**Approved Patient Information Leaflet for ZYROVA**

# PATIENT INFORMATION LEAFLET

**SCHEDULING STATUS:** S4

**ZYROVA 5, 5 mg film-coated tablets**

**ZYROVA 10, 10 mg film-coated tablets**

**ZYROVA 20, 20 mg film-coated tablets**

**Rosuvastatin calcium**

**Contains sugar:**

**Each 5 mg film-coated tablet contains 55,432 mg lactose monohydrate.**

**Each 10 mg film-coated tablet contains 110,865 mg lactose monohydrate.**

**Each 20 mg film-coated tablet contains 221,729 mg lactose monohydrate.**

**Read all of this leaflet carefully before you start taking ZYROVA:**

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist, nurse or other healthcare provider.
- ZYROVA 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**

6. Contents of the pack and other information.

## 1. What ZYROVA is and what it is used for

ZYROVA contains 5 mg, 10 mg or 20 mg of rosuvastatin, as rosuvastatin calcium, per film-coated tablet and belongs to the pharmacotherapeutic group called HMG-CoA reductase inhibitors.

ZYROVA 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.
ZYROVA 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. ZYROVA, in addition to diet, lowers “bad” cholesterol (LDL) and increases “good” cholesterol (HDL) in the blood.
ZYROVA 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.

40 mg of ZYROVA 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 ZYROVA or alternative therapy.
Specialist supervision is recommended when the 40 mg dose is initiated.
ZYROVA 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 ZYROVA

**Do not take ZYROVA**

- if you are hypersensitive (allergic) to rosuvastatin or any of the other ingredients of ZYROVA (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 ZYROVA**);
- 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 pre-disposing conditions for a muscle disease called myopathy must not take ZYROVA 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 ZYROVA:**

Tell your doctor or healthcare professional before taking ZYROVA:

- 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 ZYROVA**.
- 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 ZYROVA can lead to serious muscle problems (rhabdomyolysis), please see **Other medicine and ZYROVA**.
- 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 ZYROVA**).

Tell your doctor if you develop any general muscle weakness or eye muscle weakness while taking ZYROVA (see **Possible side effects**). These may be signs of myasthenia gravis or ocular myasthenia.

ZYROVA 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 ZYROVA.

In a small number of people, ZYROVA 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 ZYROVA, and if needed thereafter.

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 ZYROVA.

While you are on ZYROVA 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. ZYROVA should be used with care in patients with Type 2 diabetes and in patients at risk.

**Other medicines and ZYROVA**

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

Tell your doctor if you are taking any of the following medicines:

***Contraindicated combinations:***

ZYROVA 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 ZYROVA and the risk of developing serious muscle problems (see **Do not take ZYROVA** above).

Fusidic acid (an antibiotic) may increase the risk of developing serious muscle problems (see **Take special care with ZYROVA** above). If you need to take oral fusidic acid to treat a bacterial infection you will need to temporarily stop using ZYROVA. Your doctor will tell you when it is safe to restart ZYROVA. Taking ZYROVA 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 ZYROVA** above), as these medicines may increase the effect of ZYROVA and may lead to an increase in the possible side effects of

ZYROVA: ritonavir, lopinavir, atazanavir, ombitasvir, paritaprevir, dasabuvir, velpatasvir, grazoprevir, elbasvir, glecaprevir, pibrentasvir, darunavir, tipranavir.

**Effect of ZYROVA may be increased:**

- Warfarin or clopidogrel (or any other medicine used for thinning the blood) as ZYROVA may affect the way this medicine works; clopidogrel may increase the effect of ZYROVA.
- Regorafenib (used to treat cancer) as this may increase the effect of ZYROVA.
- Eltrombopag (used to treat low blood platelet counts caused by an autoimmune disorder) as this may increase the effect of ZYROVA.
- Dronedarone (used to treat abnormal heart rhythm) as this may increase the effect of ZYROVA.
- Itraconazole (used to treat fungal infections) as this may increase the effect of ZYROVA.

**Effect of ZYROVA may be decreased:**

- Indigestion remedies, such as antacids (used to neutralise acid in your stomach) as these medicines may decrease the effect of ZYROVA.
- Erythromycin (an antibiotic) as this may decrease the effect of ZYROVA.

**ZYROVA may increase the effect of other medicines:**

- Oral contraceptives (the pill) as ZYROVA may increase the effect of contraceptives.
- Hormone replacement therapy as ZYROVA may increase the effect of these medicines.

**Taking ZYROVA with food and alcohol**

You can take ZYROVA 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 health care provider for advice before taking ZYROVA.

Women of child-bearing potential should use appropriate contraceptive measures. Do not take ZYROVA if you are pregnant or breastfeeding.

**Driving and using machines**

ZYROVA may cause dizziness, therefore you should not drive or use machines until you know how ZYROVA affects you.

It is not always possible to predict to what extent ZYROVA may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which ZYROVA affects them.

**ZYROVA contains lactose monohydrate**

If you have been told by your doctor that you have an intolerance to some sugars, consult your doctor before taking ZYROVA.

## 3. How to take ZYROVA

Do not share medicines prescribed for you with any other person.

Always take ZYROVA 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 ZYROVA 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 ZYROVA-therapy. The majority of patients are controlled at the 10 mg dose. However, if necessary, dose adjustment can be made 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:**

***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 ZYROVA 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 ZYROVA 5 mg, doses above 10 mg should be carefully considered.

***Race:***

A 5 mg starting dose of ZYROVA should be considered for Asian patients.

Your doctor will tell you how long your treatment with ZYROVA 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 ZYROVA is started. Do not stop treatment early.
If you have the impression that the effect of ZYROVA is too strong or too weak, tell your doctor or pharmacist.

**If you take more ZYROVA than you should**

In the event of an overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

**If you forget to take ZYROVA:**

Do not take a double dose to make up for the forgotten individual doses.

## 4. Possible side effects

ZYROVA can have side effects.
Not all side effects reported for ZYROVA are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking ZYROVA, please consult your healthcare provider for advice.
If any of the following happens, stop taking ZYROVA 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 (Stevens-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 ZYROVA. 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 frequently 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.
- Diarrhoea.
- An increase in the amount of protein in the urine.
- Numbness and tingling in hands or feet (peripheral neuropathy).
- Myasthenia gravis, causing muscle weakness in the skeletal muscles (the muscles that connect to your bones to allow body movement).
- Ocular myasthenia, causing eye muscle weakness, double vision, trouble focusing, drooping eyelids.

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 or pharmacist. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: http://www.sahpra.org.za/Publications/Index/8.

By reporting side effects, you can help provide more information on the safety of ZYROVA.

## 5. How to store ZYROVA

- Store at or below 25 °C.
- Keep the blister strips in the outer carton until required for use.
- Store all medicines out of reach of children.
- Do not use after the expiry date printed on the label or carton.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains and sewerage systems (e.g. toilets).

## 6. Contents of the pack and other information

### What ZYROVA contains

ZYROVA 5: Each film-coated tablet contains 5 mg rosuvastatin (as rosuvastatin calcium).

ZYROVA 10: Each film-coated tablet contains 10 mg rosuvastatin (as rosuvastatin calcium).

ZYROVA 20: Each film-coated tablet contains 20 mg rosuvastatin (as rosuvastatin calcium).

The other ingredients are crospovidone (E1202), magnesium stearate (E572), meglumine, microcrystalline cellulose (E460(i)), lactose monohydrate.

ZYROVA 5: Opadry Yellow (containing hypromellose (E464), FD&C blue No. 2 (E133), FD&C red No. 40 (E129), FD&C yellow No. 6 (E102), lactose monohydrate, titanium dioxide (E171) and triacetin (E1518)).

ZYROVA 10 / 20: Opadry Pink (containing hypromellose (E464), FD&C blue No. 2 (E133), FD&C red No. 40 (E129), FD&C yellow No. 6 (E102), lactose monohydrate, titanium dioxide (E171) and triacetin (E1518)).

### What ZYROVA looks like and contents of the pack

ZYROVA 5: Yellow, round shaped, biconvex, bevelled edge, film-coated tablets, plain on both sides.

ZYROVA 10: Pink, round shaped, biconvex, bevelled edge, film-coated tablets, with a diameter of 7

mm and plain on both sides.

ZYROVA 20: Pink, round shaped biconvex, bevelled edge, film-coated tablets, with a diameter of 9 mm and debossed with ‘20’ on one side and plain on other side.

Aluminium/aluminium blister strips in a carton containing 30 tablets.

**Holder of Certificate of Registration**

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