

Applicant: Aurogen South Africa (Pty) Ltd
Product Name: ANNIN CO 50/12.5 mg and ANNIN CO 100/25 mg
Dosage form and strength: Film coated Tablet, each tablet contains Losartan potassium/Hydrochlorothiazide 50/12.5 mg and 100/25 mg

Patient Information Leaflet

SCHEDULE STATUS

S3

PATIENT INFORMATION LEAFLET

ANNIN CO 50/12,5 mg

Losartan potassium 50 mg and hydrochlorothiazide 12,5 mg.

Contains sugar: 111 mg of lactose

ANNIN CO 100/25 mg

Losartan potassium 100 mg and hydrochlorothiazide 25 mg.

Contains sugar: 222 mg of lactose

Read all of this leaflet carefully before you start taking ANNIN CO.

- 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.
- **ANNIN CO** 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 **ANNIN CO** is and what it is used for
2. What you need to know before you use **ANNIN CO**
3. How to use **ANNIN CO**
4. Possible side effects
5. How to store **ANNIN CO**
6. Contents of the pack and other information

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1. What ANNIN CO is and What it is used for

ANNIN CO is a combination of an angiotensin II receptor antagonist (losartan) and a diuretic (hydrochlorothiazide). Angiotensin II is a substance produced in the body which binds to receptors in blood vessels, causing them to tighten. This results in an increase in blood pressure. Losartan prevents the binding of angiotensin II to these receptors, causing the blood vessels to relax which in turn lowers the blood pressure.

Hydrochlorothiazide works by making the kidneys pass more water and salt. This also helps to reduce blood pressure.

ANNIN CO is indicated for the treatment of essential hypertension (high blood pressure).

2. What you need to know before you take ANNIN CO

Do not take ANNIN CO:

- If you are hypersensitive (allergic) to losartan, hydrochlorothiazide or to any of the other ingredients of this medicine (listed in section 6).
- If you have previously been treated with a medication in the same group of medicines as **ANNIN CO** (angiotensin receptor antagonists) or with a medication in the group of medicines known as ACE inhibitors and have had allergic reactions with swelling of the face, lips, tongue, and/or throat with difficulty in swallowing or breathing.
- If you have severely impaired liver function.
- If you have low potassium, low sodium or high calcium levels which cannot be corrected by treatment.
- If you have hereditary or idiopathic angioedema (swelling of the face, lips, mouth, tongue or throat with or without difficulty in swallowing or breathing).
- If you have hypertrophic obstructive cardiomyopathy, a heart disorder in which the walls of the ventricles (lower heart chambers) thicken (hypertrophy) and become stiff and the thickened muscle blocks the flow of blood out of the heart.
- If you have severely impaired kidney function or your kidneys are not producing any urine.
- If you have narrowing of the blood vessels to both kidneys or to a single kidney.

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- If you have aortic stenosis, a narrowing of the aortic valve opening between the left ventricle (large pumping chamber of the heart) and the aorta (the main artery leading away from the heart).
- If you are taking diuretics (water pills) that cause your body to retain potassium such as spironolactone, triamterene and amiloride.
- If you have porphyria.
- Thiazide water tablets in (fixed dose) combination as with **ANNIN CO** should not be given to patients with Addison's disease (a long-term endocrine disorder in which the adrenal glands do not produce enough steroid hormones). This therapy should also not be used in patients with severe kidney disease or patients not passing urine, and in patients who show allergy to other sulphonamide-derived medicines (ask your doctor if you are not sure what sulphonamide-derived medicines are).
- Lithium therapy: Concomitant administration with **ANNIN CO** may lead to toxic blood concentrations of lithium.
- If you are pregnant or breastfeeding (see Pregnancy and Breastfeeding).
- If you have liver disease.
- The concomitant use with antibiotics that belong in the class “fluoroquinolones” should be avoided.
- The concomitant use of **ANNIN CO** with aliskiren-containing products should be avoided.

Take special care with ANNIN CO:

Talk to your doctor, pharmacist or nurse before taking **ANNIN CO**. You must tell your doctor if you think you are (or might become) pregnant. **ANNIN CO** is not recommended in pregnancy, and must not be taken if you are pregnant, as it may cause serious harm to your baby.

It is important to tell your doctor before taking ANNIN CO:

- If you have previously suffered from swelling of the face, lips, throat or tongue.
- If you take diuretics (water pills).
- If you are on a salt restricted diet.

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- If you have or have had severe vomiting and/or diarrhoea.
- If you have heart failure.
- If your liver function is impaired (see section 2 “Do not take **ANNIN CO**”).
- If you have narrow arteries to your kidneys (renal artery stenosis) or only have one functioning kidney, or you have recently had a kidney transplant.
- If you have narrowing of the arteries (atherosclerosis), angina pectoris (chest pain due to poor heart function).
- If you have ‘aortic or mitral valve stenosis’ (narrowing of the valves of the heart) or ‘hypertrophic cardiomyopathy’ (a disease causing thickening of heart muscle).
- If you are diabetic.
- If you have had gout.
- If you have or have had an allergic condition, asthma or a condition that causes joint pain, skin rashes and fever (systemic lupus erythematosus).
- If you have high calcium or low potassium levels or you are on a low potassium diet.
- If you need to have an anaesthetic (even at the dentist) or before surgery, or if you are going to have tests to check your parathyroid function, you must tell the doctor or medical staff that you are taking losartan potassium and hydrochlorothiazide tablets, as there may be a sudden fall in blood pressure associated with the anaesthetic.
- If you suffer from primary hyperaldosteronism (a syndrome associated with increased secretion of the hormone aldosterone by the adrenal gland, caused by an abnormality within the gland).
- If you are taking any of the following medicines used to treat high blood pressure: an ACE-inhibitor (for example enalapril, lisinopril, ramipril), in particular if you have diabetes-related kidney problems.
- If you are taking lithium (a medicine used to treat a certain kind of depression)
- Aliskiren
- Your doctor may check your kidney function, blood pressure, and the amount of electrolytes (e.g. potassium) in your blood at regular intervals.
- If you are taking other medicines that may increase serum potassium (see section 2 “Other medicines and **ANNIN CO**”).
- If you have had skin cancer or if you develop an unexpected skin lesion during the treatment.

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Treatment with hydrochlorothiazide, particularly long-term use with high doses, may increase the risk of some types of skin and lip cancer (non-melanoma skin cancer). Protect your skin from sun exposure and UV rays while taking **ANNIN CO**.

Use in children

As there is no experience with the use of **ANNIN CO** in children, **ANNIN CO** should not be given to children.

Taking other medicines with ANNIN CO

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

Other medicines and ANNIN CO

ANNIN CO may have an effect on other medicines or other medicines may have an effect on **ANNIN CO**.

- It is especially important for your doctor to know if you are taking other medicines to reduce blood pressure, other diuretics (water tablets),
- medication used to treat diabetes including insulin,
 - resins which reduce high cholesterol,
 - muscle relaxants, pressor amines such as adrenaline, steroids, certain pain and arthritis medicines, or
 - lithium (a medicine used to treat a certain kind of depression). Lithium excretion may be reduced. Therefore, lithium should not be taken at the same time with **ANNIN CO**.
- Sedatives, tranquilizers, narcotics, alcohol and analgesics may increase the blood pressure-lowering effect of **ANNIN CO**, so tell your doctor if you take any of these medicines.
- When Non-steroidal anti-inflammatory drugs (NSAIDs), which is used to treat patients with reduced kidney function, is taken together with **ANNIN CO**, further deterioration of kidney function may result.

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Pregnancy and Breastfeeding

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking ANNIN CO. When pregnancy is detected or suspected ANNIN CO should be discontinued as soon as possible. ANNIN CO should not be used in pregnancy as teratogenicity has been shown in experimental animals.

Pregnancy

You must tell your doctor if you think you are (or might become) pregnant. Your doctor will normally advise you to stop taking **ANNIN CO** before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of **ANNIN CO**.

ANNIN CO is not recommended during pregnancy

Women of childbearing age should ensure effective contraception.

Breast-feeding

Tell your doctor if you are breast-feeding or about to start breast-feeding. Safety in breastfeeding has not been established. Thiazides appear in human milk. **ANNIN CO** is not recommended for mothers who are breast-feeding, and your doctor may choose another treatment for you if you wish to breast-feed your baby.

Driving and using machinery:

When you begin treatment with this medication, you should not perform tasks, which may require special attention (for example, driving an automobile or operating dangerous machinery) until you know how you tolerate your medicine.

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Important information about some of the ingredients of ANNIN CO

ANNIN CO contains lactose therefore you should tell your doctor if you are sugar intolerant or have a history of lactose intolerance.

3. How to take ANNIN CO

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

Always take **ANNIN CO** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. Your doctor will tell you how long your treatment with **ANNIN CO** will last. If you have the impression that the effect of **ANNIN CO** is too strong or too weak, talk to your doctor or pharmacist.

Taking ANNIN CO with food and drink:

ANNIN CO tablets may be taken with or without food.

Adult dose:

The maximum dose is one tablet of **ANNIN CO** 100 mg losartan potassium and 25 mg hydrochlorothiazide) once daily. The maximum antihypertensive effect is attained within three weeks after initiation of therapy.

Try to take **ANNIN CO** daily as prescribed. However, if you miss a dose, do not take an extra dose. Just resume your usual schedule.

Paediatric Use:

Safety and efficacy in children has not been established.

Your doctor will tell you how long your treatment with **ANNIN CO** will last. Do not stop treatment early because this may lead to reoccurrence of your condition. If you have the impression that the effect of **ANNIN CO** is too strong or too weak, tell your doctor or pharmacist.

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If you take more ANNIN CO 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.

In case of an overdose, contact your doctor immediately so that medical attention may be given promptly. Overdose can cause a drop in blood pressure, palpitations, slow pulse, changes in blood composition, and dehydration.

If you forget to take ANNIN CO:

If you forgot to take a dose, take it as soon as you remember unless it is nearly time for your next dose. Do not take a double dose to make up for forgotten individual doses.

4. POSSIBLE SIDE EFFECTS

ANNIN CO can have side effects:

Not all side effects reported for **ANNIN CO** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking this medicine, please consult your doctor, pharmacist or other health care professional for advice.

If any of the following happens, stop taking **ANNIN CO** and tell your doctor immediately or go to the casualty department at your nearest hospital:

- A severe allergic reaction (rash, itching, swelling of the face, lips, mouth or throat that may cause difficulty in swallowing or breathing).

This is a serious side effect. You may need urgent medical attention or hospitalisation.

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

Tell your doctor if you notice any of the following:

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The following side effects occur frequently:

- Cough, upper airway infection, congestion in the nose, sinusitis, sinus disorder
- Diarrhoea, abdominal pain, nausea, indigestion
- Muscle pain or cramps, leg pain, back pain
- Insomnia, headache, dizziness
- Weakness, tiredness, chest pain
- Increased potassium levels (which can cause an abnormal heart rhythm), decreased haemoglobin levels
- Changes in kidney function including kidney failure
- Too low sugar in the blood (hypoglycaemia)
- Low blood pressure, which may be associated with changes in posture (feeling light-headed or weak when you stand up, angina (chest pain), abnormal heartbeat, cerebrovascular accident (TIA, "mini-stroke"), heart attack, palpitations
- Improper beating of the heart, whether irregular, too fast or too slow.

The following side effects occur less frequently:

- Anaemia, red or brownish spots on the skin (sometimes especially on the feet, legs, arms and buttocks, with joint pain, swelling of the hands and feet and stomach pain), bruising, reduction in white blood cells, clotting problems
- Loss of appetite, increased uric acid levels or frank gout, increased blood sugar levels, abnormal blood electrolyte levels
- Anxiety, nervousness, panic disorder (recurring panic attacks), confusion, depression, abnormal dreams, sleep disorders, sleepiness, memory impairment
- Blurred vision, burning or stinging in the eyes, conjunctivitis, worsening eyesight, seeing things in yellow
- Ringing, buzzing, roaring or clicking in the ears, vertigo
- Inflammation of blood vessels, which is often associated with a skin rash or bruising
- Sore throat, breathlessness, bronchitis, pneumonia, water on the lungs (which causes difficulty breathing), nosebleed, runny nose, congestion

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- Constipation, obstipation, wind, stomach upsets, stomach spasms, vomiting, dry mouth, inflammation of a salivary gland, toothache
- Jaundice (yellowing of the eyes and skin), inflammation of the pancreas
- Itching, inflammation of the skin, rash, redness of the skin, sensitivity to light, dry skin, flushing, sweating, hair loss
- Pain in the arms, shoulders, hips, knees or other joints, joint swelling, stiffness, muscle weakness
- Frequent urination including at night, abnormal kidney function including inflammation of the kidneys, urinary tract infection, sugar in the urine
- Swelling of the face, localised swelling (oedema), fever
- Pins and needles or similar sensations, pain in the extremities, trembling, migraine, fainting
- Increased urea and creatinine levels, increased liver enzymes

The following side effects occur less frequently:

- Hepatitis (inflammation of the liver), abnormal liver function tests

The following side effects occur with an unknown frequency:

- Thrombocytopenia (a low number of platelets in the blood)
- Pancreatitis (inflammation of the pancreas)
- Flu-like symptoms such as fever, chills, muscle aches, cough, congestion, runny nose, headaches and fatigue
- Liver problems
- Rhabdomyolysis (A breakdown of muscle tissue that causes muscle pain with dark (tea-coloured) urine)
- Decreased sex drive or impotence
- Orthostatic hypotension (A form of low blood pressure that happens when standing up from sitting or lying down)
- Hyponatraemia (A condition that occurs when the level of sodium in the blood is too low)
- Skin and lip cancer (Non-melanoma skin cancer)

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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. 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 Reactions Reporting Form. Found 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 this medicine.

5. How to store ANNIN CO

- Keep out of the sight and reach of children.
- Do not store above 25 °C.

Store in the original package in order to protect from light and moisture.

- Do not use **ANNIN CO** after the expiry date, which is stated on the package. The expiry date refers to the last day of that month.
- If your tablets become discoloured or show any other signs of deterioration, consult your doctor or pharmacist who will tell you what to do.
- Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

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 ANNIN CO contains

There are two active ingredients in **ANNIN CO**. These are losartan potassium and hydrochlorothiazide.

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ANNIN CO 50 mg/12,5 mg

Each film-coated tablet contains 50 mg losartan potassium and 12,5 mg of hydrochlorothiazide.

ANNIN CO 100 mg/25 mg

Each film-coated tablet contains 100 mg losartan potassium and 25 mg of hydrochlorothiazide.

Other ingredients:

Cellulose, Microcrystalline Ph.Eur (Avicel PH 101)

Cellulose, Microcrystalline Ph.Eur (Avicel PH 200)

Starch, Pre-gelatinised Ph.Eur (Starch 1500)

Silica Colloidal anhydrous Ph.Eur (Aerosil® 200 Pharma)

Magnesium Stearate Ph.Eur

Ingredients of Coating material:

Opadry Yellow 20A52067

What ANNIN CO looks like and contents of the pack

ANNIN CO 50 mg/12,5 mg

Yellow coloured, oval shaped, beveled edge, biconvex film-coated tablets debossed with 'E' on one side and '48' on the other side.

ANNIN CO 100 mg/25 mg

Yellow coloured, oval shaped, beveled edge, biconvex film-coated tablets debossed with 'E' on one side and '49' on the other side.

Blister pack

PVC / Aclar

Blister pack comprises of 250 micron white opaque PVC film laminated with 50 micron aclar as the forming material and 25 micron aluminum foil with 7gsm heat seal lacquer as the lidding material.

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PVC / PE / PVdc

Blister pack comprises of 250 micron white opaque PVC film laminated with 25 micron PE, coated with 90 gsm PVdc as the forming material and 25 micron aluminum foil with 7gsm heat seal lacquer as the lidding material

Pack size: 30's. Each container contains 3 blisters of 10 tablets each.

HDPE

White opaque round 40 mL HDPE container with 33 mm neck finish closed with 33 mm -400 RS white opaque polypropylene stock ribbed closure with wad having induction sealing liner.

Pack Size: 30's: Each HDPE container contains 30 tablets each.

Holder of Certificate of Registration

AUROGEN SOUTH AFRICA (PTY) Ltd

Woodhill Office Park,

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Meyersdal, Ext. 12, 1448

Johannesburg

South Africa

Registration Number

ANNIN CO 50 mg/12.5 mg: 45/7.1.3/1054

ANNIN CO 100 mg/25 mg: 45/7.1.3/1055

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