CREVAS

SCHEDULING STATUS S4

1. NAME OF THE MEDICINE

CREVAS 5 mg (5 mg film coated tablets)
CREVAS 10 mg (10 mg film coated tablets)
CREVAS 15 mg (15 mg film coated tablets)
CREVAS 20 mg (20 mg film coated tablets)
CREVAS 30 mg (30 mg film coated tablets)
CREVAS 40 mg (40 mg film coated tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

CREVAS 5 mg: Each film coated tablet contains 5 mg rosuvastatin (as rosuvastatin calcium)
CREVAS 10 mg: Each film coated tablet contains 10 mg rosuvastatin (as rosuvastatin calcium)
CREVAS 15 mg: Each film coated tablet contains 15 mg rosuvastatin (as rosuvastatin calcium)
CREVAS 20 mg: Each film coated tablet contains 20 mg rosuvastatin (as rosuvastatin calcium)
CREVAS 30 mg: Each film coated tablet contains 30 mg rosuvastatin (as rosuvastatin calcium)
CREVAS 40 mg: Each film coated tablet contains 40 mg rosuvastatin (as rosuvastatin calcium)

Excipients with known effect
Each 5 mg film coated tablet contains 45,72 mg lactose monohydrate.
Each 10 mg film coated tablet contains 90,90 mg lactose monohydrate.
Each 15 mg film coated tablet contains 137,16 mg lactose monohydrate.
Each 20 mg film coated tablet contains 181,80 mg lactose monohydrate.
Each 30 mg film coated tablet contains 274,32 mg lactose monohydrate.
Each 40 mg film coated tablet contains 233,01 mg lactose monohydrate.
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

CREVAS 5 mg: Round, biconvex, yellowish film coated tablets, 6 mm in diameter, debossed with "5" on one side.
CREVAS 10 mg: Round, biconvex, light pink film coated tablets, 7 mm in diameter, debossed with "10" on one side.
CREVAS 15 mg: Round, biconvex, yellow film coated tablets, 8 mm in diameter, debossed with "15" on one side and "15" on the other side.
CREVAS 20 mg: Round, biconvex, dark pink film coated tablets, 9 mm in diameter, debossed with "20" on one side.
CREVAS 30 mg: Round, biconvex, yellow film coated tablets, 10 mm in diameter, debossed with "30" on one side.
CREVAS 40 mg: Round, biconvex, red film coated tablets, 10 mm in diameter, debossed with "40" on one 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, CREVAS is indicated to reduce the risk of non-fatal stroke, non-fatal MI, and the need for arterial revascularisation.

In adult patients with hypercholesterolaemia:
CREVAS 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.

CREVAS is indicated to treat patients with primary dysbetalipoproteinaemia (Fredrickson Type III hyperlipoproteinaemia).
CREVAS 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).
CREVAS 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 CREVAS or alternative therapy. Specialist supervision is recommended when the 40 mg dose is initiated (see section 4.4).

Children and adolescents 10 to 17 years of age:
CREVAS 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 dosage range for CREVAS is 5 - 40 mg orally once a day. The recommended starting dose is 5 mg once a day.

The dose 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.

Adults:
Primary hypercholesterolaemia (including heterozygous familial hypercholesterolaemia), mixed dyslipidaemia, dysbetalipoproteinaemia (Frederickson Type III hyperlipoproteinaemia), 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.

Special populations
Use in the elderly:
The usual dose range applies.

Dosage in patients with renal insufficiency:
The starting dose applies in patients with mild to moderate renal impairment.
For patients with severe renal impairment the dose of CREVAS 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 CREVAS 5 mg. Increased systemic exposure to rosuvastatin has been observed in these patients, therefore the use of doses above 10 mg should be carefully considered (see section 5.2).

Ethnic differences:
A 5 mg starting dose of CREVAS should be considered for Asian patients. Increased plasma concentration of rosuvastatin is seen in Asian subjects (see sections 4.4 and 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:
CREVAS has shown 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.
CREVAS can also be used in combination with ezetimibe or bile acid sequestrants (see section 4.5).

Interactions requiring dose adjustments:
Ciclosporin:
Increased systemic exposure to rosuvastatin has been observed in patients taking concomitant rosuvastatin and ciclosporin. For the CREVAS dose range (10 - 40 mg) this combination is not recommended (see section 4.3).

Gemfibrozil:
Increased systemic exposure to rosuvastatin has been observed in subjects taking concomitant rosuvastatin and gemfibrozil. Patients taking this combination should start with therapy of CREVAS 5 mg once daily and should not exceed a dose of CREVAS 20 mg once daily (see section 4.5).

Paediatric population
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 approximately 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).

Method of administration
For oral administration
CREVAS may be given at any time of day, with or without food.

4.3 Contraindications

CREVAS is contraindicated:
- in patients with hypersensitivity to rosuvastatin or to any of the excipients of CREVAS listed in section 6.1
- in patients with active liver disease including unexplained, persistent elevations of serum transaminases and any serum transaminase elevation exceeding 3 times the upper limit of normal (ULN)
- in patients with severe renal impairment (creatinine clearance < 30 mL/min)
- in patients receiving concomitant ciclosporin (see section 4.5)
- during pregnancy and lactation and in women of childbearing potential not using appropriate contraceptive measures (see section 4.6)
- in patients with myopathy.

The 40 mg dose is contraindicated in patients with predisposing factors for myopathy/rhabdomyolysis. Such factors include:
- moderate renal impairment (creatinine clearance < 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 an increase in rosuvastatin-plasma levels may occur
- Asian patients
- concomitant use of fibrates (see sections 4.4 and 4.5).

4.4 Special warnings and precautions for use

Renal effects
Proteinuria, detected by dipstick testing and mostly tubular in origin, has been observed in patients treated with higher doses of CREVAS, in particular 40 mg. This condition was transient or intermittent in most cases. Proteinuria has not been shown to be a precursor to acute or progressive renal disease (see section 4.8).
The reporting rate for serious renal events in post-marketing use is higher at the 40 mg dose. An assessment of renal function must be considered during routine follow-up of patients treated with a dose of 40 mg.

Skeletal muscle effects
Risk of myasthenia gravis and ocular myasthenia.
Effects on skeletal muscle e.g. myalgia, myopathy and, rarely, rhabdomyolysis have been reported in patients at all doses, particularly at doses higher than 20 mg.
The reporting rate for rhabdomyolysis in post-marketing use is higher at the highest marketed dose. Patients who develop any signs or symptoms suggestive of myopathy should have their Creatine Kinase (CK) levels measured. CREVAS therapy should be discontinued if myopathy is diagnosed or suspected.
An increase in the incidence of myositis and myopathy has been seen in patients receiving other HMG-CoA reductase inhibitors together with ciclosporin, fibric acid derivatives, including gemfibrozil, nicotinic acid, azole antifungals and macrolide antibiotics.
CREVAS should be prescribed with caution in patients with predisposing factors for myopathy, such as renal impairment, advanced age and hypothyroidism, or situations where an increase in plasma levels may occur (see section 5.2).

Creatine Kinase Measurement
Creatine Kinase (CK) should not be measured following strenuous exercise or in the presence of alternative causes of CK increase which may influence the interpretation of the result. If CK levels are significantly elevated at baseline (> 5 x ULN) a confirmatory test should be carried out within 5 - 7 days. If the repeat test confirms a baseline CK > 5 x ULN, treatment must not be started.

Before treatment
HMG-CoA reductase inhibitors, such as CREVAS, should be prescribed with caution in patients with predisposing factors for myopathy/rhabdomyolysis. Such factors 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
- above 70 years of age
- situations where an increase in plasma levels may occur (see sections 4.2, 4.5 and 5.2)
- concomitant use of fibrates.

In this patient group, the risk of treatment should be considered in relation to possible benefit. Clinical monitoring is recommended. If CK levels are significantly elevated at baseline (> 5 x ULN) treatment must not be initiated.

During treatment
Patients must be advised to report inexplicable muscle pain, weakness or cramps immediately, particularly if associated with malaise or fever. CK levels should be measured in these patients. Therapy must be discontinued if CK levels are markedly elevated (> 5 x ULN) or if muscular symptoms are severe and cause daily discomfort (even if CK levels are ≤ 5 x ULN).
If symptoms resolve and CK levels return to normal, then consideration should be given to reintroducing CREVAS or an alternative HMG-CoA reductase inhibitor at the lowest dose with close monitoring. Routine monitoring of CK levels in asymptomatic patients is not warranted.
There have been reports of an immune-mediated necrotising myopathy (IMNM) during or after treatment with statins, including rosuvastatin. IMNM is clinically characterised by proximal muscle weakness and elevated serum creatine kinase, which persist despite discontinuation of statin treatment.
An increase in the incidence of myositis and myopathy has been seen in patients receiving other HMG-CoA reductase inhibitors together with fibric acid derivatives including gemfibrozil, ciclosporin, nicotinic acid, azole antifungals, protease inhibitors and macrolide antibiotics.

Gemfibrozil
Gemfibrozil increases the risk of myopathy when given concomitantly with some HMG-CoA reductase inhibitors, such as CREVAS. Therefore, the combination of CREVAS and gemfibrozil is not recommended. The benefit of further alterations in lipid levels by the combined use of CREVAS with fibrates or niacin should be carefully weighed against the potential risks of such combinations.
The 40 mg dose is contraindicated with concomitant use of a fibrate (see sections 4.5 and 4.8).

Fusidic acid
CREVAS must not be co-administered with systemic formulations of fusidic acid or within 7 days of stopping fusidic acid treatment. In patients where the use of systemic fusidic acid is considered essential, statin treatment should be discontinued throughout the duration of fusidic acid treatment. There have been reports of rhabdomyolysis (including some fatalities) in patients receiving fusidic acid and statins in combination (see section 4.5).
Patients are to be advised to seek medical advice immediately if they experience any symptoms of muscle weakness, pain or tenderness. Statin therapy may be reintroduced 7 days after the last dose of fusidic acid.
In exceptional circumstances, where prolonged systemic fusidic acid is needed, e.g. for the treatment of severe infections, the need for concomitant administration of CREVAS and fusidic acid should only be considered on a case by case basis and under close medical supervision.

CREVAS must not be used in patients with acute, serious conditions suggestive of myopathy or predisposing to the development of renal failure secondary to rhabdomyolysis (e.g. sepsis, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders; or uncontrolled seizures).

Liver effects
HMG-CoA reductase inhibitors, such as CREVAS, must be used with caution in patients who consume excessive quantities of alcohol and/or have a history of liver disease.

It is recommended that liver function tests be carried out prior to, and 3 months following, the initiation of treatment. CREVAS must be discontinued or the dose reduced if the level of serum transaminases is greater than 3 times the upper limit of normal. The reporting rate for serious hepatic events (consisting mainly of increased hepatic transaminases) in post-marketing use is higher at the 40 mg dose.

In patients with secondary hypercholesterolaemia, caused by hypothyroidism or nephrotic syndrome, the underlying disease should be treated prior to initiating therapy with CREVAS.

Ethnic differences
Pharmacokinetic studies show an increase in exposure in Asian subjects compared with Caucasian subjects (see sections 4.2, 4.3 and 5.2).

Protease inhibitors
Increased systemic exposure to rosuvastatin has been observed in subjects receiving rosuvastatin concomitantly with various protease inhibitors in combination with ritonavir.
Consideration should be given both to the benefit of lipid lowering by use of CREVAS in HIV patients receiving protease inhibitors and the potential for increased rosuvastatin plasma concentrations when initiating and up-titrating CREVAS doses in patients treated with protease inhibitors. The concomitant use with certain protease inhibitors is not recommended unless the dose of CREVAS is adjusted (see sections 4.2 and 4.5).

Interstitial lung disease
Cases of interstitial lung disease have been reported with some statins, especially with long-term therapy (see section 4.8). Presenting features may include dyspnoea, non-productive cough and deterioration in general health (fatigue, weight loss and fever). If it is suspected a patient has developed interstitial lung disease, statin therapy must be discontinued.

Diabetes mellitus
Statins, as a class of medicine, may raise blood glucose. In some patients, at high risk of future diabetes, it may produce a level of hyperglycaemia where formal diabetes care is appropriate. This risk, however, is outweighed by the reduction in vascular risk with statins and therefore should not be a reason for stopping statin treatment.
CREVAS should be used with care in patients with Type 2 diabetes and in patients at risk, being patients with a fasting glucose of 5,6 to 6,9 mmol/L, BMI > 30 kg/m², raised triglycerides or hypertension. Patients at risk must be clinically and biochemically monitored.

Children and adolescents 10 - 17 years of age
The safety profile of CREVAS is similar in children or adolescent patients and adults, although CK elevations > 10 x ULN and muscle symptoms following exercise or increased physical activity, which resolved with continued treatment, were observed more frequently in children and adolescents. However, the same special warnings and special precautions for use in adults also apply to children and adolescents.

Lactose intolerance
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take CREVAS.

Excipients
CREVAS 5 mg, 15 mg and 30 mg contains quinoline yellow aluminium lake (E104).
CREVAS 10 mg contains alura red aluminium lake (E129).
CREVAS 40 mg contains sunset yellow aluminium lake (E110) and ponceau aluminium lake (E124).
The above colourants may cause allergic reactions.

4.5 Interaction with other medicines and other forms of interaction

Effect of co-administered medicines on CREVAS
Transporter protein inhibitors:
Rosuvastatin, as contained in CREVAS, is a substrate for certain transporter proteins including the hepatic uptake transporter organic-anion-transporting polypeptide 1B1 (OATP1B1) and efflux transporter breast-cancer-resistance protein (BCRP). Concomitant administration of CREVAS with medicines that are inhibitors of these transporter proteins may result in increased rosuvastatin plasma concentrations and an increased risk of myopathy (see sections 4.2, 4.4 and 4.5 Table 1).

Ciclosporin:
During concomitant treatment with rosuvastatin and ciclosporin, rosuvastatin AUC values were on average 7 times higher than those observed in healthy volunteers (see Table 1). CREVAS is contraindicated in patients receiving concomitant ciclosporin (see section 4.3). Concomitant administration did not affect plasma concentrations of ciclosporin.

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 (see Table 1 below). This increase in systemic exposure to rosuvastatin may lead to an increased incidence of adverse events.
The concomitant use of CREVAS and some protease inhibitor combinations may be considered after careful consideration of CREVAS dose adjustments based on the expected increase in rosuvastatin exposure (see sections 4.4 and Table 1 below).

Gemfibrozil and other lipid-lowering medicines:
Concomitant use of rosuvastatin and gemfibrozil resulted in a 2-fold increase in rosuvastatin C_{max} and AUC (see section 4.4).
No pharmacokinetic relevant interaction with fenofibrate has been reported, however, a pharmacodynamic interaction may occur. Gemfibrozil, fenofibrate, other fibrates and lipid lowering doses (> or equal to 1 g/day) of niacin (nicotinic acid) increase the risk of myopathy when given concomitantly with HMG-CoA reductase inhibitors such as rosuvastatin contained in CREVAS, probably because they can produce myopathy when given alone. The 40 mg dose is contraindicated with concomitant use of a fibrate (see sections 4.3 and 4.4). These patients should start with the 5 mg dose.

Ezetimibe:
Concomitant use of 10 mg rosuvastatin and 10 mg ezetimibe resulted in a 1,2-fold increase in AUC of rosuvastatin in hypercholesterolaemic subjects (Table 1). A pharmacodynamic interaction, in terms of adverse effects, between CREVAS and ezetimibe cannot be ruled out (see section 4.2).

Antacid:
The simultaneous dosing of rosuvastatin 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 CREVAS. The clinical relevance of this interaction has not been studied.

Erythromycin:
Concomitant use of rosuvastatin and erythromycin resulted in a 20 % decrease in AUC and a 30 % decrease in C_{max} of rosuvastatin. This interaction may be caused by the increase in gut motility caused by erythromycin.

Cytochrome P450 enzymes:
In vitro and *in vivo* data indicate that rosuvastatin has no clinically significant cytochrome P450 interactions (as a substrate, inhibitor or inducer). Therefore, medicine interactions resulting from cytochrome P450-mediated metabolism are not expected. No clinically relevant interactions have been observed between rosuvastatin and either fluconazole (an inhibitor of CYP2C9 and CYP3A4) or ketoconazole (an inhibitor of CYP2A6 and CYP3A4).

Interactions requiring rosuvastatin dose adjustments (see also Table 1 below):
When it is necessary to co-administer CREVAS with other medicines known to increase exposure to rosuvastatin, doses of CREVAS should be adjusted.
Start with a 5 mg once daily dose of CREVAS if the expected increase in exposure (AUC) is approximately 2-fold or higher.
The maximum daily dose of CREVAS should be adjusted so that the expected rosuvastatin exposure would not likely exceed that of a 40 mg daily dose of CREVAS taken without interacting medicines, for example a 20 mg dose of CREVAS with gemfibrozil (1,9-fold increase), and a 10 mg dose of CREVAS with combination ritonavir/atazanavir (3,1-fold increase).

Table 1 Effect of co-administered medicines on rosuvastatin exposure (AUC; in order of decreasing magnitude) from published clinical trials

Interacting medicine dose regimen	Rosuvastatin dose regimen	Change in rosuvastatin AUC*
Ciclosporin 75 mg twice daily to 200 mg twice daily, 6 months	10 mg once daily, 10 days	7,1-fold ↑
Regorafenib 160 mg, once daily, 14 days	5 mg, single dose	3,8-fold ↑
Atazanavir 300 mg/ritonavir 100 mg once daily, 8 days	10 mg, single dose	3,1-fold ↑
Velpatasvir 100 mg once daily	10 mg, single dose	2,7-fold ↑
Ombitasvir 25 mg/ paritaprevir 150 mg/ ritonavir 100 mg once daily/ dasabuvir 400 mg twice daily, 14 days	5 mg, single dose	2,6-fold ↑
Grazoprevir 200 mg/elbasvir 50 mg once daily, 11 days	10 mg, single dose	2,3-fold ↑
Glecaprevir 400 mg/ pibrentasvir 120 mg once daily, 7 days	5 mg once daily, 7 days	2,2-fold ↑
Lopinavir 400 mg/ritonavir 100 mg twice daily, 17 days	20 mg once daily, 7 days	2,1-fold ↑
Clopidogrel 300 mg loading, followed by 75 mg at 24 hours	20 mg, single dose	2-fold ↑
Gemfibrozil 600 mg twice daily, 7 days	80 mg, single dose	1,9-fold ↑
Eltrombopag 75 mg once daily, 5 days	10 mg, single dose	1,6-fold ↑
Darunavir 600 mg/ritonavir 100 mg twice daily, 7 days	10 mg once daily, 7 days	1,5-fold ↑
Tipranavir 500 mg/ritonavir 200 mg twice daily, 11 days	10 mg, single dose	1,4-fold ↑
Dronedarone 400 mg twice daily	Not available	1,4-fold ↑
Itraconazole 200 mg once daily, 5 days	10 mg, single dose	**1,4-fold ↑
Ezetimibe 10 mg once daily, 14 days	10 mg, once daily, 14 days	**1,2-fold ↑
Fosamprenavir 700 mg/ ritonavir 100 mg twice daily, 8 days	10 mg, single dose	↔
Aleglitazar 0,3 mg, 7 days	40 mg, 7 days	↔
Silymarin 140 mg three times daily, 5 days	10 mg, single dose	↔
Fenofibrate 67 mg three times daily, 7 days	10 mg, 7 days	↔
Rifampicin 450 mg once daily, 7 days	20 mg, single dose	↔
Ketoconazole 200 mg twice daily, 7 days	80 mg, single dose	↔
Fluconazole 200 mg once daily, 11 days	80 mg, single dose	↔
Erythromycin 500 mg four times daily, 7 days	80 mg, single dose	20 % ↓
Baicalin 50 mg three times daily, 14 days	20 mg, single dose	47 % ↓

* Data given as x-fold change represent a simple ratio between co-administration and rosuvastatin alone. Data given as % change represent % difference relative to rosuvastatin alone. Increase is indicated as "↑", no change as "↔", decrease as "↓".
** Several interaction studies have been performed at different dosages, the table shows the most significant ratio.

Effect of rosuvastatin on co-administered medicines:
Warfarin:
The pharmacokinetics of warfarin are not significantly affected following co-administration with CREVAS. However, as with other HMG-CoA reductase inhibitors, co-administration of CREVAS and warfarin may result in a rise in International Normalised Ratio (INR) compared to warfarin alone. In patients taking warfarin, monitoring of INR is recommended both at initiation or cessation of therapy with CREVAS or following dose adjustment.

Oral contraceptive/hormone replacement therapy (HRT):
Concomitant use of rosuvastatin and an oral contraceptive resulted in an increase in ethinyl estradiol and norgestrel AUC of 26 % and 34 %, respectively. These increased plasma levels should be considered when selecting oral contraceptive doses. There are no pharmacokinetic data available in subjects taking concomitant CREVAS and hormone replacement therapy, therefore, a similar effect cannot be excluded.

Other medicines:
Digoxin:
Based on data from specific interaction studies no clinically relevant interaction with digoxin is expected.

Fusidic acid:
Interaction studies with rosuvastatin and fusidic acid have not been conducted. The risk of myopathy, including rhabdomyolysis may be increased by the concomitant administration of systemic fusidic acid with statins. The mechanism of this interaction (whether it is pharmacodynamic or pharmacokinetic, or both) is yet unknown. There have been reports of rhabdomyolysis (including some fatalities) in patients receiving this combination.
If treatment with systemic fusidic acid is necessary, CREVAS treatment should be discontinued throughout the duration of the fusidic acid treatment (see section 4.4).

Paediatric population
Interaction studies have only been performed in adults. The extent of interactions in the paediatric population is not known.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/contraception in males and females
Women of childbearing potential should use appropriate contraceptive measures.

Pregnancy
CREVAS is contraindicated in pregnancy (see section 4.3).

Breastfeeding
CREVAS is contraindicated in lactation. Rosuvastatin is excreted in the milk of rats. There is no data available with respect to excretion of rosuvastatin in milk in humans (see section 4.3).

Fertility
No data is available on fertility.

4.7 Effects on ability to drive and use machines

CREVAS may cause dizziness, therefore patients taking CREVAS should not drive or use machines until their individual susceptibility to dizziness is known.

4.8 Undesirable effects

The adverse reactions seen with CREVAS are generally mild and transient.

Table 2: Tabulated list of adverse reactions

System Organ Class	Frequency	Side effects
Blood and lymphatic system disorders	*Less frequent*	Thrombocytopenia
Immune system disorders	*Less frequent*	Hypersensitivity reactions including angioedema
Endocrine disorders	*Frequent*	Diabetes mellitus[1]
Psychiatric disorders	*Frequency unknown*	Depression
Nervous system disorders	*Frequent*	Headache dizziness
	Less frequent	Polyneuropathy, memory loss
	Frequency unknown	Peripheral neuropathy, sleep disturbance (including insomnia and nightmares), myasthenia gravis
Eye disorders	*Frequency unknown*	Ocular myasthenia
Respiratory, thoracic and mediastinal disorders	*Frequency unknown*	Cough, dyspnoea
Gastro-intestinal disorders	*Frequent*	Constipation, nausea, abdominal pain
	Less frequent	Pancreatitis
	Frequency unknown	Diarrhoea
Hepatobiliary disorders	*Less frequent*	Increased hepatic transaminases, jaundice, hepatitis
Skin and subcutaneous tissue disorders	*Less frequent*	Pruritus, rash, urticaria
	Frequency unknown	Stevens-Johnson syndrome
Musculoskeletal and connective tissue disorders	*Frequent*	Myalgia
	Less frequent	Myopathy (including myositis), rhabdomyolysis, Lupus-like syndrome, muscle rupture, arthralgia
	Frequency unknown	Tendon disorders, sometimes complicated by rupture, immune-mediated necrotising myopathy
Renal and urinary disorders	*Less frequent*	Haematuria
	Frequency unknown	Proteinuria
Reproductive system and breast disorders	*Less frequent*	Gynaecomastia
General disorders and administration site conditions	*Frequent*	Asthenia
	Less frequent	Oedema

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).
As with other HMG-CoA reductase inhibitors, such as CREVAS, the incidence of adverse reactions tends to be dose dependent.

Description of selected adverse reactions
Renal effects:
Proteinuria, detected by dipstick testing and mostly tubular in origin, has been observed in patients treated with CREVAS. Shifts in urine protein from none or trace to 100 mg/dL or more were seen in < 1 % of patients at some time during treatment with 10 and 20 mg, and in approximately 3 % of patients treated with 40 mg.
A minor increase in shift from none or trace to 30 mg/dL was observed with the 20 mg dose. In most cases, proteinuria decreases or disappears spontaneously on continued therapy. Review of data from clinical trials and post-marketing experience to date has not identified a causal association between proteinuria and acute or progressive renal disease. Haematuria has been observed in patients treated with CREVAS and clinical trial data show that the occurrence is low.

Skeletal muscle effects:
Effects on skeletal muscle e.g. myalgia, myopathy (including myositis) and, rarely, rhabdomyolysis with and without acute renal failure have been reported in CREVAS-treated patients with all doses and in particular with doses > 20 mg.
A dose-related increase in CK levels has been observed in patients taking rosuvastatin; the majority of cases were mild, asymptomatic and transient. If CK levels are elevated (> 5 x ULN), treatment should be discontinued (see section 4.4).

Liver effects:
A dose-related increase in transaminases has been observed in a small number of patients taking rosuvastatin as in CREVAS; the majority of cases were mild, asymptomatic and transient.

The following adverse events have been reported with some statins:
- sexual dysfunction
- exceptional cases of interstitial lung disease, especially with long term therapy (see section 4.4)
- the reporting rates for rhabdomyolysis, serious renal events and serious hepatic events (consisting mainly of increased hepatic transaminases) is higher at the 40 mg dose.

Paediatric population:
Children and adolescents 10 - 17 years of age
Creatine kinase elevations > 10 x ULN and muscle symptoms following exercise or increased physical activity were observed more frequently in a 52-week clinical trial of children and adolescents compared to adults (see section 4.4).
In other respects, the safety profile of rosuvastatin was similar in children and adolescents compared to adults.

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 online service for adverse drug reaction reporting by using either of the following links: https://www.sahpra.org.za/Publications/Index/8 or http://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/.
An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

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. 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
Pharmacological classification: A 7.5 Serum-cholesterol reducers

Mechanism of action
Rosuvastatin is a selective and competitive inhibitor of 3-hydroxy-3-methylglutaryl-CoA (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 of rosuvastatin is the liver, the target organ for cholesterol lowering.
Rosuvastatin produces its lipid-modifying effects in 2 ways; it increases the number of hepatic low density lipoprotein (LDL) receptors on the cell-surface, enhancing uptake and catabolism of LDL and it inhibits the hepatic synthesis of very low density lipoprotein (VLDL), thereby reducing the total number of VLDL and LDL particles.

High density lipoprotein (HDL), which contains apolipoprotein A-1 (Apo A-1) is involved, amongst other things, in transport of cholesterol from tissues back to liver (reverse cholesterol transport).
Rosuvastatin reduces elevated LDL-cholesterol (LDL-C), Total Cholesterol and triglycerides (TG) and increases HDL-cholesterol (HDL-C). It also lowers apolipoprotein B (Apo B) non-HDL-C, VLDL-C, VLDL-TG and increases Apo A-1. Rosuvastatin also lowers the LDL-C/HDLC, total C/HDL-C and non-HDL-C/HDL-C and the Apo B/Apo A-1 ratios.
A therapeutic response to rosuvastatin is evident within 1 week of commencing therapy and 90 % of maximum response is usually achieved by 4 weeks and is maintained after that.

5.2 Pharmacokinetic properties

Absorption:
Maximum rosuvastatin plasma concentrations are achieved approximately 5 hours after oral administration. The absolute bioavailability is approximately 20 %.

Distribution:
Approximately 90 % of rosuvastatin is bound to plasma proteins, mainly to albumin. The parent compound accounts for greater than 90 % of the circulating active HMG-CoA reductase inhibitor activity.

Biotransformation:
Rosuvastatin undergoes limited metabolism in humans (approximately 10 %) mainly to the N-desmethyl form.

Elimination:
Approximately 90 % of the rosuvastatin dose is excreted unchanged in the faeces and the remaining part is excreted in the urine.

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

Special populations:
Age and sex:
There was no clinically relevant effect of age or sex on the pharmacokinetics of rosuvastatin. The pharmacokinetics of rosuvastatin in children and adolescents with heterozygous familial hypercholesterolaemia was similar to that of adult volunteers.

Ethnic differences:
Pharmacokinetic studies show a 1,26 - 2,31-fold elevation in geometric mean $AUC_{(0-t)}$ in Asian subjects compared with 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 analyses in these 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, Ethnic differences).

Renal insufficiency:
In a study in subjects with varying degrees of renal impairment, mild to moderate renal disease had little influence on plasma concentration of rosuvastatin. However, subjects with severe impairment (CrCl < 30 mL/min) had a 3-fold increase in plasma concentration compared to healthy volunteers. Haemodialysis is unlikely to be of benefit for rosuvastatin removal.

Hepatic insufficiency:
In a 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 CREVAS is recommended.

Paediatric population:
Two 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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet cores
Crospovidone
Lactose monohydrate
Magnesium stearate
Microcrystalline cellulose

Opadry coating[1]
Hypromellose
Lactose monohydrate
Titanium dioxide (E171)
Triacetin (E1518)

Opadry II 31K38097 Yellow (5 mg, 15 mg, 30 mg)
Quinoline yellow aluminium lake (E104)

Opadry II 32K240042 Pink (10 mg)
Allura red aluminium lake (E129)

Opadry II 32K240039 Pink (20 mg)
Carmine (E120)

Opadry II 32K250001 (40 mg)
Ponceau aluminium lake (E124)
Sunset yellow aluminium lake (E110)
[1] Applicable to the coating of all strengths

6.2 Incompatibilities

Not applicable

6.3 Shelf life

48 Months

6.4 Special precautions for storage

Store at or below 30 °C in a cool, dry place.
Protect from light.
Keep the tablets in the outer carton until required for use.

6.5 Nature and contents of container

CREVAS is available in polyamide/aluminium/PVC/aluminium foil blister strips, packed in an outer carton, in packs of 7, 14, 28, 30, 56 or 98 film coated tablets.
Not all pack sizes are marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Pharma Dynamics (Pty) Ltd
1st Floor Grapevine House, Steenberg Office Park
Silverwood Close
Westlake, 7945
Cape Town, South Africa

8 REGISTRATION NUMBERS

CREVAS 5 mg: A46/7.5/0313
CREVAS 10 mg: A46/7.5/0314
CREVAS 15 mg: A55/7.5/0453*
CREVAS 20 mg: A46/7.5/0315
CREVAS 30 mg: A55/7.5/0454*
CREVAS 40 mg: A46/7.5/0316*

9. DATE OF FIRST AUTHORISATION

CREVAS 5 mg: 12 July 2022
CREVAS 10 mg: 12 July 2022
CREVAS 15 mg: 02 May 2023
CREVAS 20 mg: 12 July 2022
CREVAS 30 mg: 02 May 2023
CREVAS 40 mg: 12 July 2022

10. DATE OF REVISION OF TEXT

1 August 2023

NAMIBIA
CREVAS 5 mg: NAM NS2 21/7.5/0057
CREVAS 10 mg: NAM NS2 21/7.5/0058
CREVAS 20 mg: NAM NS2 21/7.5/0059
CREVAS 40 mg: NAM NS2 21/7.5/0060

MOZAMBIQUE*
CREVAS 5 mg: C6912
CREVAS 10 mg: C6913
CREVAS 20 mg: C6914

*CREVAS 15 mg, CREVAS 30 mg and CREVAS 40 mg are not marketed in Mozambique.

D5640

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PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

CREVAS 5 mg (5 mg film coated tablets)
Contains sugar (lactose monohydrate 45,72 mg)
CREVAS 10 mg (10 mg film coated tablets)
Contains sugar (lactose monohydrate 90,90 mg)
CREVAS 15 mg (15 mg film coated tablets)
Contains sugar (lactose monohydrate 137,16 mg)
CREVAS 20 mg (20 mg film coated tablets)
Contains sugar (lactose monohydrate 181,80 mg)
CREVAS 30 mg (30 mg film coated tablets)
Contains sugar (lactose monohydrate 274,32 mg)
CREVAS 40 mg (40 mg film coated tablet)
Contains sugar (lactose monohydrate 233,01 mg)

Rosuvastatin calcium

Read all of this leaflet carefully before you start taking CREVAS
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- CREVAS has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet
1. What CREVAS is and what it is taken for
2. What you need to know before you take CREVAS
3. How to take CREVAS
4. Possible side effects
5. How to store CREVAS
6. Contents of the pack and other information

1. What CREVAS is and what it is taken for
CREVAS contains 5 mg, 10 mg, 15 mg, 20 mg, 30 mg or 40 mg of rosuvastatin, as rosuvastatin calcium, per film coated tablet and belongs to the pharmacotherapeutic group called HMG-CoA reductase inhibitors.

CREVAS is used to reduce the risk of incidents that may cause damage to the heart muscle in patients at risk of developing heart disease as a result of build-up of fats in and on the blood vessels of the heart.
CREVAS is used, together with diet, to lower high levels of fats in the blood, which are called lipids, usually when changes to diet and exercise have failed to do this. CREVAS, in addition to diet, lowers "bad" cholesterol (LDL) and increases "good" cholesterol (HDL) in the blood.
CREVAS is also used to reduce Total Cholesterol and "bad" cholesterol (LDL) in adult patients with very high cholesterol and a family history of high cholesterol, either alone or together with diet and other lipid lowering treatments.

CREVAS 40 mg should only be considered in patients with severe high cholesterol and high cardiovascular risk who do not achieve their treatment goal on 20 mg of CREVAS or alternative therapy.
Specialist supervision is recommended when the 40 mg dose is initiated.
CREVAS can be used in children and adolescents (10 to 17 years of age) to reduce the Total Cholesterol, "bad" cholesterol (LDL) and lipids in patients with genetically inherited high cholesterol called heterozygous familial hypercholesterolaemia (HeFH).

2. What you need to know before you take CREVAS
Do not take CREVAS:
- if you are hypersensitive (allergic) to rosuvastatin or any of the other ingredients of CREVAS (listed in section 6)
- if you currently have a liver disease
- if you have severe kidney problems
- if you take a medicine called ciclosporin (used, for example, after organ transplants) (see Other Medicines and CREVAS)
- if you are pregnant or breastfeeding or if you are a woman of childbearing potential not using appropriate contraceptive measures (see Pregnancy, breastfeeding and fertility).

Patients with the following predisposing conditions for a muscle disease called myopathy must not take CREVAS 40 (the highest dose).

The following conditions may increase the risk of muscle disorders:
- if you have moderate kidney problems (if in doubt, please ask your doctor)
- if you have a condition called hypothyroidism (underactive thyroid)
- if you have had any repeated or unexplained muscle aches or pains, a personal or family history of muscle problems, or a previous history of muscle problems when taking other cholesterol-lowering medicines
- if you regularly drink large amounts of alcohol
- if you are taking other medicines called fibrates (for high cholesterol)
- if you are of Asian descent.

Warnings and precautions
Take special care with CREVAS:
Tell your doctor or healthcare professional before taking CREVAS:
- if you have problems with your kidneys
- if you have unexplained muscle aches and pains, muscle weakness, cramps and especially if you feel unwell or have a fever, tell your doctor immediately
- if your thyroid gland is not working properly (hypothyroidism)
- if you have a personal or family history of hereditary muscular disorders
- if you have a previous history of muscle problems when using cholesterol lowering medicines
- if you regularly consume large amounts of alcohol
- if you are above 70 years of age
- if you are taking fibrates (cholesterol lowering medicine) please see Other medicine and CREVAS
- if you are taking or have taken in the last 7 days a medicine called fusidic acid (a medicine for bacterial infection), orally or by injection. The combination of fusidic acid and CREVAS can lead to serious muscle problems (rhabdomyolysis), please see Other medicine and CREVAS
- if you are taking other HMG-CoA reductase inhibitors together with fibric acid derivatives including gemfibrozil, ciclosporin, nicotinic acid, azole antifungals, protease inhibitors (such as lopinavir/ritonavir – medicines used to treat HIV infection) and macrolide antibiotics (see Other medicine and CREVAS).

CREVAS may cause interstitial lung disease, especially with long-term treatment. Tell your doctor if you experience difficulty breathing, develop a non-productive cough and/or deterioration in general health (e.g. fatigue, weight loss and fever) while taking CREVAS.

In a small number of people, CREVAS can affect the liver. This is identified by a test which looks for increased levels of liver enzymes in the blood. For this reason, your doctor will usually carry out this blood test (liver function test) before treatment starts with CREVAS, and if needed thereafter.

CREVAS may cause myasthenia gravis and ocular myasthenia, which are conditions that cause muscle weakness, impaired speech, difficulty swallowing and drooping of one or both eyelids or double vision. Tell your doctor if you experience any of these symptoms while taking CREVAS.

In patients whose high cholesterol is caused by another disease, such as thyroid or kidney problems, the underlying disease should be treated prior to initiating therapy with CREVAS.

While you are on CREVAS your doctor will monitor you closely if you have diabetes or are at risk of developing diabetes. You are likely to be at risk of developing diabetes if you have high levels of sugars and fats in your blood, are overweight and have high blood pressure. CREVAS should be used with care in patients with Type 2 diabetes and in patients at risk.

Other medicines and CREVAS
Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

Tell your doctor if you are taking any of the following medicines:
Contraindicated combinations
CREVAS should not be used together with ciclosporin (used for example, after organ transplants).
The 40 mg dose is contraindicated with concomitant use of a fibrate.

There may be a higher than usual chance of other side effects
Fibrates (such as gemfibrozil, fenofibrate) or any other medicine used to lower cholesterol (such as ezetimibe) as these medicines may increase the effect of CREVAS and the risk of developing serious muscle problems (see Do not take CREVAS above).

Fusidic acid (an antibiotic) may increase the risk of developing serious muscle problems (see Take special care with CREVAS above). If you need to take oral fusidic acid to treat a bacterial infection you will need to temporarily stop using CREVAS. Your doctor will tell you when it is safe to restart CREVAS. Taking CREVAS with fusidic acid may lead to muscle weakness, tenderness or pain (rhabdomyolysis).

Medicines used to treat viral infections, including HIV or hepatitis C infection, alone or in combination (please see Take special care with CREVAS above), as these medicines may increase the effect of CREVAS and may lead to an increase in the possible side effects of CREVAS: ritonavir, lopinavir, atazanavir, ombitasvir, paritaprevir, dasabuvir, velpatasvir, grazoprevir, elbasvir, glecaprevir, pibrentasvir, darunavir, tipranavir.

Effect of CREVAS may be increased:
- warfarin or clopidogrel (or any other medicine used for thinning the blood) as CREVAS may affect the way this medicine works; clopidogrel may increase the effect of CREVAS
- regorafenib (used to treat cancer) as this may increase the effect of CREVAS
- eltrombopag (used to treat low blood platelet counts caused by an autoimmune disorder) as this may increase the effect of CREVAS
- dronedarone (used to treat abnormal heart rhythm) as this may increase the effect of CREVAS
- itraconazole (used to treat fungal infections) as this may increase the effect of CREVAS.

Effect of CREVAS may be decreased:
- indigestion remedies, such as antacids (used to neutralise acid in your stomach) as these medicines may decrease the effect of CREVAS
- erythromycin (an antibiotic) this may decrease the effect of CREVAS.

CREVAS may increase the effect of other medicines:
- oral contraceptives (the pill) as CREVAS may increase the effect of contraceptives
- hormone replacement therapy as CREVAS may increase the effect of these medicines.

Taking CREVAS with food and alcohol
You can take CREVAS with or without food.
If you regularly drink large amounts of alcohol, it may increase your risk of muscle disorders.

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before taking this medicine.
You should use appropriate contraceptive measures, if you are a woman of childbearing potential.
You should not take CREVAS if you are pregnant or breastfeeding your baby.

Driving and using machines
CREVAS may cause dizziness, therefore you should not drive or use machines until you know how CREVAS affects you.
It is not always possible to predict to what extent CREVAS may interfere with your daily activities. You should ensure that you do not engage in the above activities until you are aware of the measure to which CREVAS affects you.

CREVAS contains colourants
CREVAS 5 mg, 15 mg and 30 mg contains quinoline yellow aluminium lake (E104).
CREVAS 10 mg contains allura red aluminium lake (E129).
CREVAS 40 mg contains sunset yellow aluminium lake (E110) and ponceau aluminium lake (E124).
The above colourants may cause allergic reactions.

CREVAS contains lactose monohydrate
If you have been told by your doctor that you have an intolerance to some sugars, contact your

3. How to take CREVAS
Do not share medicines prescribed for you with any other person.
Always take CREVAS exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Before starting treatment, your doctor should place you on a standard cholesterol-lowering diet that should continue during treatment.
The dosage range for CREVAS is 5 - 40 mg orally once a day. The recommended start dose is 5 mg once a day.
Your dosage will be individualised according to your cholesterol levels, your risk factors and your response to CREVAS-therapy. The majority of patients are controlled at the 10 mg dose. However, if necessary, your doctor will adjust your dose at 2 - 4-week intervals.
A 5 mg starting dose is recommended for patients of Asian ancestry and for patients requiring a smaller reduction in "bad" cholesterol (LDL-C) to achieve treatment target.
For patients with severely high cholesterol (including genetically inherited high cholesterol), a start dose of 20 mg may be considered.
For patients with genetically inherited high cholesterol, a start dose of 20 mg once a day is recommended.

Children and adolescents 10 - 17 years of age:
In children and adolescents with genetically inherited high cholesterol, the usual dose range is 5 - 20 mg orally once daily.

Special populations
Your doctor will prescribe a suitable dosage if you are elderly, if you have a kidney or liver disorder.

Your doctor will tell you how long your treatment with CREVAS will last. It may take weeks or months of treatment for you to see any improvement in your symptoms and your symptoms might even worsen when CREVAS is started. Do not stop treatment early.
If you have the impression that the effect of CREVAS is too strong or too weak, tell your doctor or pharmacist.

If you take more CREVAS than you should
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take CREVAS
Do not take a double dose to make up for the forgotten individual doses.

4. Possible side effects
CREVAS can have side effects.
Not all side effects reported for CREVAS are included in this leaflet. Should your general health worsen or if you experience untoward effects while taking CREVAS, please consult your healthcare provider for advice.

If any of the following happens, stop taking CREVAS and tell your doctor immediately or go to the casualty department at your nearest hospital:
- difficulty in breathing, with or without swelling of the face, lips, tongue and/or throat which may cause difficulty in swallowing, severe itching of the skin (with raised lumps)
- blistering of the skin, mouth and eyes (Steven-Johnson syndrome)
- jaundice (yellowing of the skin and eyes).

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to CREVAS. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:
- any unusual aches and pains in your muscles which go on for longer than you might expect, especially if you develop a fever or feel unwell. Unpleasant muscle effects may become a potentially life-threatening muscle damage known as rhabdomyolysis. Muscle symptoms are more frequent in children and adolescents than in adults
- tendon disorders sometimes complicated by rupture
- serious muscle damage presenting as unexplained muscle aches and pains, feeling unwell and a fever (immune-mediated necrotising myopathy)
- a severe stomach pain (inflamed pancreas)
- increase in liver enzymes in the blood
- hepatitis (an inflamed liver).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:
Frequent side effects:
- increased glucose levels, diabetes
- headache, dizziness
- constipation, nausea, stomach pain
- muscle pain
- feeling weak or a lack of energy.

Less frequent side effects:
- abnormal bleeding or bruising
- memory loss
- numbness, tingling, loss of sensation in the arms and legs, burning feeling in the hands or feet (polyneuropathy)
- rash, itching or other skin reactions
- oedema (swelling under the skin)
- cough, shortness of breath, difficulty breathing
- lupus-like disease syndrome (including rash, joint disorders and effects on blood cells)
- muscle rupture
- joint pain
- traces of blood in your urine
- breast enlargement in men (gynaecomastia).

Side effects with unknown frequency:
- depression
- sleep disturbances including insomnia and nightmares
- diarrhoea
- an increase in the amount of protein in the urine
- numbness and tingling in hands or feet (peripheral neuropathy)
- muscle weakness, impaired speech, difficulty swallowing and drooping of one or both eyelids or double vision (myasthenia gravis and ocular myasthenia).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects
If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the online service for adverse drug reaction reporting by using either of the following links: https://www.sahpra.org.za/Publications/Index/8 or http://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/.
By reporting side effects, you can help provide more information on the safety of CREVAS. You can also send an email directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

5. How to store CREVAS
Store all medicines out of reach of children.
Store at or below 30 °C in a cool, dry place.
Protect from light.
Keep the tablets in the outer carton until required for use.
Do not use after the expiry date stated on the carton.
Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information
What CREVAS contains:
The active substance is rosuvastatin calcium.
Each film coated tablet contains rosuvastatin calcium equivalent to either 5, 10,15, 20, 30 or 40 mg rosuvastatin.

The other ingredients are:
Tablet cores
Crospovidone, lactose monohydrate, magnesium stearate, microcrystalline cellulose.

Opadry-coating/film coating
Allura red aluminium lake (E129)[2], carmine (E120)[3], hypromellose (E464), lactose monohydrate, ponceau aluminium lake (E124)[4], quinolone yellow aluminium lake (E104)[1], sunset yellow aluminium lake (E110)[4], titanium dioxide (E171), triacetin (E1518).
[1] Applicable to 5 mg, 15 mg and 30 mg strengths only
[2] Applicable to 10 mg strength only
[3] Applicable to 20 mg strength only
[4] Applicable to 40 mg strength only

What CREVAS looks like and contents of the pack
CREVAS 5 mg: Round, biconvex, yellowish film coated tablets, 6 mm in diameter, debossed with "5" on one side.
CREVAS 10 mg: Round, biconvex, light pink film coated tablets, 7 mm in diameter, debossed with "10" on one side.
CREVAS 15 mg: Round, biconvex, yellow film coated tablets, 8 mm in diameter, debossed with "15" on one side and "15" on the other side.
CREVAS 20 mg: Round, biconvex, dark pink film coated tablets, 9 mm in diameter, debossed with "20" on one side.
CREVAS 30 mg: Round, biconvex, yellow film coated tablets, 10 mm in diameter, debossed with "30" on one side.
CREVAS 40 mg: Round, biconvex, red film coated tablets, 10 mm in diameter, debossed with "40" on one side.

CREVAS is available in polyamide/aluminium/PVC/aluminium foil blister strips, packed in an outer carton, in packs of 7, 14, 28, 30, 56 or 98 film coated tablets.
Not all pack sizes are marketed.

Holder of Certificate of Registration
Pharma Dynamics (Pty) Ltd
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This leaflet was last revised in
1 August 2023

Registration numbers
CREVAS 5 mg: A46/7.5/0313
CREVAS 10 mg: A46/7.5/0314
CREVAS 15 mg: A55/7.5/0453*
CREVAS 20 mg: A46/7.5/0315
CREVAS 30 mg: A55/7.5/0454*
CREVAS 40 mg: A46/7.5/0316*

NAMIBIA
CREVAS 5 mg: NAM NS2 21/7.5/0057
CREVAS 10 mg: NAM NS2 21/7.5/0058
CREVAS 20 mg: NAM NS2 21/7.5/0059
CREVAS 40 mg: NAM NS2 21/7.5/0060

MOZAMBIQUE*
CREVAS 5 mg: C6912
CREVAS 10 mg: C6913
CREVAS 20 mg: C6914

*CREVAS 15 mg, CREVAS 30 mg and CREVAS 40 mg are not marketed in Mozambique.

D5640

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PASIËNTINLIGTINGSBLAD

SKEDULERINGSTATUS: S4

CREVAS 5 mg (5 mg filmbedekte tablette)
Bevat suiker (45,72 mg laktosemonohidraat)
CREVAS 10 mg (10 mg filmbedekte tablette)
Bevat suiker (90,90 mg laktosemonohidraat)
CREVAS 15 mg (15 mg filmbedekte tablette)
Bevat suiker (137,16 mg laktosemonohidraat)
CREVAS 20 mg (20 mg filmbedekte tablette)
Bevat suiker (181,80 mg laktosemonohidraat)
CREVAS 30 mg (30 mg filmbedekte tablette)
Bevat suiker (274,32 mg laktosemonohidraat)
CREVAS 40 mg (40 mg filmbedekte tablette)
Bevat suiker (233,01 mg laktosemonohidraat)

Kalsiumrosuvastatien

Lees hierdie hele inligtingsblad deeglik deur, voordat u begin om CREVAS te neem
- Hou hierdie inligtingsblad. Dit mag nodig wees vir u om dit weer te lees.
- Indien u verdere vrae het, vra asseblief u dokter, apteker, verpleegkundige of ander gesondheidsorgverskaffer.
- CREVAS is vir u persoonlik voorgeskryf en u moet nie u medisyne met ander persone deel nie. Dit mag skadelik wees vir hulle, selfs al is hulle simptome dieselfde as u eie.

Wat hierdie inligtingsblad bevat
1. Wat CREVAS is en waarvoor dit geneem word
2. Wat u nodig het om te weet, voordat u CREVAS neem
3. Hoe om CREVAS te neem
4. Moontlike newe-effekte
5. Hoe om CREVAS te bewaar
6. Verpakkingsinhoud en ander inligting

1. Wat CREVAS is en waarvoor dit geneem word
CREVAS bevat 5 mg, 10 mg, 15 mg, 20 mg, 30 mg of 40 mg rosuvastatien, as kalsiumrosuvastatien, per filmbedekte tablet en behoort aan die farmakoterapeutiese groep wat HMG-CoA-reduktaseremmers genoem word.

CREVAS word gebruik om die risiko vir voorvalle wat beskadiging van die hartspier by pasiënte met 'n risiko vir hartsiekte (as gevolg van die opbou van vette in en op die bloedvate van die hart) mag veroorsaak, te verlaag.
CREVAS word in kombinasie met 'n dieet gebruik om hoë vetvlakke in die bloed (ook lipiede genoem), te verlaag, gewoonlik wanneer veranderinge in dieet en oefening alleen onsuksesvol was. CREVAS, saam met 'n dieet, verlaag "slegte" cholesterol (LDL) en verhoog "goeie" cholesterol (HDL) in die bloed.
CREVAS word ook gebruik om algehele cholesterol en "slegte" cholesterol (LDL) by volwassenes met baie hoë cholesterol en 'n familiegeskiedenis van hoë cholesterol het, te verlaag, óf, alleen, óf, tesame met 'n dieet en ander lipied-verlagende behandelings.

CREVAS 40 mg moet slegs oorweeg word by pasiënte wie baie hoë cholesterol en 'n hoë kardiovaskulêre risiko het en wie nie hulle behandelingsdoelwit met 20 mg CREVAS of alternatiewe behandeling, bereik het nie.
Gespesialiseerde toesig word aanbeveel wanneer die 40 mg dosis begin word.
CREVAS kan deur kinders en adolessente (10 tot 17 jaar oud) gebruik word om algehele cholesterol, "slegte" cholesterol (LDL) en lipiede by pasiënte met geneties oordraagbare hoë cholesterol (ook heterosigotiese familiële hipercholesterolemie genoem (HeFH)), te verlaag.

2. Wat u nodig het om te weet, voordat u CREVAS gebruik
Moet nie CREVAS neem:
- indien u hipersensitief (allergies) is vir rosuvastatien, of vir enige van die ander bestanddele van CREVAS nie (gelys in afdeling 6)
- indien u tans 'n lewersiekte het nie
- indien u erge nierprobleme het nie
- indien u medisyne, wat siklosporien genoem word, gebruik nie (word byvoorbeeld gebruik na orgaanoorplantings) (kyk Ander medisyne en CREVAS)
- indien u swanger is of borsvoed nie, of indien u 'n vrugbare vrou is en nie gepaste voorbehoedmaatreëls toepas nie (kyk Swangerskap, borsvoeding en fertiliteit).

Pasiënte wie die volgende voorafgaande toestande vir 'n spiersiekte wat miopatie genoem word het, moet nie CREVAS 40 mg (die hoogste dosis), neem nie.

Die volgende toestande mag die risiko vir spierversteurings verhoog:
- indien u matige nierprobleme het (indien onseker, vra asseblief u dokter)
- indien u aan 'n toestand wat hipotiroïdisme genoem word, ly (onderaktiewe skildklier)
- indien u enige herhaalde of onverklaarbare spierpyne of -skete gehad het, 'n persoonlike of familiegeskiedenis van spierprobleme het, of 'n vorige geskiedenis van spierprobleme, wanneer ander cholesterol-verlagende medisyne gebruik is, het
- indien u gereeld groot hoeveelhede alkohol inneem
- indien u ander medisyne, wat fibrate genoem word, neem (vir hoë cholesterol)
- indien u van Asiatiese afkoms is.

Waarskuwings en voorsorgmaatreëls
Neem spesiale sorg met CREVAS:
Vertel u dokter of gesondheidsorgverskaffer voordat u CREVAS neem:
- indien u nierprobleme het
- indien u onverklaarbare spierpyne en -skete het, spierswakheid en krampe ervaar en veral indien u ongesteld voel of 'n koors het. Vertel u dokter onmiddellik.
- indien u skildklier nie behoorlik funksioneer nie (hiptiroïdisme)
- indien u 'n persoonlike, of familiegeskiedenis van oorerflike spierversteurings het
- indien 'n vorige geskiedenis van spierprobleme het, of spierprobleme ervaar het, wanneer ander cholesterol-verlagende medisyne gebruik was
- indien u gereeld groot hoeveelhede alkohol inneem
- indien u ouer as 70 jaar oud is
- indien u fibrate neem (cholesterol-verlagende medisyne) (kyk asseblief Ander medisyne en CREVAS)
- indien u tans of tydens die afgelope 7 dae, 'n medisyne wat fusidiensuur genoem word ('n medisyne vir bakteriële infeksie), mondeliks, of deur middel van 'n inspuiting, neem of ontvang het. Die kombinasie van fusidiensuur en CREVAS mag lei tot ernstige spierprobleme (rabdomiolise) (kyk asseblief Ander medisyne en CREVAS)
- indien u ander HMG-CoA-reduktaseremmers saam met fibriensuurderivate, insluitend gemfibrosil, siklosporien, nikotiensuur, asool-swamwerende middels, protease inhibitors (soos lopinavir/ritonavir – medisyne wat gebruik word om MIV-infeksie te behandel) en makroliede antibiotika, gebruik (kyk Ander medisyne en CREVAS).

CREVAS mag interstisiële longsiekte, veral met langtermyn gebruik, veroorsaak. Vertel u dokter indien u dit moeilik vind om asem te haal, 'n nie-produktiewe hoes ontwikkel en/of 'n agteruitgang in u algemene gesondheid (bv. uitputting, gewigsverlies en koors) ervaar terwyl u CREVAS neem.

CREVAS tas die lewer aan by 'n klein hoeveelheid mense. Dit word geïdentifiseer deur 'n toets wat verhoogde lewerensieme in die bloed vasstel. Vir hierdie rede, sal u dokter gewoonlik hierdie bloedtoets aanvra (lewerfunksietoets), voordat behandeling met CREVAS begin word, en indien nodig, daarna.

Crevas mag myasthenia gravis en okulêre miastenie veroorsaak, wat toestande soos spierswakheid, belemmerde spraak, moeisame sluk, een of beide hangende ooglede, of dubbelvisie, tot gevolg het. Vertel u dokter indien u enige van hierdie simptome ervaar, terwyl u CREVAS neem.

By pasiënte wie se hoë cholesterol deur 'n ander siekte, soos skildklier- of nierprobleme veroorsaak word, moet die onderliggende siekte eers behandel word, voordat behandeling met CREVAS begin word.

U dokter sal u noukeurig waarneem, tydens die gebruik van CREVAS indien u diabetes het, of 'n risiko toon om diabetes te ontwikkel. U het waarskynlik 'n risiko om diabetes te ontwikkel, indien u hoë suiker- en vetvlakke in die bloed het, oorgewig is en 'n hoë bloedruk het. CREAVS moet omsigtig gebruik word by pasiënte met Tipe 2 diabetes en by pasiënte wie 'n risiko hiervoor toon.

Ander medisyne en CREVAS
Vertel altyd u gesondheidsorgverskaffer indien u enige ander medisyne neem. (Dit sluit aanvullende of tradisionele medisyne in).

Vertel u dokter indien u enige van die volgende medisyne neem:
Kombinasies wat teenaangedui word
CREVAS moet nie saam met siklosporien (byvoorbeeld gebruik na orgaanoorplantings), gebruik word nie.
Die 40 mg dosis word teenaangedui saam met die gelyktydige gebruik van 'n fibraat.

Daar mag 'n groter moontlikheid vir ander newe-effekte wees, as wat normaalweg verwag sou word
Fibrate (soos gemfibrosil, fenofibraat) of enige ander medisyne wat gebruik word om cholesterol te verlaag (soos esetimib), aangesien hierdie medisyne die uitwerking van CREVAS mag versterk en die risiko om ernstige spierprobleme te ontwikkel, verhoog (kyk Moet nie CREVAS neem bo).

Fusidiensuur ('n antibiotikum) mag die risiko om ernstige spierprobleme te ontwikkel, verhoog (kyk Neem spesiale sorg met CREVAS bo). Indien u mondelikse fusidiensuur benodig om 'n bakteriële infeksie te behandel, moet u die gebruik van CREVAS tydelik staak. U dokter sal u inlig wanneer dit weer veilig is om CREVAS te begin gebruik. Die gebruik van CREVAS saam met fusidiensuur, mag lei tot spierswakheid, teerheid, of pyn (rabdomiolise).
Medisyne wat gebruik word om virusinfeksies te behandel, insluitend MIV of hepatitis C-infeksie, alleen of in kombinasie (kyk asseblief Neem spesiale sorg met CREVAS bo), aangesien hierdie medisyne die werking van CREVAS mag versterk en lei tot 'n toename in die moontlike newe-effekte van CREVAS: ritonavir, lopinavir, atasanavir, ombitasvir, paritaprevir, dasabuvir, velpatasvir, grasoprevir, elbasvir, glekaprevir, pibrentasvir, darunavir, tipranavir.

Effek van CREVAS mag versterk word:
- warfarien of klopidogrel (of enige ander medisyne wat gebruik word vir bloedverdunning), aangesien CREVAS die werking van hierdie medisyne beïnvloed; klopidogrel mag die effek van CREVAS versterk
- regorafenib (gebruik om kanker te behandel), aangesien dit die werking van CREVAS mag versterk
- eltrombopag (gebruik om lae bloedplaatjietellings, veroorsaak deur 'n outo-immuunversteuring te behandel), aangesien dit die werking van CREVAS mag versterk
- dronedaroon (gebruik om abnormale hartritme te behandel), aangesien dit die uitwerking van CREVAS mag versterk
- itrakonasool (gebruik om swaminfeksies te behandel), aangesien dit die uitwerking van CREVAS mag versterk.

Effek van CREVAS mag verswak met:
- indigestiemiddels soos teensuurmiddels (gebruik om die suur in u maag te neutraliseer), aangesien hierdie medisyne die uitwerking van CREVAS mag verswak
- eritromisien ('n antibiotikum), aangesien dit die uitwerking van CREVAS mag verswak.

CREVAS mag die uitwerking van ander medisyne versterk:
- orale voorbehoedmiddels (die pil), aangesien CREVAS die werking van voorbehoedmiddels mag versterk
- hormoonvervangingsterapie, aangesien CREVAS die uitwerking van hierdie medisyne mag versterk.

Die gebruik van CREVAS saam met kos en drinkgoed
U kan CREVAS saam met, of sonder kos neem. Indien u gereeld groot hoeveelhede alkohol inneem, mag dit u risiko vir spierversteurings verhoog.

Swangerskap, borsvoeding en fertiliteit
Indien u swanger is of borsvoed, vermoed dat u swanger is of 'n baba beplan, raadpleeg asseblief u dokter, apteker of ander gesondheidsorgverskaffer vir advies, voordat u hierdie medisyne neem.
U moet toepaslike voorbehoedmaatreëls tref, indien u 'n vrugbare vrou is, wat steeds aan kinders geboorte mag skenk.
U moet nie CREVAS neem, indien u swanger is of u baba borsvoed nie.

Bestuur en die hantering van masjiene
CREVAS mag duiseligheid veroorsaak. U moet dus nie bestuur of masjiene hanteer, totdat u weet hoe CREVAS u aantas nie.
Dit is nie altyd moontlik om te voorspel tot watter mate CREVAS met u daaglikse aktiwiteite sal inmeng nie. U moet verseker dat u nie betrokke raak by bogenoemde aktiwiteite, totdat u weet hoe CREVAS u aantas nie.

CREVAS bevat kleurstowwe
CREVAS 5 mg, 15 mg en 30 mg bevat kinolien geel aluminium-lakkleurstof (E104).
CREVAS 10 mg bevat allura rooi aluminiumlakkleurstof (E129).
CREVAS 40 mg bevat sunset geel aluminiumlakkleurstof (E110) en ponceau aluminiumlakkleurstof (E124).
Die bogenoemde kleurstowwe mag allergiese reaksies veroorsaak.

CREVAS bevat laktosemonohidraat
Indien u deur u dokter meegedeel is dat u 'n onverdraagsaamheid teenoor sekere suikers het, kontak u dokter voordat u hierdie medisinale produk neem.

3. Hoe om CREVAS te gebruik
Moet nie medisyne wat vir u voorgeskryf is met enige ander persoon deel nie.
Neem CREVAS altyd presies soos deur u dokter aanbeveel word. U moet u dokter of apteker raadpleeg indien u onseker is.

Voordat u met behandeling begin moet u dokter u op 'n standaard cholesterol-verlagende dieet plaas, wat voortduur tydens behandeling.
Die doseringsreeks vir CREVAS is 5 - 40 mg mondeliks, een keer per dag. Die aanbevole aanvangsdosis is 5 mg een keer per dag.
U dosis sal individueel aangepas word, in ooreenstemming met u cholesterolvlakke, u risikofaktore en u reaksie teenoor CREVAS-behandeling. Die oorgrote meerderheid pasiënt word beheer met 'n 10 mg dosis. Indien dit egter nodig geag word, sal u dokter u dosis aanpas met 2 - 4-week intervalle.
'n 5 mg aanvangsdosis word aanbeveel vir pasiënte van Asiatiese afkoms en vir pasiënte wie 'n kleiner afname in "slegte" cholesterol (LDL-C) benodig om die behandelingsdoelwit te bereik.
'n Aanvangsdosis van 20 mg mag oorweeg word vir pasiënte met baie hoë cholesterol (insluitend geneties oordraagbare hoë cholesterol).
'n Aanvangsdosis van 20 mg een keer per dag word aanbeveel by pasiënte met geneties oordraagbare hoë cholesterol.

Kinders en adolessente 10 - 17 jaar oud:
By kinders en adolessente met geneties oordraagbare hoë cholesterol, is die dosisreeks 5 - 20 mg mondeliks een keer daagliks.

Spesiale bevolkingsgroepe
U dokter sal 'n gepaste dosis voorskryf indien u bejaard is, of 'n nier- of lewerversteuring het.

U dokter sal aandui hoe lank u behandeling met CREVAS sal duur. Dit mag weke of maande van behandeling neem vir u om enige verbetering in u simptome op te merk en u simptome mag selfs vererger wanneer CREVAS behandeling begin word. Moet nie behandeling vroegtydig staak nie. Indien u onder die indruk is dat die werking van CREVAS té sterk of té swak is, vertel u dokter of apteker.

Indien u meer CREVAS neem as wat u behoort
In die geval van oordosering, raadpleeg u dokter of apteker. Indien beide nie beskikbaar is nie, kontak die naaste hospitaal, of gifbeheersentrum.

Indien u vergeet om CREVAS te neem
Moet nie 'n dubbeldosis neem om op te maak vir die vergete, individuele doserings nie.

4. Moontlike newe-effekte
CREVAS kan newe-effekte hê.
Nie alle newe-effekte wat vir CREVAS aangemeld is, word in hierdie inligtingsblad ingesluit nie.
Sou u algemene gesondheid versleg, of indien u enige ongewenste effekte ervaar, tydens die gebruik van CREVAS, raadpleeg asseblief u gesondheidsorgverskaffer vir advies.

Indien enige van die volgende gebeur, staak die gebruik van CREVAS en vertel u dokter onmiddellik, of gaan na die ongevalle-afdeling by u naaste hospitaal:
- moeilike asemhaling, met of sonder swelling van die gesig, lippe, tong en/of keel, wat sluk mag bemoeilik, erge jeuk van die vel (met verhewe swelsels)
- blaasvorming van die vel, mond en oë (Steven-Johnson-sindroom)
- geelsug (vergeling van die vel en oë).

Hierdie is alles baie ernstige newe-effekte. Indien u dit ervaar, kon u 'n ernstige allergiese reaksie vir CREVAS gehad het. U mag dringende mediese aandag of hospitalisasie benodig.

Vertel u dokter onmiddellik, of gaan na die ongevalle-afdeling by u naaste hospitaal indien u enige van die volgende opmerk:
- enige ongewone pyne en skete in u spiere, wat langer duur as wat verwag word, veral indien u ook 'n koors ontwikkel, of ongesteld voel. Ongemaklike spiereffekte mag ontaard in moontlik lewensbedreigende spierskade, bekend as rabdomiolise. Spiersimptome kom meer dikwels voor by kinders en adolessente, as by volwassenes
- tendonsteurnisse word somtyds gekompliseer deur skeuring
- ernstige spierskade wat presenteer as onverklaarbare spierpyne en -skete, voel ongesteld en koors (immuun-gemedieerde nekrotiserende miopatie)
- 'n erge maagpyn (pankreasinflammasie)
- verhoging in lewerensieme in die bloed
- hepatitis (lewerinflammasie).

Hierdie is alles ernstige newe-effekte. U mag dringende mediese aandag benodig.

Vertel u dokter indien u enige van die volgende opmerk:
Newe-effekte wat dikwels voorkom:
- verhoging in glukosevlakke, diabetes
- hoofpyn, duiseligheid
- hardlywigheid, naarheid, maagpyn
- spierpyn
- voel swak, of ervaar 'n energietekort.

Newe-effekte wat minder dikwels voorkom:
- abnormale bloeding of kneusing
- geheueverlies
- gevoelloosheid, tinteling of sensasieverlies in die arms en bene, brandende gevoel in die hande of voete (polineuropatie)
- uitslag, gejeuk of ander velreaksies
- edeem (swelling onder die vel)
- hoes, asemnood, moeilike asemhaling
- lupus-soortige siekte-sindroom (insluitend uitslag, gewrigsversteurings en effekte op bloedselle)
- spierskeuring
- gewrigspyn
- teenwoordigheid van bloed in u urine
- borstevergroting by mans (ginekomastie).

Newe-effekte met 'n onbekende voorkoms:
- depressie
- slaapsteurnisse, insluitend slaaploosheid en nagmerries
- diarree
- 'n toename in die hoeveelheid proteïen in die urine
- gevoelloosheid en tinteling in die hande of voete (perifere neuropatie)
- spierswakheid, belemmerde spraak, moeisame sluk, een of beide ooglede wat hang, of dubbelvisie (myasthenia gravis en okulêre miastenie).

Indien u enige newe-effekte opmerk, wat nie in hierdie inligtingsblad genoem word nie, raadpleeg asseblief u dokter of apteker.

Aanmelding van newe-effekte
Indien u newe-effekte ervaar, praat met u dokter, apteker of verpleegkundige. U kan ook newe-effekte by SAHPRA via die aanlynskakel vir ongewenste geneesmiddelreaksie rapporteer: https://www.sahpra.org.za/Publications/Index/8 of http://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/.
Deur die aanmelding van newe-effekte, kan u help om meer inligting aangaande die veiligheid van CREVAS in te win. U kan ook 'n epos direk na die maatskappy stuur, pharmacovigilance@pharmadynamics.co.za om veiligheid van die produk te verseker.

5. Hoe om CREVAS te bewaar
Bewaar alle medisyne buite die bereik van kinders.
Bewaar teen of benede 30 °C op 'n koel, droë plek.
Beskerm teen lig.
Hou die tablette in die buitenste kartonhouer, totdat dit benodig word vir gebruik.
Moet nie gebruik na die vervaldatum wat op die kartonhouer aangedui word nie.
Neem alle ongebruikte medisyne na u apteker terug.
Moet nie ongebruikte medisyne in dreine of rioolstelsels (bv. toilette), weggooi nie.

6. Verpakkingsinhoud en ander inligting
Wat CREVAS bevat:
Die atiewe bestanddeel is kalsiumrosuvastatien.
Elke filmbedekte tablet bevat kalsiumrosuvastatien gelykstaande aan of 5, 10, 15, 20, 30 of 40 mg rosuvastatien.

Die ander bestanddele is:
Tabletkerne
Kruisgekoppelde povidoon, laktosemonohidraat, magnesiumstearaat, mikrokristallyne sellulose.

Opadry-deklaag/Filmbedekking
Allura rooi aluminium-lakkleurstof (E129)[2], karmyn (E120)[3], hipromellose (E464), laktosemonohidraat, ponceau aluminium-lakkleurstof (E124)[4], kinolien geel aluminium-lakkleurstof (E104)[1], sunset geel aluminium-lakkleurstof (E110)[4], titaandioksied (E171), triasetien (E1518).
[1] Slegs van toepassing op 5 mg, 15 mg en 30 mg sterktes
[2] Slegs van toepassing op 10 mg sterkte
[3] Slegs van toepassing op 20 mg sterkte
[4] Slegs van toepassing op 40 mg sterkte

Hoe CREVAS lyk en die verpakkingsinhoud
CREVAS 5 mg: Ronde, bikonvekse, gelerige, filmbedekte tablette, 6 mm in deursnee, gedebosseleer met "5" aan een kant.
CREVAS 10 mg: Ronde, bikonvekse, ligpienk, filmbedekte tablette, 7 mm in deursnee, gedebosseleer met "10" aan een kant.
CREVAS 15 mg: Ronde, bikonvekse, geel, filmbedekte tablette, 8 mm in deursnee, gedebosseleer met "15" aan een kant en "15" aan die teenoorgestelde kant.
CREVAS 20 mg: Ronde, bikonvekse, donkerpienk, filmbedekte tablette, 9 mm in deursnee, gedebosseleer met "20" aan een kant.
CREVAS 30 mg: Ronde, bikonvekse, geel, filmbedekte tablette, 10 mm in deursnee, gedebosseleer met "30" aan een kant.
CREVAS 40 mg: Ronde, bikonvekse, rooi, filmbedekte tablette, 10 mm in deursnee, gedebosseleer met "40" aan een kant.

CREVAS is beskikbaar in poliamied/aluminium/PVC-aluminiumfoeliestulpstroke, verpak in 'n buitenste kartonhouer, in verpakkingsgroottes van 7, 14, 28, 30, 56 of 98 filmbedekte tablette.
Nie alle verpakkingshoeveelhede word bemark nie.

Eienaar van die Registrasiesertifikaat
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1 Augustus 2023

Registrasienommers
CREVAS 5 mg: A46/7.5/0313
CREVAS 10 mg: A46/7.5/0314
CREVAS 15 mg: A55/7.5/0453*
CREVAS 20 mg: A46/7.5/0315
CREVAS 30 mg: A55/7.5/0454*
CREVAS 40 mg: A46/7.5/0316*

NAMIBIË
CREVAS 5 mg: NAM NS2 21/7.5/0057
CREVAS 10 mg: NAM NS2 21/7.5/0058
CREVAS 20 mg: NAM NS2 21/7.5/0059
CREVAS 40 mg: NAM NS2 21/7.5/0060

MOSAMBIEK*
CREVAS 5 mg: C6912
CREVAS 10 mg: C6913
CREVAS 20 mg: C6914

*CREVAS 15 mg, CREVAS 30 mg en CREVAS 40 mg word nie bemark in Mosambiek nie.

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