PROPOSED PATIENT INFORMATION LEAFLET

SCHEDULING STATUS:

S4

MEZIBE PLUS 10/10 tablet

Simvastatin/Ezetimibe

Contains sugar: Lactose monohydrate 57,23 mg/tablet

MEZIBE PLUS 10/20 tablet

Simvastatin/Ezetimibe

Contains sugar: Lactose monohydrate 124,45 mg/tablet

MEZIBE PLUS 10/40 tablet

Simvastatin/Ezetimibe

Contains sugar: Lactose monohydrate 258,90 mg/tablet

Read all of this leaflet carefully before you start taking MEZIBE PLUS

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- MEZIBE PLUS 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 MEZIBE PLUS IS AND WHAT IT IS USED FOR

MEZIBE PLUS contains ezetimibe and simvastatin, one of a group of medicines called serum cholesterol reducers.

MEZIBE PLUS is taken by patients who cannot control their cholesterol levels by diet alone.

You should stay on a cholesterol-lowering diet while taking MEZIBE PLUS.

MEZIBE PLUS is used in addition to your cholesterol-lowering diet if you have:

a raised cholesterol level in your blood (primary hypercholesterolaemia [heterozygous familial and non-familial] or elevated fat levels in your blood (mixed hyperlipidaemia)

- that is not well controlled with a statin alone
- for which you have used a statin and ezetimibe as separate tablets
- a hereditary illness (homozygous familial hypercholesterolaemia) that increases the cholesterol level in your blood. You may also receive other treatments

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE MEZIBE PLUS

Do not take MEZIBE PLUS:

- If you are hypersensitive (allergic) to ezetimibe, simvastatin or to any of the ingredients of MEZIBE PLUS (see section 5)
- if you have liver disease
- • if you are pregnant or breastfeeding your baby
- if you are a child.
- you are taking medicine(s) with one or more than one of the following active ingredients:

- itraconazole, ketoconazole, posaconazole, or voriconazole (used to treat fungal infections),
- erythromycin, clarithromycin, or telithromycin (used to treat infections),
- protease inhibitors such as indinavir, nelfinavir, ritonavir, and saquinavir (HIV protease inhibitors are used to treat HIV infections),
- boceprevir or telaprevir (used to treat hepatitis C virus infections)
- nefazodone (used to treat depression),
- cobicistat,
- gemfibrozil (used to lower cholesterol),
- ciclosporin (often used in organ transplant patients),
- danazol (a man-made hormone used to treat endometriosis, a condition in which the lining of the uterus grows outside the uterus).

- 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 MEZIBE PLUS can lead to serious muscle problems (rhabdomyolysis).

Do not take more than 10/40 mg MEZIBE PLUS if you are taking lomitapide (used to treat a serious and rare genetic cholesterol condition).

Warnings and precautions

Take special care with MEZIBE PLUS:

- if you have moderate to severe liver problems

- if you are taking medicines containing danazol (to treat endometriosis), niacin (nicotinic acid), acipimox (also used to lower cholesterol)
- if you are taking medicine containing ciclosporin (used in organ transplant patients), as your doctor will want to monitor your progress
- if you are taking medicine to treat fungal or bacterial infections (e.g. itraconazole, ketoconazole, erythromycin, clarithromycin, telithromycin),
- if you are taking medicine to treat HIV or medicine to treat depression (nefazodone)
- if you are taking fibrates (to lower cholesterol levels), especially gemfibrozil and bezafibrate
- if you are taking medicines to treat a heart condition (amiodarone or verapamil)
- **if you experience any unexplained muscle pain, tenderness, or weakness contact your doctor immediately.** This is because on rare occasions, muscle problems can be serious, including muscle breakdown resulting in kidney damage.
- The risk of muscle breakdown is greater at higher doses of MEZIBE PLUS. The risk of muscle breakdown is also greater in certain patients:
    - if you have kidney problems
    - if you have thyroid problems
    - if you are 65 years old or older
    - if you are female
    - if you have ever had muscle problems during treatment with cholesterol lowering medicines called “statins” (such as simvastatin, atorvastatin, and rosuvastatin)
    - if you or close family members have a hereditary

muscle disorder

- if you drink large amounts of alcohol
- if you are taking any medicines that may increase the risk of myopathy and rhabdomyolysis

  (disease of the muscle tissue)
- if you are taking medicines to thin your blood (e.g. warfarin)
- if you have diabetes or at risk of developing diabetes
- if you have severe lung disease
- if you have porphyria (a rare hereditary blood disease)

Children

MEZIBE PLUS is not recommended in children under age of 10.

Other medicines and MEZIBE PLUS

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

Tell your doctor if you are taking, have recently taken or might take any other medicine(s) with any of the following active ingredients. Taking MEZIBE PLUS with any of the following medicines can increase the risk of muscle problems (some of these have already been listed in the above section Do not take MEZIBE PLUS).

- medicines with an active ingredient like itraconazole, ketoconazole, fluconazole, posaconazole, or voriconazole (used to treat fungal infections)
- fibrates with active ingredients like gemfibrozil and bezafibrate (used to lower cholesterol)
- ciclosporin (often used in organ transplant patients)
- danazol (used to treat endometriosis, a condition in which the lining of the uterus grows outside the uterus)

- amiodarone (used to treat an irregular heartbeat)
  verapamil, diltiazem, or amlodipine (used to treat high blood pressure, chest pain associated with heart disease, or other heart conditions)
- fusidic acid (to treat a bacterial infection)
  if you need to take oral fusidic acid, you will need to temporarily stop using this medicine.
  Your doctor will tell you when it is safe to restart MEZIBE PLUS. Taking MEZIBE PLUS with fusidic acid may lead to muscle weakness, tenderness or pain (rhabdomyolysis). See more information regarding rhabdomyolysis in section 4.
- HIV protease inhibitors such as indinavir, nelfinavir, ritonavir, and saquinavir (used to treat AIDS)
- hepatitis C antiviral medicines such as boceprevir, telaprevir, elbasvir, or grazoprevir (used treat hepatitis C virus infection)
- nefazodone (used to treat depression)
- medicines with the active ingredient cobicistat
- erythromycin, clarithromycin, daptomycin or telithromycin (used to treat bacterial infections)
- cholestyramine (also used to lower cholesterol), because it affects the way MEZIBE PLUS works
- medicines with an active ingredient to prevent blood clots, such as warfarin, fluindione (anticoagulants)
- lomitapide (used to treat a serious and rare genetic cholesterol condition)

- grapefruit juice (may increase your risk of experiencing muscle problems)
- colchicine (used to treat gout)
- rifampicin (used to treat tuberculosis)
- large amounts (1 gram or more each day) of niacin or nicotinic acid (also used to lower cholesterol)

MEZIBE PLUS with food and drink

MEZIBE PLUS can be taken with or without food.

Grapefruit juice contains one or more components that alter the metabolism of some medications, including MEZIBE PLUS. Consuming grapefruit juice should be avoided as it may increase your risk of muscle problems.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before using MEZIBE PLUS.

Do not take MEZIBE PLUS if you are pregnant, trying to get pregnant or are breastfeeding your baby (see Do not take MEZIBE PLUS).

Driving and using machines

MEZIBE PLUS can cause dizziness.

It is not always possible to predict to what extent MEZIBE PLUS 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 MEZIBE PLUS affects them.

MEZIBE PLUS contains lactose monohydrate

MEZIBE PLUS contains lactose monohydrate. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking MEZIBE PLUS.

3. HOW TO TAKE MEZIBE PLUS

Do not share medicines prescribed for you with any other person. Always use MEZIBE PLUS exactly as your doctor has instructed. You should check with your doctor or pharmacist if you are unsure.

Before starting, and during treatment with MEZIBE PLUS, you should be on a diet to lower your cholesterol.

Adults:

The usual starting dose, depending on your condition, is one MEZIBE PLUS 10/20 mg tablet per day.

One tablet is to be taken in the evening, either with or without food. The dosage range is 10/10 mg to 10/40 mg per day

If your doctor has prescribed MEZIBE PLUS with a bile acid sequestrant such as cholestyramine (a medicine to lower cholesterol), MEZIBE PLUS should be taken at least 2 hours before or 4 hours after taking the bile acid sequestrant.

Children:

MEZIBE PLUS is not for use in children (see Do not take MEZIBE PLUS).

Your doctor will tell you how long your treatment with MEZIBE PLUS will last. Do not stop treatment early because cholesterol level may increase again. If you have the impression that the effect of MEZIBE PLUS is too strong or too weak, tell your doctor or pharmacist.

If you take more MEZIBE PLUS 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 MEZIBE PLUS

If you forget to take **MEZIBE PLUS**, take a dose as soon as you remember, then continue to take **MEZIBE PLUS** at the usual times. Do not take a double dose to make up for forgotten individual doses.

If you stop taking MEZIBE PLUS

If you stop taking MEZIBE PLUS without consulting your doctor, your cholesterol levels may rise again.

4. POSSIBLE SIDE EFFECTS

Not all side effects reported for MEZIBE PLUS are included in this leaflet. Should your general health worsen, or if you experience any untoward effects while using MEZIBE PLUS, please consult your healthcare provider for advice.

If any of the following happens, stop using MEZIBE PLUS and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips, mouth or throat, which may cause difficulty in swallowing or breathing
- rash or itching
- pain or inflammation of the joints, unusual bruising, skin eruptions and swelling, skin sensitivity to the sun, fever, flushing, feeling unwell

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to MEZIBE PLUS. 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:

- muscle breakdown (with symptoms such as muscle pain, tenderness, weakness, swollen muscles, tendon rupture/tear, kidney disorder with reddish-brown urine
- liver problems (you may experience jaundice – yellowing of the skin and eyes – stomach pain and swelling, dark coloured urine)
- an increase in blood sugar which could lead to problems if you are a diabetic (your diabetic medicine may need to be adjusted)

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:

- headache
- cough
- Viral infections, sore throat (pharyngitis), sinusitis, chest infections
- stomach pain/disturbances, flatulence, diarrhoea
- muscle pain, back pain
- extreme tiredness, chest pain
- elevations in laboratory blood tests of liver (transaminases) and/or muscle (CK) function

Less frequent side effects:

- low red blood cell count (anaemia); reduction in blood cell counts, which may cause bruising/bleeding (thrombocytopenia), increased blood clotting time (longer than normal bleeding)
- Weight loss

- sleep disorder, trouble sleeping, depression
- dizziness, pins and needles, poor memory, weakness/ numbness/pain (peripheral neuropathy)
- inflammation of the pancreas often with severe abdominal pain, pain that worsens with deep

  breathing or pain that travels to the right shoulder or

  back
- gastrointestinal problems such as wind, discomfort or bloating, indigestion or heartburn nausea, vomiting, dry mouth, constipation
- itchy or red skin, rash, hair loss, skin or mouth lesions that have a pink-red centre surrounded by a pale ring border and an outer pink-red ring (erythema multiforme)
- pain in the joints or neck, back pain, muscle pain and weakness with skin rash, muscle cramps, muscle spasm, inflammation of the muscle, weakness in the arm and leg muscles,double vision and difficulties with speech and chewing (myasthenia gravis)
- abnormal lack of energy, feeling generally unwell, swelling of the hands or feet abnormal liver function test results

The following side effects have been reported but the frequency for them to occur is not known:

- difficulty breathing, chest infection
- decrease in appetite
- changes to the content of your urine which will be seen in a test performed by your doctor,kidney failure
- trouble remembering, learning new things, concentrating, or making decisions, nightmares,sleep disturbances

- hot flush, high blood pressure
- gall stones, inflammation of the gall bladder
- erectile dysfunction, sexual dysfunction, decreased sex drive, testicular pain, impotence

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 "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of MEZIBE PLUS.

5. HOW TO STORE MEZIBE PLUS

Store all medicines out of reach of children.

Store at or below 25 °C in the original pack.

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

Do not dispose of unused medicine in drains or sewage systems.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

WHAT MEZIBE PLUS CONTAINS

Each **MEZIBE PLUS 10/20** tablet contains 10 mg ezetimibe and 10 mg simvastatin.

Contains sugar: lactose monohydrate 57.23 mg per tablet

Each **MEZIBE PLUS 10/20** tablet contains 10 mg ezetimibe and 20 mg simvastatin.

Contains sugar: lactose monohydrate 124,45 mg per tablet

Each **MEZIBE PLUS 10/40** tablet contains 10 mg ezetimibe and 20 mg simvastatin.

Contains sugar: lactose monohydrate 258,90 mg per tablet

The other ingredients are: Butylated hydroxylanisole 0,02%, citric acid monohydrate, croscarmellose sodium, hypromellose, lactose monohydrate, magnesium stearate, microcrystalline cellulose, and propyl gallate 0,005%

WHAT MEZIBE PLUS LOOKS LIKE AND CONTENTS OF THE PACK

MEZIBE PLUS 10/10

White to off-white, capsule shaped uncoated tablets, debossed with **'L'** on one side and plain on other side.

MEZIBE PLUS 10/20

White to off-white, capsule shaped uncoated tablets, debossed with **'I'** on one side and plain on other side.

MEZIBE PLUS 10/40

White to off-white, capsule shaped uncoated tablets, debossed with **'F'** on one side and plain on other side.

Cartons containing 3 strips of 10 tablets packed in Cold form blister laminate packs composed of oriented polyamide, aluminium foil and PVC with backing of aluminium foil coated with heat seal lacquer on the inner side.

HOLDER OF CERTIFICATE OF REGISTRATION

RANBAXY PHARMACEUTICAL (PTY) LTD

14 Lautre Road

Stormill, Ext.1, Roodepoort, 1724

South Africa

THIS LEAFLET WAS LAST REVISED IN

To be allocated by SAHPRA

REGISTRATION NUMBER

To be allocated by SAHPRA upon registration

ACCESS TO THE CORRESPONDING PROFESSIONAL INFORMATION

To be updated upon approval of the PIL