
| Reproductive disorders | | | | Gynaecomastia (very rare) |
| General disorders | Asthenia | | | Oedema (not known) |
| Blood disorders | | | Thrombocytopenia | |
| Immune disorders | | | Hypersensitivity reactions including angioedema | |

*[1] Frequency will depend on the presence or absence of risk factors (fasting blood glucose ≥5.6 mmol/L, BMI >30 kg/m², raised triglycerides, history of hypertension).*

**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 Regulatory Authority.

### 4.9 Overdose
There is no specific treatment in the event of overdose. The patient should be treated symptomatically and supportive measures instituted as required. Liver function and CK levels should be monitored. Haemodialysis is unlikely to be of benefit.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties
Pharmacotherapeutic group: 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 for cholesterol. The primary site of action is the liver. 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 the total number of VLDL and LDL particles.

Rosuvastatin reduces elevated LDL-cholesterol, total cholesterol and triglycerides, and increases HDL-cholesterol. It also lowers ApoB, non-HDL-C, VLDL-C, VLDL-TG and increases ApoA-I.

A therapeutic effect is obtained within 1 week following treatment initiation, and 90% of the maximum response is achieved in 2 weeks; the maximum response is usually achieved by 4 weeks and maintained thereafter.

In the JUPITER study in patients with hsCRP ≥2 mg/L, LDL-C <3.4 mmol/L and without lipid-lowering treatment, rosuvastatin 20 mg significantly reduced the risk of the primary composite endpoint (cardiovascular death, non-fatal MI, non-fatal stroke, arterial revascularisation, or hospitalisation for unstable angina) compared to placebo.

### 5.2 Pharmacokinetic properties
**Absorption**
Maximum rosuvastatin plasma concentrations are achieved approximately 5 hours after oral administration. Absolute bioavailability is approximately 20%.

**Distribution**
The volume of distribution is approximately 134 L. Approximately 90% is bound to plasma proteins, mainly albumin. Rosuvastatin is taken up extensively by the liver.

**Biotransformation**
Limited metabolism (approximately 20%). CYP2C9 is the principal isoenzyme, with CYP2C19, CYP3A4 and CYP2D6 involved to a lesser extent. The main metabolites are N-desmethyl (approximately 50% less active than rosuvastatin) and lactone metabolites (clinically inactive). Rosuvastatin accounts for >90% of the circulating HMG-CoA reductase inhibitory activity.

**Elimination**
Approximately 90% of the rosuvastatin dose is excreted unchanged in faeces; the remaining part is excreted in urine. The plasma elimination half-life is approximately 19 hours. The elimination half-life does not increase at higher doses. The geometric mean plasma clearance is approximately 50 litres/hour. Hepatic uptake involves the membrane transporter OATP-C.

**Linearity**
Systemic exposure increases in proportion to dose. There are no changes in pharmacokinetic parameters following multiple daily doses.

**Special populations**
Race: Approximately 2-fold elevation in median AUC and Cmax in Asian subjects (Japanese, Chinese, Filipino, Vietnamese, Korean). Asian-Indians show approximately 1.3-fold elevation.

Renal impairment: Mild to moderate renal disease has no influence on plasma rosuvastatin concentrations. Subjects with severe impairment (CrCl <30 ml/min) had a 3-fold increase in plasma concentration.

Hepatic impairment: No increased exposure in subjects with Child-Pugh scores of 7 or below. Child-Pugh scores of 8 and 9 showed at least 2-fold increases.

Genetic polymorphisms: SLCO1B1 (OATP1B1) c.521CC and ABCG2 (BCRP) c.421AA are associated with higher rosuvastatin exposure. A lower daily dose is recommended in patients known to have these polymorphisms.

### 5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, genotoxicity and carcinogenicity. In repeated-dose toxicity studies, histopathological liver changes were observed in mouse, rat and (to a lesser extent) dog at exposure levels similar to clinical exposure levels. Testicular toxicity was observed in monkeys and dogs at higher dosages. Reproductive toxicity was evident in rats at maternally toxic doses at exposures several times above the therapeutic exposure level.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

The following excipients are present in the film-coated tablet (core and coat):

| Excipient |
|---|
| Calcium hydrogen phosphate |
| Maize starch |
| Microcrystalline cellulose phosphate |
| Purified talc |
| Iron oxide red (tablet coat — excipient with known effect) |
| Hypromellose (tablet coat) |
| Purified talc (tablet coat) |
| Isopropyl alcohol (tablet coat) |
| Dichloromethane (tablet coat) |
| Allura red AC (E129) (azo colouring agent with known effect) |
| Sunset yellow FCF (E120) (azo colouring agent with known effect) |

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

36 months.

### 6.4 Special precautions for storage

Do not store at a temperature above 30°C. Keep out of the reach and sight of children.

### 6.5 Nature and contents of container

30 tablets packed in one ALU blister; 3 such blisters packed in one mono carton with package insert. Pack size: 90 tablets.

### 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

**SHALINA HEALTHCARE KENYA LIMITED (Marketed by)**

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## 8. MARKETING AUTHORISATION NUMBER (PPB REGISTRATION NUMBER)

CTD10179

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

07.09.2025

## 10. DATE OF REVISION OF THE TEXT

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