Professional Information

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

ROSVATOR 5 Tablets

ROSVATOR 10 Tablets

ROSVATOR 20 Tablets

ROSVATOR 40 Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ROSVATOR 5

Each film-coated tablet contains Rosuvastatin calcium equivalent to Rosuvastatin 5 mg.

Contains sugar: Lactose monohydrate 42,952 mg per film-coated tablet.

ROSVATOR 10

Each film-coated tablet contains Rosuvastatin calcium equivalent to Rosuvastatin 10 mg.

Contains sugar: Lactose monohydrate 85,905 mg per film-coated tablet.

ROSVATOR 20

Each film-coated tablet contains Rosuvastatin calcium equivalent to Rosuvastatin 20 mg.

Contains sugar: Lactose monohydrate 171,810 mg per film-coated tablet.

ROSVATOR 40

Each film-coated tablet contains Rosuvastatin calcium equivalent to Rosuvastatin 40 mg.

Contains sugar: Lactose monohydrate 343,619 mg per film-coated tablet.

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

ROSVATOR 5

Light yellow to yellow coloured round film coated tablets with 'RT 1' debossed on one side and plain on other side.

ROSVATOR 10

Light pink to pink coloured round film coated tablets with 'RT 2' debossed on one side and plain on other side.

ROSVATOR 20

Light pink to pink coloured round film coated tablets with 'RT 3' debossed on one side and plain on other side.

ROSVATOR 40

Light pink to pink coloured oval film coated tablets with 'RT 4' debossed on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

To reduce the risk of cardiovascular events:

In adult patients with an increased risk of atherosclerotic cardiovascular disease based on the presence of cardiovascular disease risk markers such as an elevated high-sensitivity C-reactive protein (hsCRP) level, age, hypertension, low HDL-C, smoking or a family history of premature coronary heart disease, ROSVATOR is indicated to reduce the risk of non-fatal stroke, non-fatal MI, and the need for arterial revascularisation.

In adult patients with hypercholesterolaemia:

ROSVATOR is indicated for patients with primary hypercholesterolaemia, mixed dyslipidaemia and isolated hypertriglyceridaemia (including Fredrickson Type IIa, IIb and IV; and

heterozygous familial and non-familial hypercholesterolaemia) as an adjunct to diet when response to diet and exercise is inadequate.

ROSVATOR is indicated to treat patients with primary dysbetalipoproteinaemia (Fredrickson Type III hyperlipoproteinaemia).

ROSVATOR is also indicated to reduce Total Cholesterol and LDL-C in patients with homozygous familial hypercholesterolaemia, either alone or as an adjunct to diet and other lipid lowering treatments (e.g. LDL apheresis).

ROSVATOR 40 mg should only be considered in patients with severe hypercholesterolaemia and high cardiovascular risk who do not achieve their treatment goal on 20 mg of **ROSVATOR** or alternative therapy.

Specialist supervision is recommended when the 40 mg dose is initiated. (See: Section 4.4).

Children and adolescents 10-17 years of age:

ROSVATOR is indicated to reduce the Total Cholesterol, LDL-C and Apo B in patients with heterozygous familial hypercholesterolaemia (HeFH).

4.2 Posology and method of administration

Before treatment initiation, the patient should be placed on a standard cholesterol-lowering diet that should continue during treatment.

Posology

The dose-range for **ROSVATOR** is 5-40 mg orally once a day. The recommended starting dose is 5 mg once a day.

The dosage of **ROSVATOR** should be individualised according to the goal of therapy and patient response. The majority of patients are controlled at the 10 mg dose. However, if necessary, dose adjustment can be made at 2-4 week intervals (see Section 5.1).

Adults:

Primary hypercholesterolaemia, (including heterozygous familial hypercholesterolaemia), mixed dyslipidaemia and isolated hypertriglyceridaemia:

The recommended starting dose is 5 mg once a day.

A 5 mg starting dose is recommended for patients of Asian ancestry and for patients requiring a smaller reduction in LDL-C to achieve treatment target.

For patients with severe hypercholesterolaemia (including heterozygous familial hypercholesterolaemia), a starting dose of 20 mg may be considered.

Homozygous familial hypercholesterolaemia:

For patients with homozygous familial hypercholesterolaemia a starting dose of 20 mg once a day is recommended.

Children and adolescents 10-17 years of age:

In children and adolescents with heterozygous familial hypercholesterolaemia the usual dose range is 5-20 mg orally once daily. The dose should be appropriately titrated to achieve treatment goal. Safety and efficacy of doses greater than 20 mg have not been studied in this population.

In children and adolescents with homozygous familial hypercholesterolaemia experience is limited to a small number of patients (aged 8 years and above).

Special populations

Use in elderly

The usual dose range applies to the elderly patients.

Dosage in patients with renal insufficiency

The starting dose of 5 mg applies in patients with mild to moderate renal impairment. For patients with severe renal impairment the dose of ROSVATOR should not exceed 10 mg once daily.

Dosage in patients with hepatic insufficiency

The usual starting dose applies in patients with mild to moderate hepatic impairment. Patients with severe hepatic impairment should start therapy with ROSVATOR 5 mg. Increased systemic exposure to rosuvastatin has been reported in these patients, therefore the use of doses above rosuvastatin 10 mg should be carefully considered (see Section 5.2).

Race

A 5 mg starting dose of **ROSVATOR** should be considered for Asian patients. Increased plasma concentration of rosuvastatin has been reported in Asian subjects (see Section 5.2). The increased systemic exposure should be taken into consideration when treating Asian patients whose hypercholesterolaemia is not adequately controlled at doses up to 20 mg daily.

Concomitant therapy

Rosuvastatin has been reported to have additive efficacy in lowering triglycerides when used in combination with fenofibrate and in increasing HDL-C levels when used in combination with niacin.

ROSVATOR can also be used in combination with bile acid sequestrants or ezetimibe (see Section 4.4).

Interactions requiring dose adjustments:

Ciclosporin:

Increased systemic exposure to rosuvastatin has been observed in patients taking concomitant **ROSVATOR** and Ciclosporin. For the **ROSVATOR** dose range (10-40 mg) this combination is not recommended. (See Section 4.3)

Gemfibrozil

Increased systemic exposure to rosuvastatin has been reported in subjects taking concomitant **ROSVATOR** and gemfibrozil. Patients taking this combination should start therapy with **ROSVATOR 5** mg once daily and should not exceed a dose of **ROSVATOR** 20 mg once daily (see Section 4.5).

Method of administration

Oral use.

ROSVATOR is taken once a day, at any time of the day, with or without food.

4.3 Contraindications

- Patients with a known hypersensitivity to **ROSVATOR,** or other HMG-CoA reductase inhibitors, or any other component of this product.
- Patients with active liver disease
- Concomitant use with ciclosporin (see Section 4.5)
- Patients with myopathy
- Safety in pregnancy and lactation has not been established (see Section 4.6)

4.4 Special warnings and precautions for use

Warnings:

Skeletal muscle

Effects on skeletal muscle e.g. uncomplicated myalgia, myopathy and rhabdomyolysis have been reported in patients treated with **ROSVATOR**. The reporting rate for rhabdomyolysis in post-marketing use is higher at the highest dose. Patients who develop any signs or symptoms suggestive myopathy should have their creatine kinase (CK) levels measured. **ROSVATOR** therapy should be discontinued if myopathy is diagnosed or suspected.

An increase in the incidence of myositis and myopathy has been reported in patients receiving other HMG-CoA reductase inhibitors such as **ROSVATOR** together with cyclosporine, fibric acid derivatives, including gemfibrozil, nicotinic acid, azole antifungals and macrolide antibiotics.

ROSVATOR should be prescribed with caution in patients with pre-disposing factors for myopathy, such as renal impairment, advanced age and hypothyroidism, history of hereditary muscular disorders, history of muscular toxicity with another statin or fibrate, alcohol abuse, or situations where an increase in plasma levels may occur (see Section 5.1).

ROSVATOR should be temporarily withheld in any patient with an acute serious condition suggestive of myopathy or pre-disposing to the development of renal failure secondary to rhabdomyolysis (e.g. sepsis, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorder; or uncontrolled seizures).

Concomitant use with protease inhibitors in HIV patients (see Section 5.5).

Special precautions

Liver Enzyme Abnormalities and Monitoring

It is recommended that liver enzyme tests be performed before and at 12 weeks following both the initiation of **ROSVATOR** therapy and any elevation of dose, and periodically (e.g., semiannually) thereafter. If serious liver injury with clinical symptoms and/or hyperbilirubinaemia or jaundice occurs during treatment, therapy should be interrupted. If an alternate aetiology is not found, **ROSVATOR** should not be restarted.

ROSVATOR should be used with caution in patients who consume substantial quantities of alcohol and/or have a history of chronic liver disease. Active liver disease, which may include unexplained persistent transaminase elevations, is a contra-indication to the use of **ROSVATOR** (see Section 4.3).

Renal effects

An assessment of renal function should be considered during routine follow-up of patients treated with a dose of 40 mg.

Endocrine Effects

Increases in glycosylated haemoglobin (HbA1c), fasting serum glucose levels and worsening of glycaemic control have been reported with the use of statins, such as **ROSVATOR** it should therefore be used with care in patients with type 2 diabetes.

Although reported clinical studies have shown that rosuvastatin alone does not reduce basal plasma cortisol concentration or impair adrenal reserve, caution should be exercised if **ROSVATOR** is administered concomitantly with agents that may decrease the levels or activity of endogenous steroid hormones such as ketoconazole, spironolactone, and cimetidine.

Nervous system effects

There have been reports of cognitive impairment (such as memory loss, forgetfulness, amnesia, memory impairment, and confusion) associated with the use of statins such **ROSVATOR**. These reported symptoms were generally not serious and reversible upon discontinuation with variable times to symptom onset (between a day to years) and symptom resolution with a median of 3 weeks.

Risk of myasthenia gravis and ocular myasthenia.

Race

Pharmacokinetic studies reported an increase in exposure in Asian subjects compared with Caucasians (See Sections 4.2 and 5.2).

ROSVATOR should be used with caution in patients taking the combination of protease inhibitors such as lopinavir/ritonavir as pharmacokinetic studies have reported an increase in the AUC and Cmax of rosuvastatin (see Section 4.5)

Excipients

ROSVATOR contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take **ROSVATOR**.

4.5 Interaction with other medicinal products and other forms of interaction

Interactions with other medicinal products and other form of interaction:

Warfarin:

The pharmacokinetics of warfarin is not significantly affected following co-administration with **ROSVATOR**. However, as with other HMG-CoA reductase inhibitors, co-administration of **ROSVATOR** and warfarin may result in a rise in INR compared to warfarin alone. In patients

taking warfarin monitoring of INR is recommended both at initiation or cessation of therapy with **ROSVATOR** or following dose adjustment.

Ciclosporin:

Co-administration of **ROSVATOR** with ciclosporin resulted in no significant changes in ciclosporin plasma concentration. However, after co-administration with ciclosporin, rosuvastatin steady plasma concentration state AUC(0-t) increased up to 7-fold over that reported in healthy volunteers administered the same dose of rosuvastatin (see Section 4.3).

Gemfibrozil:

Concomitant use of **ROSVATOR** and gemfibrozil resulted in a 2-fold increase in rosuvastatin C_{max} and $AUC_{(0-t)}$ (see Section 4.2).

Protease inhibitors:

Increased systemic exposure to rosuvastatin has been observed in subjects in pharmacokinetic studies receiving rosuvastatin with various protease inhibitors in combination with ritonavir. This increase in systemic exposure to rosuvastatin may lead to increased incidence of adverse effects.

Antacids:

The simultaneous dosing of **ROSVATOR** with an antacid suspension containing aluminium and magnesium hydroxide resulted in a decrease in rosuvastatin plasma concentration of approximately 50 %. This effect was mitigated when the antacid was dosed 2 hours after **ROSVATOR**. The clinical relevance of this interaction has not been reported.

Cytochrome P450 enzymes:

In vivo and in vitro data indicate that rosuvastatin has no clinically significant Cytochrome P450 interactions (as a substrate, inhibitor or inducer).

Niacin:

The risk of skeletal muscle effects may be enhanced when **ROSVATOR** is used in combination with niacin; a reduction in **ROSVATOR** dosage should be considered in this setting.

Fenofibrate:

When **ROSVATOR** was co-administered with fenofibrate no clinically significant increase in the AUC of rosuvastatin or fenofibrate was reported. The benefit of further alterations in lipid levels by the combined use of **ROSVATOR** with fibrates should be carefully weighed against the potential risks of this combination.

Erythromycin:

Concomitant use of **ROSVATOR** and erythromycin can result in a 20 % decrease in the $AUC_{(0-t)}$ and a 30 % decrease in C_{max} of rosuvastatin. This interaction may be caused by the increase in gastro-intestinal motility caused by erythromycin.

Oral contraceptive/hormone replacement therapy (HRT):

Concomitant use of **ROSVATOR** and an oral contraceptive can result in an increase in ethinyl oestradiol and norgestrel AUC of 26 % and 34 % respectively. These increased plasma levels should be considered when selecting oral contraceptive doses. Although there are no pharmacokinetic data available in women taking concomitant HRT, a similar effect cannot be excluded.

Ezetimibe:

Concomitant use of ROSVATOR and ezetimibe will not result in any change of AUC or Cmax for either medicine. However, cases of rhabdomyolysis have been reported when ezetimibe is used in combination with rosuvastatin (see Section 4.8).

Other medications:

In reported clinical studies rosuvastatin was co-administered with antihypertensive agents, anti-diabetic agents and hormone replacement therapy. These reported studies did not produce any evidence of clinically significant adverse reactions.

4.6 Fertility, pregnancy and lactation

ROSVATOR is contra-indicated in pregnancy and lactation (see Section 4.3). Women of child-bearing potential should use appropriate contraceptive measures.

Pregnancy

The safety of **ROSVATOR** during pregnancy has not been established.

Breast-feeding

The safety of **ROSVATOR** whilst breast-feeding has not been established.

Fertility

No available data.

4.7 Effects on ability to drive and use machines

Pharmacology testing revealed no evidence of a sedative effect of rosuvastatin. **ROSVATOR** may however cause dizziness, therefore patients should not drive or use machines, until their individual susceptibility to dizziness is known (see Section 4.8).

4.8 Undesirable effects

Table 1. Tabulated list of adverse events observed and reported during treatment with rosuvastatin

SYSTEM ORGAN CLASS	FREQUENCY	ADVERSE REACTION
Immune system disorders	Less frequent	Hypersensitivity reactions including angioedema.
Blood and lymphatic system disorders	Less frequent	Thrombocytopaenia
Endocrine disorders	Frequent	Diabetes Mellitus
Psychiatric disorders	Frequency unknown	Depression
Metabolism and nutrition disorders	Frequent	Increased serum glucose levels.
Nervous system disorders	Frequent	Dizziness, headache.
	Less frequent	Cognitive impairment such as memory loss, forgetfulness, amnesia, memory impairment and confusion, polyneuropathy.
	Frequency unknown	Sleep disturbances including nightmares and insomnia. Peripheral neuropathy. Myasthenia gravis.

Eye disorders	Frequency unknown	Ocular myasthenia
Respiratory, thoracic and mediastinal disorders	Frequency unknown	Cough Dyspnoea
Gastrointestinal disorders	Frequent	Nausea, constipation, abdominal pain.
	Less frequent	Pancreatitis
	Frequency not known	Diarhoea
Hepatobiliary disorders	Less frequent	Jaundice, hepatitis, increased hepatic transaminases
Skin and subcutaneous tissue disorders	Frequent	Rash, pruritus (includes pruritus generalised)
	Less frequent	Pruritus, rash, urticaria.
	Frequency unknown	Stevens-Johnson syndrome. Drug reaction with eosinophilia and systemic symptoms(DRESS)
Muscoskeletal and connective tissue disorders	Frequent	Myalgia.
	Frequency Unknown	Immune mediated necrotising myopathy Tendon disorders, sometimes complicated by rupture
	Less frequent	Myopathy (including myositis) rhabdomyolysis, arthralgia, Lupus-like syndrome, muscle rupture
Renal and urinary disorders	Less frequent	Proteinuria, hematuria
Reproductive system	Less Frequent	Gynaecomastia
General disorders and administration site conditions	Frequent	Asthenia.
	Frequency unknown	Oedema

Investigations: A dose related increase in liver transaminases and creatine kinase (CK) has been observed in patients taking rosuvastatin. Abnormal urinalysis testing (dipstick-positive proteinuria with haematuria) has been seen in patients taking ROSVATOR. The protein detected was mostly tubular in origin. In most cases, proteinuria decreases or disappears

spontaneously on continued therapy and is not predictive of acute or progressive renal disease.

Table 2: Adverse reactions from post-marketing experience

SYSTEM ORGAN CLASS	ADVERSE REACTION
Hepatobiliary:	Jaundice, hepatitis, increased hepatic transaminases.
Musculoskeletal	Artralgia. The reporting rate for rhabdomyolysis in post-marketing use is higher at the highest marketed dose. Rhabdomyolysis, which may occasionally be associated with impairment of renal function, has been reported with rosuvastatin.
Renal effects	Proteinuria.
Nervous system disorders	Memory loss.
Laboratory effects	A dose-related increase in liver transaminases and Creatine kinase (CK) has been observed in patients taking rosuvastatin. Abnormal urinalysis testing (dipstick-positive proteinuria with haematuria) has been seen in patients taking rosuvastatin. The protein detected was mostly tubular in origin. In most cases, proteinuria decreases or disappears spontaneously on continued therapy, and is not predictive of acute or progressive renal disease.
Other effects	No harmful effects on the ocular lens have been reported in clinical trials.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

There is no specific treatment in the event of overdose. In the event of overdose, the patient should be treated symptomatically and supportive measures instituted as required.

Haemodialysis is unlikely to be of benefit.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacological classification: A 7.5 Serum-cholesterol reducers

Pharmacotherapeutic group: HMG-CoA reductase inhibitors;

ATC code: C10A A07

Mechanism of action

Rosuvastatin is a selective, competitive inhibitor of HMG-CoA reductase, the rate-limiting enzyme that converts 3-hydroxy-3-methylglutaryl coenzyme A to mevalonate, a precursor of cholesterol.

Pharmacodynamic effects

The lipid-modifying effects of rosuvastatin are produced in two ways; it 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.

High density lipoprotein (HDL), which contains ApoA-I is involved, amongst other things, in transport of cholesterol from tissues back to the liver (reverse cholesterol transport).

5.2 Pharmacokinetic properties

Absorption

Maximum rosuvastatin plasma concentrations are achieved approximately 5 hours after oral administration. Absorption increases linearly over the dose range. The absolute bioavailability is approximately 20%. There is minimal accumulation on repeated once daily dosing.

Distribution

Rosuvastatin is taken up extensively by the liver which is the primary site of cholesterol synthesis and LDL-C clearance. The volume of distribution of rosuvastatin is approximately 134 L. Approximately 90% of rosuvastatin is bound to plasma proteins, mainly to albumin.

Biotransformation

Rosuvastatin undergoes limited metabolism (approximately 10%), mainly to the N-desmethyl form. *In vitro* metabolism studies using human hepatocytes indicate that rosuvastatin is a poor substrate for cytochrome P450-based metabolism. CYP2C9 was the principal isoenzyme involved, with 2C19, 3A4 and 2D6 involved to a lesser extent. The main metabolites identified are the N-desmethyl and lactone metabolites. The N-desmethyl metabolite is approximately 50% less active than rosuvastatin whereas the lactone form is considered clinically inactive. Rosuvastatin accounts for greater than 90% of the circulating HMG-CoA reductase inhibitor activity

Elimination

Approximately 90% of the rosuvastatin dose is excreted unchanged in the faeces (consisting of absorbed and non-absorbed active substance) and the remaining part is excreted in urine. Approximately 5% is excreted unchanged 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 (coefficient of variation 21.7%). As with other HMG-CoA reductase inhibitors, the hepatic uptake of rosuvastatin involves the membrane transporter OATP-C. This transporter is important in the hepatic elimination of rosuvastatin.

Special populations:

Age and sex:

There was no clinically relevant effect of age or sex on the pharmacokinetics of rosuvastatin in adults. The exposure in children and adolescents with heterozygous familial hypercholesterolemia appears to be similar to or lower than that in adult patients with dyslipidaemia (see “Paediatric population” below).

Race:

Reported pharmacokinetic studies show an approximate 1,26 to 2,31 fold elevation in mean $AUC_{(0\text{-}t)}$ and C_{max} in Asian subjects compared to Caucasians. A total of 62 (19 %) Caucasian, 61 (19 %) Chinese, 61 (19 %) Asian-Indian, 35 (11 %) Malay, 27 (8 %) Japanese, 27 (8 %) Philipino, 26 (8 %) Korean and 25 (8 %) Vietnamese subjects were evaluated for pharmacokinetic analysis in the reported studies. A population pharmacokinetic analysis revealed no clinically relevant differences in pharmacokinetics among Caucasian, Hispanic and Black or Afro-Caribbean groups (see Section 4.2: Race

Renal insufficiency:

In a reported study in subjects with varying degrees of renal impairment, mild to moderate renal disease had no influence on plasma concentration of rosuvastatin or the N-desmethyl metabolite. Subjects with severe impairment (CrCl <30 ml/min) had a 3-fold increase in plasma concentration and a 9-fold increase in the N-desmethyl metabolite concentration compared to healthy volunteers. Steady-state plasma concentrations of rosuvastatin in subjects undergoing haemodialysis were approximately 50% greater compared to healthy volunteers. Haemodialysis is unlikely to be of benefit for medicine removal.

Hepatic insufficiency:

In a reported study with subjects with varying degrees of hepatic impairment, there was no evidence of increased exposure to rosuvastatin in subjects with Child-Pugh scores of 7 or below. However, two subjects with Child-Pugh scores of 8 and 9 showed an increase in systemic exposure of at least 2-fold compared to subjects with lower Child-Pugh scores. There is no experience in subjects with Child-Pugh scores above 9.

Genetic polymorphisms:

Disposition of HMG-CoA reductase inhibitors, including rosuvastatin, involves OATP1B1 and BCRP transporter proteins. In patients with SLCO1B1 (OATP1B1) and/or ABCG2 (BCRP) genetic polymorphisms there is a risk of increased rosuvastatin exposure. Individual polymorphisms of SLCO1B1 c.521CC and ABCG2 c.421AA are associated with a higher rosuvastatin exposure (AUC) compared to the SLCO1B1 c.521TT or ABCG2 c.421CC genotypes. This specific genotyping is not established in clinical practice, but for patients who are known to have these types of polymorphisms, a lower daily dose of ROSVATOR is recommended.

Paediatric population:

Two reported pharmacokinetic studies with rosuvastatin (given as tablets) in paediatric patients with heterozygous familial hypercholesterolaemia 10 to 17 or 6 to 17 years of age (total of 214 patients) demonstrated that exposure in paediatric patients appears comparable to or lower than that in adult patients. Rosuvastatin exposure was predictable with respect to dose and time over a 2-year period.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, genotoxicity and carcinogenicity potential.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

ROSVATOR contains the following excipients: crospovidone, magnesium stearate, microcrystalline cellulose, opadry yellow or opadry pink and sodium citrate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store at or below 25 °C in the original pack, protected from light and moisture.

Do not remove the blisters from the carton until required for use.

6.5 Nature and contents of container

Cartons contain 28 or 30 tablets packed in silver cold form blister packs or desiccant embedded silver cold form blister packs, each blister strip of silver cold form blister pack and desiccant embedded silver cold form blister pack contains 7 or 10 tablets.

The carton contains 4 blister strips of 7 tablets each for the 28’s pack and 3 blister strips of 10 tablets each for the 30’s pack.

6.6 Special precautions for disposal and other handling

No special requirements

7. MARKETING AUTHORISATION HOLDER

Ranbaxy Pharmaceuticals (Pty) Ltd

14 Lautre Road, Stomill, Ext 1

Roodepoort, 1724

8. MARKETING AUTHORISATION NUMBER(S)

ROSVATOR 5: 45/7.5/0955

ROSVATOR 10: 45/7.5/0956

ROSVATOR 20: 45/7.5/0957

ROSVATOR 40: 45/7.5/0958

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01 March 2013

10. DATE OF REVISION OF THE TEXT

24 July 2022