PATIENT INFORMATION LEAFLET

EZETIMIBE/SIMVASTATIN RANGE

SCHEDULING STATUS

S4

TRYZETOR PLUS 10/10 mg tablets

TRYZETOR PLUS 10/20mg tablets

TRYZETOR PLUS 10/40 mg tablets

Ezetimibe and Simvastatin

TRYZETOR PLUS 10/10 mg contains sugar (lactose monohydrate 51,63mg)

TRYZETOR PLUS 10/20 mg contains sugar (lactose monohydrate 113,26 mg)

TRYZETOR PLUS 10/40 mg contains sugar (lactose monohydrate 236,52mg)

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

- 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.
- TRYZETOR 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

PATIENT INFORMATION LEAFLET

EZETIMIBE/SIMVASTATIN RANGE

1. What TRYZETOR PLUS is and what it is used for

TRYZETOR PLUS contains ezetimibe which is part of a group of medicines called lipid modifying agents and simvastatin part of a group of medicines called serum-cholesterol reducers.

TRYZETOR PLUS is taken by patients who cannot control their cholesterol levels by diet alone. You should stay on a cholesterol-lowering diet while taking TRYZETOR PLUS.

TRYZETOR 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 TRYZETOR PLUS

Do not take TRYZETOR PLUS:

- if you are hypersensitive (allergic) to ezetimibe, simvastatin or to any of the ingredients of TRYZETOR PLUS (see section 6)
- 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 TRYZETOR PLUS can lead to serious muscle problems (rhabdomyolysis).

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

Warnings and precautions

Take special care with TRYZETOR 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 TRYZETOR 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

TRYZETOR PLUS is not recommended in children under the age of 10.

Other medicines and TRYZETOR PLUS

Always tell your healthcare 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 TRYZETOR 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 TRYZETOR 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 TRYZETOR PLUS. Taking TRYZETOR 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 agents such as boceprevir, telaprevir, elbasvir, or grazoprevir (used to 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 TRYZETOR 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).

TRYZETOR PLUS with food and drink

TRYZETOR PLUS can be taken with or without food. Grapefruit juice contains one or more components that alter the metabolism of some medicines, including TRYZETOR 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, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking TRYZETOR PLUS.

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

Driving and using machines

TRYZETOR PLUS can cause dizziness.

It is not always possible to predict to what extent TRYZETOR PLUS 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 TRYZETOR PLUS affects you.

TRYZETOR PLUS contains lactose monohydrate

TRYZETOR 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 TRYZETOR PLUS.

3. How to take TRYZETOR PLUS

Do not share medicines prescribed for you with any other person. Always take TRYZETOR 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 TRYZETOR PLUS, you should be on a diet to lower your cholesterol.

Adults
The usual starting dose, depending on your condition, is one TRYZETOR 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 TRYZETOR PLUS with a bile acid sequestrant such as cholestyramine (a medicine to lower cholesterol), TRYZETOR PLUS should be taken at least 2 hours before or 4 hours after taking the bile acid sequestrant.

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

Your doctor will tell you how long your treatment with TRYZETOR PLUS will last. Do not stop treatment early because cholesterol levels may increase again. If you have the impression that

the effect of TRYZETOR PLUS is too strong or too weak, tell your doctor or pharmacist.

If you take more TRYZETOR 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 TRYZETOR PLUS

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

If you stop taking TRYZETOR PLUS

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

4. Possible side effects

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

If any of the following happens, stop using TRYZETOR 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 TRYZETOR 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.

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

- 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 any side effects to SAHPRA via the online service for reporting 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 TRYZETOR PLUS. You can also send an email directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure the safety of the product.

5. How to store TRYZETOR PLUS

Store all medicines out of reach of children.

Blister strip: Store at or below 30 °C.

Store in a cool, dry place.

Do not take tablets from the blisters until time for use.

Keep blisters in carton until required for use.

Do not use after the expiry date stated on the blister/label/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 TRYZETOR PLUS contains:

The active substances are ezetimibe and simvastatin.

Each TRYZETOR PLUS 10/10 mg tablet contains 10 mg ezetimibe and 10 mg simvastatin.

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

Each TRYZETOR PLUS 10/40 mg tablet contains 10 mg ezetimibe and 40 mg simvastatin.

TRYZETOR PLUS tablets contain sugar in the form of lactose monohydrate.

The other ingredients are

Ascorbic acid, butylhydroxyanisole (BHA), citric acid anhydrous (pH-adjuster), croscarmellose sodium, hypromellose, lactose monohydrate, magnesium stearate and microcrystalline cellulose, pigment blend PB-220001 Yellow (lactose monohydrate, iron oxide (yellow, red, black)), propyl gallate.

What TRYZETOR PLUS looks like and contents of the pack

TRYZETOR PLUS 10/10 mg: Light tan, mottled, round about 6 mm, biconvex tablets. Marking 511 on one side.

TRYZETOR PLUS 10/20 mg: Light tan, mottled, round about 8 mm, biconvex tablets. Marking 512 on one side.

TRYZETOR PLUS 10/40 mg: Light tan, mottled, round about 10 mm, biconvex tablets. Marking 513 on one side.

TRYZETOR PLUS is packed in:

- Blister strips with aluminium foil base and PVC lidding, containing 30 tablets in a carton.

Holder of Certificate of Registration

Pharma Dynamics (Pty) Ltd

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7945, South Africa

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TRYZETOR PLUS 10/10 mg: A51/7.5/1007

TRYZETOR PLUS 10/20 mg: A51/7.5/1008

TRYZETOR PLUS 10/40 mg: A51/7.5/1009

MOZAMBIQUE

TRYZETOR PLUS 10/10 mg: C6915

TRYZETOR PLUS 10/20 mg: C6916

TRYZETOR PLUS 10/40 mg: C6917