PATIENT INFORMATION LEAFLET

CALSAR CO RANGE

SCHEDULING STATUS

S3

CALSAR CO 5 mg/160 mg /12,5 mg film coated tablets

CALSAR CO 5 mg/160 mg /25 mg film coated tablets

CALSAR CO 10 mg/160 mg /12,5 mg film coated tablets

CALSAR CO 10 mg/160 mg /25mg film coated tablets

CALSAR CO 10 mg/320 mg/25 mg film coated tablets

Amlodipine, valsartan and hydrochlorothiazide

CALSAR CO contains sugar (sugar alcohol – mannitol) (58,8 mg: 5/160/12,5 mg; 10/160/12,5 mg; 5/160/25 mg; 10/160/25 mg. 117,5 mg: 10/320/25 mg)

Essentially 'sodium free'

Read all of this leaflet carefully before you start taking CALSAR CO

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

1. What CALSAR CO is and what it is used for

CALSAR CO contains three active substances, amlodipine, valsartan and hydrochlorothiazide. All of these substances help to control high blood pressure.

- amlodipine belongs to a group of substances called calcium channel blockers. Amlodipine stops calcium from moving into the blood vessel wall, which stops the blood vessels from tightening
- valsartan belongs to a group of substances called angiotensin-II receptor antagonists. Angiotensin II is produced by the body and makes the blood vessels tighten, thus increasing the blood pressure. Valsartan works by blocking the effect of angiotensin II. As a result, blood vessels relax and blood pressure is lowered
- hydrochlorothiazide belongs to a group of substances called thiazide diuretics. Hydrochlorothiazide increases urine output, which also lowers blood pressure.

CALSAR CO is used to treat high blood pressure in patients whose blood pressure has been stabilised on the combination of the three medicines contained in CALSAR CO, given as individual doses, at the same time.

CALSAR CO is not prescribed for the initial treatment of high blood pressure.

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

Do not take CALSAR CO:

- if you are hypersensitive (allergic) to amlodipine, valsartan, hydrochlorothiazide and other sulphonamides (medicines used to treat chest or urinary infections), dihydropyridine derivatives (used in the treatment of high blood pressure) or any of the other ingredients of CALSAR CO listed in section 6

- if you have previously suffered from the rapid swelling of the skin or mucous membranes of the face (angioedema) while taking this type of medicines, called angiotensin receptor blockers (ARBs). This medicine must never be taken again
- if you have moderate or severe kidney problems, or are an elderly patient and are being treated with a fluroquinolone antibiotic
- if you are treated with a blood pressure lowering medicine containing aliskiren
- if you are on lithium therapy (a medicine used to treat some types of depression)
- if you are taking other medicines or substances, which increase the potassium levels in your blood (such as certain types of diuretics, e.g. spironolactone, triamterene, amiloride and potassium supplements). These medicines are usually used to treat high blood pressure or swelling (see Other medicines with CALSAR CO)
- if you have hereditary or spontaneous development of swelling under the skin (angioedema)
- if you have severe liver problems
- if you have Addison's disease, a rare, chronic disease of the adrenal glands
- if you have an inability to produce urine, or are undergoing dialysis
- if you have imbalances in your blood chemistry, such as low sodium and potassium levels, or high calcium or urea levels
- if you suffer from a narrowing of valves in your heart (called aortic or mitral stenosis), or abnormally increased thickness of your heart muscle with narrowing (called hypertrophic obstructive cardiomyopathy - HOCM)
- if you have only one kidney or you suffer from a narrowing or blockage of the arteries that supply blood to your kidney (renal artery stenosis)
- if you are pregnant, planning to become pregnant, or breastfeeding your baby
- if you have porphyria, a rare disease of a deficiency of certain enzymes. The disease can be recognised by nerve pain and skin problems
- if you are under the age of 18 as CALSAR CO should not be given to children
- if you have or previously had cancer of the skin or lips.

Warnings and precautions

Take special care with CALSAR CO:

If you are pregnant or fall pregnant while taking CALSAR CO, therapy should be stopped immediately and switched to a different class of high blood pressure medicine (see sections Do not take CALSAR CO and Pregnancy and breastfeeding)

- if you have mild to moderate kidney problems, your doctor will monitor your electrolyte levels periodically
- if you are on a low-salt diet, have lost a lot of fluids recently (due to excessive sweating, hot weather, exercising, diarrhoea, vomiting or dialysis) or are taking high doses of water tablets; you may experience dehydration or a serious drop in blood pressure (hypotension) with symptoms including feeling dizzy when standing up. Should this occur, lie down flat and seek medical help if need be
- when taking CALSAR CO your doctor may wish to have your blood tested before and at regular intervals during your treatment to check the values of potassium, magnesium, calcium, sodium, sugar, cholesterol, uric acid and the amounts of red and white cells as well as platelets
- if you develop rapid swelling of the skin or mucous membranes of the face (angioedema) (see Do not take CALSAR CO). Seek medical help if you have previously been diagnosed with Systemic Lupus Erythematosus (an autoimmune disease), or you develop side effects that include fever, facial rash, and joint pain, which may be signs of lupus erythematosus
- one of the ingredients of CALSAR CO is hydrochlorothiazide, a thiazide diuretic (water tablet), and may change your glucose tolerance (used to determine your resistance to glucose and is used to test for diabetes), raise the levels of cholesterol, triglycerides (fatty acid in the blood), and uric acid (a component in your blood formed from the breakdown of proteins). Your doctor might need to adjust the dosage of your diabetic medicines

- if you have had heart failure or have experienced a heart attack. Follow your doctor's instructions for the starting dose carefully. Your doctor may also check your kidney function
- if you have a condition affecting the renal glands called primary hyperaldosteronism (a hormonal disorder) you should not used CALSAR CO
- if you suffer from kidney problems and are taking a fluoroquinolone antibiotic, your doctor will need to assess your condition before starting and during treatment with CALSAR CO. If you are already taking a fluoroquinolone antibiotic together with CALSAR CO you should contact your doctor to re-evaluate your treatment
- if you experience skin reactions such as rash after sun exposure, your doctor may change your medicine or advise you to protect your skin against sun and UV light
- if you experience a decrease in vision or eye pain, notify your doctor. These could be symptoms of an increase of pressure in your eye and can happen within hours to a week of starting this medicine. This can lead to permanent vision impairment, if not treated
- if you are over the age of 65 as your doctor will want to monitor your blood pressure closely
- if you are taking any medicines which contain aliskiren, please inform your doctor. These medicines should not be taken with CALSAR CO if you have diabetes with kidney impairment (see Do not take CALSAR CO)
- if you have had skin cancer or if you develop an unexpected skin lesion during the treatment. 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 CALSAR CO.

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

Children and adolescents:

The use of CALSAR CO in children and adolescents is not recommended (see Do not take CALSAR

CO).

Other medicines and CALSAR CO

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

The effect of the treatment can be influenced if CALSAR CO is taken together with certain other medicines. These medicines may either reduce the ability of CALSAR CO to lower blood pressure or increase blood levels which may cause unwanted adverse effects. Hence it may be necessary to change the dose, to take other precautions, or in some cases to stop taking the medicine.

Do not take together with: (see Do not take CALSAR CO)

- ACE inhibitors or aliskiren (see also information under the headings Do not take CALSAR CO and Warnings and precautions)
- fluoroquinolone antibiotics when taken with CALSAR CO may worsen kidney problems especially in elderly
- lithium (a medicine used to treat some types of depression)
- medicines or substances that increase the amount of potassium in your blood. These include potassium supplements or salt substitutes containing potassium, potassium-sparing medicines and heparin.

Caution should be used with:

- medicines to treat fungal infections (such as ketoconazole, itraconazole), antiretrovirals (e.g. ritonavir) and antibiotics (e.g. erythromycin, clarithromycin)
- anticonvulsant medicines and mood-stabilizing medicines used to treat epilepsy and bipolar disorder (e.g. carbamazepine, phenobarbitone, phenytoin, fosphenytoin, primidone) or St John's Wort (a herbal medicine)
- simvastatin (used to lower cholesterol)

- dantrolene (an infusion for severe body temperature abnormalities)
- some antibiotics (rifampicin), medicines used to protect against transplant rejection (ciclosporin) or an antiretroviral medicine used to treat HIV/AIDS infection (ritonavir).
- certain types of painkillers called nonsteroidal anti-inflammatory drugs (NSAIDs) or selective cyclooxygenase-2 inhibitors (COX-2 inhibitors) to treat pain and arthritis (such as ibuprofen, indomethacin or aspirin)
- alcohol, sleeping pills and anaesthetics (medicines allowing patients to undergo surgery and other procedures)
- amantadine (anti-Parkinson therapy, also used for influenza treatment)
- anticholinergic medicines including atropine, biperiden (medicines used to treat a variety of disorders such as gastrointestinal cramps, urinary bladder spasm, asthma, motion sickness, muscular spasms, Parkinson's disease and as an aid to anaesthesia)
- cholestyramine, colestipol or other resins (substances used mainly to treat high levels of lipids in the blood)
- diuretics (water tablets), corticosteroids, laxatives, amphotericin, or penicillin G may overly reduce the amount of potassium in your blood
- medicines that may reduce the amount of sodium in your blood, such as antidepressants, antipsychotics, antiepileptics.

CALSAR CO may also affect the way other medicines work or increase their adverse effects. Hence it may be necessary to adjust the dose or to take other precautions:

- insulin or antidiabetic medicines (insulin and those taken by mouth including metformin)
- medicines that may increase blood sugar levels (beta blockers, diazoxide) may increase the risk of hyperglycaemia
- ciclosporin (a medicine used in transplantation to prevent organ rejection or for other conditions, e.g. rheumatoid arthritis or eczema), may increase the risk of side effects such as gout
- cytotoxic medicines (cancer therapy e.g. cyclophosphamide, methotrexate) due to increased

unwanted side effects

- digoxin (a heart medicine) as unwanted side effects may occur
- iodine contrast media (agents used for imaging examinations) as there may be a risk of kidney failure should you be dehydrated
- medicines that may induce "*torsades de pointes*" (irregular heartbeat), such as antidysrhythmics (medicines used to treat heart problems) and some antipsychotics
- medicines for the treatment of gout, such as allopurinol (which may also lead to an allergic reaction), probenecid, sulphinpyrazone. The dosage of these medicines may need to be adjusted due to increased uric acid levels
- medicines used to lower blood pressure (e.g. guanethidine, methyldopa, beta-blockers, vasodilators, calcium channel blockers, ACE inhibitors, ARBs and Direct Renin Inhibitors [DRIS]) as antihypertensive effect of these medicines may be increased. Concomitant use with Methyldopa may also result in anaemia
- muscle relaxants (medicines to relax the muscles which are used during operations) as the effects of these medicines may be enhanced
- medicines to increase blood pressure such as adrenaline or noradrenaline and their effectiveness may be reduced
- Vitamin D or calcium salts as CALSAR CO may cause an increase in the levels of calcium in your blood.

CALSAR CO with food and drink

Grapefruit and grapefruit juice should not be consumed by people who take CALSAR CO. This is because grapefruit and grapefruit juice can lead to an increase in the blood levels of the active substance amlodipine, which can cause an unpredictable increase in the blood pressure lowering effect of CALSAR CO.

Avoid drinking alcohol as alcohol may make your blood pressure fall too much and/or increase the possibility of dizziness or fainting.

Pregnancy, breastfeeding and fertility

Pregnancy and breastfeeding

If you are pregnant or breastfeeding your baby, think you may be pregnant or planning to have a baby, please consult your doctor, pharmacist or other healthcare professional for advice before using CALSAR CO.

Women of childbearing age should use effective contraception.

Do not take CALSAR CO if you are pregnant or planning to become pregnant. Use during pregnancy may cause serious damage to your unborn child (see Do not take CALSAR CO).

Treatment with CALSAR CO is not recommended during breastfeeding (see Do not take CALSAR CO).

Fertility

There is no data on fertility with CALSAR CO.

Driving and using machines:

CALSAR CO may make you feel dizzy or drowsy, which may affect your ability to drive or operate machinery.

It is not always possible to predict to what extent CALSAR CO 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 CALSAR CO affects you.

CALSAR CO contains sodium

This medicine contains less than 1 mmol sodium (0,023 g) per film coated tablet, that is to say essentially 'sodium free'.

3. How to take CALSAR CO

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

Adults:

The usual dose is one tablet per day of either of the following:

CALSAR CO 5 mg/160 mg /12,5 mg

CALSAR CO 5 mg/160 mg /25 mg

CALSAR CO 10 mg/160 mg /12,5 mg

CALSAR CO 10 mg/160 mg /25 mg

CALSAR CO 10 mg/320 mg/25 mg

CALSAR CO can be taken with or without food. It is recommended to take CALSAR CO with some water.

Do not take the tablet if there are signs of cracking.

Your doctor will tell you which strength to take and for how long your treatment with CALSAR CO will last. Do not stop treatment early because your high blood pressure may return.

If you have the impression that the effect of CALSAR CO is too strong or too weak, tell your doctor or pharmacist.

CALSAR CO is not recommended for use in patients aged below 18 years (see Do not take CALSAR CO).

If you take more CALSAR 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.

Symptoms of overdose may include:

- rapid heartbeat, chest pain, fainting, low blood pressure and dizziness.
- difficulty breathing, extreme shortness of breath, feeling of suffocating or drowning, cough that produces frothy sputum that may have blood in it, rapid, irregular heartbeat, anxiety, restlessness, cold and clammy skin, wheezing.

If you forget to take CALSAR CO:

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

If you stop taking CALSAR CO

It is important that you continue the course of treatment. Stopping your treatment may cause your disease to get worse. Do not stop taking CALSAR CO unless your doctor tells you to do so.

4. Possible side effects

CALSAR CO can have side effects.

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

If any of the following happens, stop using CALSAR CO 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
- fainting.

These are all very serious side effects. If you have them, you may have had a serious reaction to CALSAR CO. 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:

- chest pain, low blood pressure, pressure, tightness, pain, or a squeezing or aching sensation in your chest or arms that may spread to your neck, jaw or back
- changes in the way your heart beats, for example, if you notice it is beating faster
- kidney problems (passing less urine than is normal for you), abnormal kidney function, kidney failure
- jaundice (yellowing of the skin and eyes)
- hepatitis (inflammation of the liver with symptoms such as nausea, mild fever, abdominal pain), abnormal liver function (clay coloured stool, dark urine, itching, loss of appetite)
- toxic epidermal necrolysis (TEN) (a life-threatening skin disorder with symptoms such as a painful red area that spreads quickly, skin peeling without blisters, raw areas of skin) or Stevens-Johnson syndrome or other serious skin disorder (begins with flu-like symptoms, followed by a painful red or purplish rash that spreads and blisters).

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:

- decrease in potassium, sodium and magnesium, increased cholesterol levels and excess of uric acid in the bloodstream (seen through blood tests)
- headache, dizziness, drowsiness
- low blood pressure, flushing, low blood pressure when standing up
- indigestion, vomiting, abdominal pain/discomfort, nausea, decreased appetite (anorexia)
- passing more urine than normal

- swelling of arms, hands, legs, ankles or feet, chronic tiredness, weakness (fatigue)
- skin rash, urticaria (a rash of round, red welts on the skin that itch intensely, sometimes with dangerous swelling)
- inability to obtain an erection (impotence).

Less frequent side effects:

- high level of sugar in the blood (hyperglycaemia), or excess of sugar in the urine, worsening of diabetes, electrolyte imbalance
- insomnia, sleep disturbances, mood changes, anxiety, depression, confusion
- taste disturbances (dysgeusia), lack of energy and enthusiasm, dizziness when standing or after exercise, pins and needles sensation, drowsiness, numbness, tremor, abnormally high level of muscle tone or tension
- vision changes, double vision, eye pain, increased pressure in the eye (glaucoma)
- vertigo (spinning sensation), tinnitus (ringing in the ears)
- swelling, reddening and pain along a vein
- cough, runny or stuffy nose, difficult or laboured breathing, throat irritation, excess fluid in lungs
- breath odour, dry mouth,
- diarrhoea or constipation
- inflammation of the pancreas, swelling of the salivary glands
- hair loss
- increased sweating
- allergic reactions and other skin conditions ranging from a rash, excessive skin pigmentation/discolouration, hives, itchy skin, blisters and peeling, sensitivity of skin to sunlight
- back pain, muscle spasm, muscle pain, joint pain, muscle weakness, pain in arms and legs
- general feeling of discomfort, illness, or unease, abnormal physical weakness or lack of energy, non-cardiac chest pain, raised body temperature, fever, walking abnormality

- weight increase, weight decrease
- increase liver enzymes, abnormal liver function test (which may be an indication of liver disease)
- increase of creatinine in the blood, kidney failure
- breast enlargement in men
- abnormal blood test results: anaemia (reduced number of red blood cells with symptoms such as feeling generally tired or lethargic, pale skin, low level of white blood cells), decrease in blood platelets which may result in unusual bruising or easy bleeding (red blood cell damage), abnormal red blood cell test, low level of a certain type of white blood cell and blood platelet, weakness, bruising and frequent infections (aplastic anaemia)
- vasculitis necrotizing (inflammation of blood vessels)
- gastritis (inflammation of the stomach lining), abnormal growth of the gums.

Side effects with unknown frequency:

- skin and lip cancer (non-melanoma skin cancer)
- involuntary or uncontrollable movements (tremors, muscle contractions)
- decreased sex drive.

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 Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of CALSAR CO.

An email can be sent directly to the company, pharmacovigilance@pharmadynamics.co.za to ensure safety of the product.

5. How to store CALSAR CO

Store all medicines out of reach of children.

Store at or below 30 °C.

Keep blisters in carton until required for use.

Do not use after the expiry date stated on the 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 CALSAR CO contains

The active substances are amlodipine besylate, valsartan and hydrochlorothiazide.

Each CALSAR CO 5 mg/160 mg /12,5 mg film coated tablet contains amlodipine besylate (equivalent to 5 mg of amlodipine), 160 mg of valsartan and 12,5 mg hydrochlorothiazide. Contains sugar (sugar alcohol - mannitol 58,8 mg).

Each CALSAR CO 5 mg/160 mg /25 mg film coated tablet contains amlodipine besylate (equivalent to 5 mg of amlodipine), 160 mg of valsartan and 25 mg hydrochlorothiazide. Contains sugar (sugar alcohol - mannitol 58,8 mg).

Each CALSAR CO 10 mg/160 mg /12,5 mg film coated tablet contains amlodipine besylate (equivalent to 10 mg of amlodipine), 160 mg of valsartan and 12,5 mg hydrochlorothiazide. Contains sugar (sugar alcohol - mannitol 58,8 mg).

Each CALSAR CO 10 mg/160 mg /25 mg film coated tablet contains amlodipine besylate (equivalent to 10 mg of amlodipine), 160 mg of valsartan and 25 mg hydrochlorothiazide. Contains sugar (sugar alcohol - mannitol 58,8 mg).

Each CALSAR CO 10 mg/320 mg/25 mg film coated tablet contains amlodipine besylate (equivalent to 10 mg of amlodipine), 320 mg of valsartan and 25 mg hydrochlorothiazide. Contains sugar (sugar alcohol - mannitol 117,5 mg).

The other ingredients are:

Tablet cores

Colloidal anhydrous silica, croscarmellose sodium, magnesium stearate, mannitol, microcrystalline cellulose, povidone, sodium lauryl sulphate.

Coating:

Ferric oxide yellow (only CALSAR CO 5/160/25 mg and CALSAR CO 10/160/25 mg), ferric oxide red (only CALSAR CO 10/160/12,5 mg and CALSAR CO 10/320/25 mg), macrogol, polyvinyl alcohol, talc, titanium dioxide.

What CALSAR CO looks like and contents of the pack

CALSAR CO 5 mg/160 mg /12,5 mg: White or almost white, oval, biconvex, film coated tablets, engraved with mark K1 on one side of the tablet.

CALSAR CO 5 mg/160 mg /25 mg: Light yellow, oval, biconvex, film coated tablets, engraved with mark K3 on one side of the tablet.

CALSAR CO 10 mg/160 mg /12,5 mg: Pink, oval, biconvex, film coated tablets, engraved with mark K2 on one side of the tablet.

CALSAR CO 10 mg/160 mg /25 mg: Brown-yellow, oval, biconvex, film coated tablets, engraved with mark K4 on one side of the tablet.

CALSAR CO 10 mg/320 mg /25 mg: Brown-red, oval, biconvex, film coated tablets.

CALSAR CO is packed in blisters (OPA/Alu/PVC – Alu): 7, 10, 14, 28, 30, 56, 60, 84, 90, 98, 100 film coated tablets, in an outer carton.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

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