APPROVED PIL

For

PREXUM 10 plus

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Confidential Information

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PATIENT INFORMATION LEAFLET

Prexum 10 plus film-coated tablets

perindopril arginine/indapamide

Contains sugar (lactose)

Prexum 10 plus contains 142,66 mg lactose monohydrate

SCHEDULING STATUS: S3

Read of this leaflet carefully before you start taking Prexum 10 plus

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **Prexum 10 plus** has been prescribed to 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 **Prexum 10 plus** is and what it is used for
2. What you need to know before you take **Prexum 10 plus**
3. How to take **Prexum 10 plus**
4. Possible side effects
5. How to store **Prexum 10 plus**
6. Contents of the pack and other information

1. What Prexum 10 plus is and what it is used for

Prexum 10 plus film-coated tablet is a combination of 10 mg perindopril arginine salt and 2,5 mg indapamide.

Prexum 10 plus is used to treat high blood pressure (hypertension).

Prexum 10 plus is prescribed for patients already receiving perindopril 10 mg and indapamide 2,5 mg from separate tablets, these patients may instead receive one tablet of **Prexum 10 plus** which contains both ingredients.

Perindopril belongs to a class of medicines called ACE-inhibitors. These work by widening the blood vessels, which makes it easier for your heart to pump blood through them.

Indapamide is a diuretic. Diuretics increase the amount of urine produced by the kidneys. However, indapamide is different from other diuretics, as it only causes a slight increase in the amount of urine produced. Each of the active ingredients reduces blood pressure and they work together to control your blood pressure.

2. What you need to know before you take Prexum 10 plus

Do not take **Prexum 10 plus**

- if you are hypersensitive (allergic) to perindopril or any other ACE-inhibitor, or to indapamide or any other sulphonamides or any of the other ingredients of **Prexum 10 plus**,
- if you have experienced symptoms such as wheezing, swelling of the face or tongue, intense itching or severe skin rashes with previous ACE-inhibitor or angiotensin receptor blockers (ARB's) treatment or if you or a member of your family have had these symptoms in any other circumstances (a condition called angioedema),
- if you have severe liver disease or suffer from a condition called hepatic encephalopathy (brain disorder caused by toxic substances in patients with liver failure),
- if you have a severe kidney disease where the blood supply to your kidneys is reduced (renal artery stenosis),
- if you are receiving dialysis, or any other type of blood filtration. Depending on the machine that is used, **Prexum 10 plus** may not be suitable for you,
- if you have low blood potassium,
- if you are suspected of having untreated decompensated heart failure (severe water retention, difficulty in breathing),
- if you are pregnant or trying to become pregnant,

- if you are breastfeeding,
- If you have porphyria,
- If you have aortic stenosis (narrowing of the main blood vessel leading from the heart) or hypertrophic cardiomyopathy (heart muscle disease) or renal artery stenosis (narrowing of the artery suppling the kidney with blood),
- if you take lithium or potassium-sparing medicines (spironolactone, triamterene,) or potassium supplements (see Taking other medicines),
- if you have diabetes mellitus or impaired kidney function problems and you are treated with a blood pressure lowering medicine containing aliskiren,
- if you are have taken or currenlty taking sacubitril/valsartan, a medicine for heart failure, as the risk of angioedema (rapid swelling under the skin in an area such as the throat) is increased (see “Warning and Precaution” and “Other medicines and **Prexum 10 plus**”),
- if you are taking fluoroquinolones (an antibiotic).

Warnings and precautions

Tell your doctor or pharmacist before taking **Prexum 10 plus**:

- if you have heart failure or any other heart problems,
- if you have kidney problems, or if you are receiving dialysis,
- if you experience a decrease in vision or eye pain. These could be symptoms of fluid accumulation in the vascular layer of the eye (choroidal effusion) or an increase of pressure in your eye and can happen within hours to weeks of taking **Prexum 10 plus**. This can lead to permanent vision loss, if not treated. If you earlier have had a penicillin or sulfonamide allergy, you can be at higher risk of developing this,
- if you have muscle disorders including muscle pain, tenderness, weakness or cramps,
- if you have abnormally increased levels of a hormone called aldosterone in your blood (primary aldosteronism),
- if you have liver problems,
- if you suffer from a collagen disease such as systemic lupus erythematosus (a type of collagen disease) or scleroderma,

- if you have atherosclerosis (hardening of the arteries),
- if you suffer from hyperparathyroidism (overactive parathyroid gland),
- if you suffer from gout,
- if you have diabetes,
- if you are on a salt restricted diet or use salt substitutes which contain potassium,
- if you take aliskiren (medicines used to treat hypertension),
- Contact your doctor to re-evaluate your treatment if you are treated with ACE-inhibitors/Angiotensin receptor blockers together with a fluoroquinolone antibiotic,
- if you are elderly,
- If you have photosensitivity reactions,
- If you have severe allergic reaction with swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing (angioedema). This may occur at any time during the treatment. If you develop such symptoms, you should stop taking the treatment and see a doctor immediately,
- if you are taking any of the following medicines used to treat high blood pressure:
  - an “angiotensin II receptor blocker” (ARBs) (also known as sartans - for example valsartan, telmisartan, irbesartan), in particular if you have diabetes-related kidney problems,
  - aliskiren.

Your doctor may check your kidney function, blood pressure, and the amount of electrolytes (e.g. potassium) in your blood at regular intervals.

See also information under the heading “Do not take **Prexum 10 plus**”,

- If you are of black origin since you may have a higher risk of angioedema and this medicine may be less effective in lowering your blood pressure than in non-black patients,
- If you are a haemodialysis patient dialysed with high-flux membranes,
- If you you are taking any of the following medicines, the risk of angioedema is increased:
  - racecadotril (used to treat diarrhoea),

- sirolimus, everolimus, temsirolimus and other medicines belonging to the class of so-called mTor inhibitors (used to avoid rejection of transplanted organs),

- sacubitril (available as fixed-dose combination with valsartan), used to treat long-term heart failure,
- linagliptin, saxagliptin, sitagliptin, vildagliptin and other drugs belonging to the class of the also called gliptins (used to treat diabetes).

Angioedema

Angioedema (a severe allergic reaction with swelling of the face, lips, tongue or throat with difficulty in swallowing or breathing) has been reported in patients treated with ACE-inhibitors, including **Prexum 10 plus**.

This may occur at any time during treatment. If you develop such symptoms, you should stop taking **Prexum 10 plus** and see a doctor immediately (see section 4).

When you are taking **Prexum 10 plus** you should also inform your doctor or the healthcare professional:

- if you are to undergo anaesthesia and/or surgery,
- if you have recently suffered from diarrhoea or vomiting, or are dehydrated,
- if you are to undergo dialysis or LDL apheresis (which is removal of cholesterol from your blood by a machine),
- if you are going to have desensitisation treatment to reduce the effects of an allergy to bee or wasp stings,
- if you are to undergo a medical test that requires injection of an iodinated contrast medicine (a substance that makes organs like kidney or stomach visible on an X-ray),
- if you have changes in your vision or pain in one or both of your eyes while taking **Prexum 10 plus**. This could be a sign that you are developing glaucoma, increased pressure in your eye(s). You should discontinue **Prexum 10 plus** treatment and seek medical attention.

Athletes should be aware that **Prexum 10 plus** contains an active ingredient (indapamide) which may give a positive reaction in drug tests.

Children and adolescents:

Prexum 10 plus should not be given to children or adolescent under 18 years of age.

Other medicines with Prexum 10 plus

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

You should avoid taking **Prexum 10 plus** with:

- lithium (used to treat mania or depression),
- aliskiren (medicine used to treat hypertension) if you have diabetes mellitus or kidney problems,
- potassium-sparing diuretics (e.g. triamterene, amiloride), potassium salts, other medicines which can increase potassium in your body (such as heparin, a medicine used to thin blood to prevent clots; trimethoprim and co-trimoxazole also known as trimethoprim/sulfamethoxazole for infections caused by bacteria),
- estramustine (used in cancer therapy),
- other medicines used to treat high blood pressure: angiotensin converting enzyme inhibitors and angiotensin receptor blockers.

Treatment with **Prexum 10 plus** can be affected by other medicines. Make sure to tell your doctor if you are taking any of the following medicines as special care may be required:

- other medicines for treating high blood pressure, including angiotensin II receptor blocker (ARB) or aliskiren (see also information under the headings “Do not take **Prexum 10 plus**” and “Take special care with **Prexum 10 plus**”) or diuretics (medicines which increase the amount of urine produced by the kidneys),
- potasium sparing medicines used in the treatment of heart failure; eplenerone and spironolactone at doses between 12,5 mg to 50 mg per day,

- medicines, which is most often used to treat diarrhoea (racecadotril) or avoid rejection of transplanted organs (sirolimus, everolimus, temsirolimus and other medicines belonging to the class of so-called mTor inhibitors). (see section Warnings and precautions),
- sacubitril/valsartan (used to treat long-term heart failure). See sections “Do not take **Prexum 10 plus**” and “Warnings and precautions”,
- anaesthetic medicines,
- iodinated contrast medicine,
- antibiotics used to treat bacterial infections (e.g moxifloxacin, sparfloxacin, erythromycin by injection),
- fluoroquinolones (an antibiotic) it may cause acute kidney disease,
- methadone (used to treat addiction),
- procainamide (for the treatment of an irregular heart beat),
- allopurinol (for the treatment of gout),
- antihistamines used to treat allergic reactions, such as hay fever (e.g mizolastine, terfenadine, astemizole),
- corticosteroids used to treat various conditions including severe asthma and rheumatoid arthritis,
- immunosuppressants used for the treatment of auto-immune disorders or following transplant surgery to prevent rejection (e.g. ciclosporin, tracolimus),
- halofantrine (used to treat certain types of malaria),
- pentamidine (used to treat pneumonia),
- injectable gold (used to treat rheumatoid polyarthritis),
- vincamine (used to treat symptomatic cognitive disorders in elderly),
- bepridil (used to treat angina pectoris),
- medicines used for heart rhythm problems (e.g. quinidine, hydroquinidine, disopyramide, amiodarone, sotalol),
- cisapride, diphemanil (used to treat gastric and digestive problems),
- digoxin (for the treatment of heart problems),
- baclofen (to treat muscle stiffness occurring in diseases such as multiple sclerosis),

- medicines to treat diabetes such as insulin, metformin or gliptins,
- calcium including calcium supplements,
- stimulant laxatives (e.g. senna),
- non-steroidal anti-inflammatory drugs (e.g. ibuprofen) or high dose salicylates (e.g. acetylsalicylic acid (an ingredient present in many medicines used to relieve pain and lower fever, as well as to prevent blood clotting),
- amphotericin B by injection (to treat severe fungal disease),
- medicines to treat mental disorders such as depression, anxiety, schizophrenia (e.g. tricyclic antidepressants, neuroleptics, (such as amisulpride, sulpiride, sultopride, tiapride, haloperidol, droperidol),
- tetracosactide (to treat Crohn's disease),
- trimethoprim (for the treatment of infections),
- vasodilators including nitrates (products that make the blood vessels become wider),
- medicines used for the treatment of low blood pressure, shock or asthma (e.g. ephedrine, noradrenaline or adrenaline).

Prexum 10 plus with food and drink

Prexum 10 plus should be taken once daily before a meal, preferably in the morning.

Pregnancy and breastfeeding

Prexum 10 plus can cause serious harm to your unborn baby.

If you are pregnant or breastfeeding your baby and think you may be pregnant or are planning to have a baby while taking Prexum 10 plus, please consult your doctor, pharmacist or other healthcare professional for advice.

Ask your doctor or pharmacist for advice before taking any medicine.

Pregnancy:

Prexum 10 plus must not be taken while pregnant. Should you become pregnant or contemplate pregnancy while using **Prexum 10 plus**, consult your doctor without delay. The switch to an alternative class of hypertensives should be initiated as soon as possible.

Breastfeeding

You must not take **Prexum 10 plus** if you are breastfeeding your infant.

Driving and using machines

Your ability to drive or to operate machinery may be impaired.

Prexum 10 plus contains lactose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking **Prexum 10 plus**.

Prexum 10 plus contains sodium

Prexum 10 plus contains less than 1 mmol sodium (23 mg) per tablet, essentially 'sodium-free'.

3. **How to take Prexum 10 plus**

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

Always take **Prexum 10 plus** exactly as directed by your doctor.

You should check with your doctor or pharmacist if you are not sure. The recommended dosage is one tablet orally taken in the morning before breakfast.

Your doctor may decide to modify the dosage regimen if you suffer from kidney function impairment.

Method of administration:

Swallow your tablet(s) with a glass of water, preferably in the morning before breakfast.

Taking your tablets at the same time each day will have the best effect on your blood pressure.

It will also help you to remember when to take the tablets.

If you take more Prexum 10 plus than you should:

In the event of overdosage, consult your doctor or pharmacist.

If neither is available seek help at the nearest hospital or poison control centre.

The most likely effect in case of overdose is low blood pressure. If marked low blood pressure occurs (associated with nausea, vomiting, cramps, dizziness, sleepiness, mental confusion, changes in the amount of urine produced by your kidneys), lying down with the legs raised can help.

If you forget to take Prexum 10 plus:

It is important to take **Prexum 10 plus** every day as regular treatment is more effective.

However, if you forget to take a dose of **Prexum 10 plus**, take the next dose at the usual time.

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

If you stop taking Prexum 10 plus:

As the treatment for high blood pressure is usually life-long, you should discuss with your doctor before stopping **Prexum 10 plus**.

"**Do not share medicines prescribed for you with others."**

4. Possible Side Effects

Prexum 10 plus can have side effects.

Not all side effects reported for Prexum 10 plus are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking Prexum 10 plus, please consult your doctor, pharmacist or other healthcare professional for advice.

Stop taking Prexum 10 plus and see a doctor immediately if you experience any of the following side effects that can be serious:

Frequent:

- Severe dizziness or fainting due to low blood pressure,

Less frequent:

- Bronchospasm (tightening of the chest, wheezing and shortness of breath),
- Swelling of the face, lips, mouth, tongue or throat, difficulty in breathing (angioedema),
- Severe skin reaction including erythema multiform (a skin rash often starts with red itchy patches on your face, arms or legs) or intense skin rash, hives, reddening of the skin over your whole body, severe itching, blistering, peeling and swelling of the skin,
- inflammation of mucous membranes (Stevens Johnson Syndrome) or other allergic reactions,
- Cardiovascular disorders (irregular heartbeat, angina pectoris (pain to the chest, jaw and back, brought on by physical effort),
- Weakness of arms or legs, or problems speaking which could be a sign of a possible stroke,
- Inflamed pancreas which may cause severe abdominal and pack pain accompanied with feeling very well,
- Yellowing of the skin or eyes (jaundice) which could be a sign of hepatitis,
- Life threatening irregular beat,
- Disorder of the brain caused by liver illness (hepatic encephalopathy),
- Inflammation of the liver (hepatitis),
- Muscle weakness, cramps, tenderness or pain and particularly, if at the same time, you feel unwell or have a high temperature it may be caused by an abnormal muscle breakdown.

In decreasing order of frequency, side effects of **Prexum 10 plus** can include:

- *Frequent:*

  Low potassium in the blood, skin reactions in subjects predisposed to allergic and asthmatic, headache, dizziness, vertigo, pins and needles, vision disturbances, tinnitus

(sensation of noises in the ears), cough, shortness of breath, (dyspnoea), gastro-intestinal disorders (nausea, anorexia, vomiting, abdominal pain, taste disturbances, dry mouth, dyspepsia or difficulty of digestion, diarrhoea, constipation), allergic reaction (skin rashes, itching), cramps, feeling of tiredness.

- *Less frequent:*

Depression, mood swings, sleep disturbances, skin reactions in subjects predisposed to allergic and asthmatic reactions, urticaria, purpura (red pinpoints on skin), blister clusters, kidney problems, impotence (inability to obtain or maintain an erection), sweating, an excess of eosinophils (a type of white blood cells), change in laboratory parameters: high blood level of potassium reversible on discontinuation, low blood level of sodium that may lead to dehydration and low blood pressure, somnolence, fainting, palpitations (awareness of your heart beat), tachycardia (fast heart beat), hypoglycaemia (very low blood sugar level) in case of diabetic patients, vasculitis (inflammation of blood vessels), dry mouth, photosensitivity reactions (increased sensitivity of the skin to sun), arthralgia (joint pain), myalgia (muscle pain), chest pain, malaise, peripheral oedema, fever, increased blood urea, increased blood creatinine, fall.

Worsening of psoriasis, changes in laboratory parameters, low chloride in the blood, low magnesium in the blood, increased level of liver enzymes, high level of serum bilirubin, high level of calcium in the blood, fatigue, flushing, decrease or absence urine output, acute renal failure.

Dark urine, feeling sick (nausea) or being sick (vomiting), muscle cramps, confusion and seizures. These may be symptoms of a condition called SIADH (inappropriate antidiuretic hormone secretion).

Confusion, eosinophilic pneumonia (a rare type of pneumonia), rhinitis (blocked up or runny nose), severe kidney problems, changes in blood values such as a lower number of white and red blood cells, lower haemoglobin, lower number of blood platelets, high levels of calcium in the blood, abnormal hepatic function, stroke possibly secondary to excessive low blood pressure.

Abdnormal ECG heart tracing, changes in laboratory parameters: high uric acid levels and high sugar levels in the blood, short sightedness (myopia), blurred vision, visual impairment, decrease in vision or pain in your eyes due to high pressure (possible signs of fluid accumulation in the vascular layer of the eye (choroidal effusion) or acute angle-closure glaucoma), discolouration, numbness and pain in fingers or toes (Raynaud's phenomenon).

If you suffer from systemic lupus erythematosus (a type of collagen disease), this might get worse.

Disorders of the blood, kidney, liver or pancreas and changes in laboratory parameters (blood tests) can occur. Your doctor may need to give you blood tests to monitor your condition.

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

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. 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 **Prexum 10 plus**.

5. How to store Prexum 10 plus

Keep all medicine out of reach of children.

Store at or below 30 °C.

Keep the bottle well closed to protect the tablets from moisture.

Do not store in bathrooms.

Do not use after the expiry date on the carton and the bottle. The expiry date refers to the last day of that month.

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 Prexum 10 plus contains

- The active substances are perindopril arginine and indapamide. One film-coated tablet contains 10 mg perindopril arginine (corresponding to 6,79 mg perindopril) and 2,5 mg indapamide.
- The other ingredients in the tablet core are: lactose monohydrate, magnesium stearate (E470B), maltodextrin, anhydrous colloidal silica (E551), sodium starch glycolate (type A), and in the tablet film-coating: glycerol (E422), hypromellose (E464), macrogol 6 000, magnesium stearate (E470B), titanium dioxide (E171).

What Prexum 10 plus looks like and contents of the pack

Prexum 10 plus: White, round, film-coated tablet.

White polypropylene tube equipped with a polyethylene flow reducer containing 30 tablets and a white polyethylene stopper containing white desiccant gel.

Holder of certificate of registration

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