APPROVED PIL

For

IDAGOR

Registration No.:

Idagor 5/1,25/5 mg: 49/7.1.3/1243

Idagor 5/1,25/10 mg: 49/7.1.3/1240

Idagor 10/2,5/5 mg: 49/7.1.3/1241

Idagor 10/2,5/10 mg: 49/7.1.3/1242

Date Approved: November 2020

Confidential Information

Registered Approved PIL
Applicant: Servier Laboratories SA (Pty) Ltd
Product: **Idagor 5 mg/1,25 mg/5 mg; 5 mg/1,25 mg/10 mg; 10 mg/2,5 mg/5 mg; 10 mg/2,5 mg/10 mg**
Date of submission: 24 November 2020

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS **S3**

Idagor 5 mg/1,25 mg/5 mg film-coated tablets

Idagor 5 mg/1,25 mg/10 mg film-coated tablets

Idagor 10 mg/2,5 mg/5 mg film-coated tablets

Idagor 10 mg/2,5 mg/10 mg film-coated tablets

perindopril arginine/ indapamide/ amlodipine

Read all of this leaflet carefully before you start taking Idagor.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse or other healthcare provider.
- **Idagor** 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 **Idagor** is and what it is used for.
2. What you need to know before you take **Idagor**.
3. How to take **Idagor**.
4. Possible side effects.
5. How to store **Idagor**.
6. Content of the pack and other information.

1. What Idagor is and what it is used for

Idagor is a combination of three active ingredients: perindopril, indapamide and amlodipine. It is an anti-hypertensive medicine used in the treatment of high blood pressure (hypertension).

If you are already taking perindopril/indapamide as fixed dose combination and amlodipine from separate tablets you may instead receive one tablet of **Idagor** which contains the three active ingredients in the same strength.

Each of the active ingredients reduces blood pressure and they work together to control your blood pressure:

- Perindopril belongs to a class of medicines called Angiotensin Converting Enzyme (ACE) inhibitors. It works by widening the blood vessels, which makes it easier for your heart to pump blood through them.
- Indapamide is a diuretic (which is a sulphonamide derivative). Diuretics increase the amount of urine produced by the kidneys. However, indapamide only causes a slight increase in the amount of urine produced.
- Amlodipine is a calcium channel blocker ~~s~~ (which belongs to a class of medicines called dihydropyridines). It works by relaxing blood vessels, so blood passes through easily.

2. What you need to know before you take Idagor

Do not take Idagor

- if you are hypersensitive (allergic) to perindopril or other ACE-inhibitors, indapamide or other sulphonamides, amlodipine or other dihydropyridines, or any of the other ingredients of **Idagor** (listed in section 6),
- if you have experienced symptoms such as wheezing, with difficult breathing, swelling of the face or tongue, intense itching or severe skin rashes with previous ACE-inhibitor 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 a liver disease with moderate to severe impairment of your liver function or suffer from a condition called hepatic encephalopathy (disease of the brain caused by liver illness),
- if you are suspected of having untreated decompensated heart failure (severe water retention, difficulty in breathing),
- if you are treated with medicines that may cause serious heart rhythm disturbances,
- if you have narrowing of the aortic heart valve (aortic stenosis) or cardiogenic shock (a condition where your heart is unable to supply enough blood to the body),
- if you suffer from heart failure after a heart attack,
- if you have severe low blood pressure (hypotension),
- if you have a low blood potassium level,
- if you have severe kidney problems where the blood supply to your kidneys is reduced (renal artery stenosis),
- if you have only one kidney,
- if you are receiving dialysis or any other type of blood filtration. Depending on the machine that is used, **Idagor** may not be suitable for you,
- if you have moderate or severe impairment of your kidney function,
- if you are pregnant or planning to become,
- if you are breastfeeding your baby,
- if you have porphyria,
- if you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren,
- if you are being treated with sacubitril/valsartan, a medicine for heart failure (see “Warnings and Precautions” and “Other medicines and **Idagor**”),
- If you are treated with Lithium,
- If you are treated with potassium sparing diuretics (water pills that increase your blood potassium e.g. spironolactone, triamterene).

Warnings and precautions

Tell your doctor or healthcare professional before taking **Idagor.**

Take special care with **Idagor**:

- if you have hypertrophic cardiomyopathy (heart muscle disease) or renal artery stenosis (narrowing of the artery supplying the kidney with blood),
- if you have heart failure or any other heart problems,
- if you have a severe increase in blood pressure (hypertensive crisis),
- if you have liver disease/disorder,
- if you suffer from a collagen disease (skin disease) such as systemic lupus erythematosus or scleroderma,
- if you have atherosclerosis (hardening of the arteries),
- if you need to have a test to check how well your parathyroid gland is working,
- if you suffer from gout,
- if you have diabetes mellitus,
- if you are on a salt restricted diet or use salt substitutes which contain potassium (a well-balanced potassium blood level is essential),
- if you take lithium or potassium-sparing diuretics (spironolactone, triamterene) as their use with **Idagor** should be avoided (see “Taking other medicines”),
- if you are elderly and your dose needs to be increased,
- if you have had photosensitivity reactions,
- if you are of black origin the blood pressure lowering effect may be less and you may have a higher incidence of angioedema (swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing),
- if you are on haemodialysis dialysed with high-flux membranes,
- if you have a kidney disease/disorder or if you are receiving dialysis,
- if you have increased levels of a hormone called aldosterone in your blood (primary aldosteronism),

- if you have too much acid in blood, which may cause an increased rate of breathing,
- if you have cerebral circulatory insufficiency (low blood pressure and blood flow in the brain),
- if you have swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing (angioedema), which can occur at any time during treatment, stop your treatment immediately and directly contact your doctor,
- if you are taking any of the following medicines, the risk of angioedema is increased:
    - racecadotril (used to treat diarrhoea),
    - sirolimus, everolimus, temsirolimus and other medicine 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.
- 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 concentration/levels of electrolytes (e.g. potassium) in your blood at regular intervals.

  See also information under the heading “Do not take **Idagor**”.

Your doctor may request laboratory blood tests to check if you have a low sodium level, a low or potassium level or a high calcium level.

When you are taking **Idagor**, you should also inform your doctor or the medical staff:

- 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).

Children and adolescents

Idagor should not be given to children and adolescents under the age of 18 years.

Other medicines and Idagor

Always tell your healthcare professional if you are taking other medicines (this include complementary or traditional medicines).

Do not take aliskiren (used to treat high blood pressure) if you have diabetes or kidney diseases/disorders or just one kidney.

You should avoid **Idagor** with:

- ✓ lithium (used to treat some mental health disorders such as mania, manic depressive illness and recurrent depression),
- ✓ potassium-sparing medicine (e.g. triamterene, amiloride), potassium supplements or potassium-containing salt substitutes, other medicines which can increase potassium in your body (such as heparin and co-trimoxazole also known as trimethoprim/sulfamethoxazole),
- ✓ dantrolene (infusion) which is ~~also~~ used to treat malignant hyperthermia during anaesthesia (symptoms including very high fever and muscle stiffness),
- ✓ estramustine (used in cancer therapy),
- ✓ medicines, which are used to treat diarrhea (racecadotril) or to 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 **Idagor**" and "Warnings and precautions",
- ✓ other medicines used to treat high blood pressure: angiotensin-converting-enzyme inhibitor and angiotensin receptor blockers.

Treatment with **Idagor** can be affected by other medicines. Your doctor may need to change your dose and/or to take other precautions. 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), aliskiren (see also information under the headings "Do not take **Idagor**" and "Warning and precaution"), or diuretics (medicines which increase the amount of urine produced by the kidneys),
- ✓ potassium-sparing medicines used in the treatment of heart failure: eplerenone and spironolactone at doses between 12,5 mg to 50 mg per day,
- ✓ anaesthetic medicines
- ✓ iodinated contrast medicines
- ✓ bepridil (used to treat angina pectoris),
- ✓ moxifloxacin, sparfloxacin (antibiotics: medicines used to treat infection),
- ✓ methadone (used to treat addiction)
- ✓ dofetilide, ibutilide, bretylium, cisapride, diphemanil, procainamide, quinidine, hydroquinidine, disopyramide, amiodarone, sotalol (for the treatment of an irregular heart beat),
- ✓ verapamil, diltiazem (heart medicines)
- ✓ digoxin (for the treatment of heart problems),
- ✓ rifampicin, erythromycin, clarithromycin (antibiotics for infection caused by bacteria),
- ✓ itraconazole, ketoconazole, amphotericin B by injection (to treat fungal disease),
- ✓ allopurinol (for the treatment of gout),
- ✓ mizolastine, terfenadine or astemizole (antihistamines for hay fever or allergies),

- ✓ corticosteroids used to treat various conditions including severe asthma and rheumatoid arthritis, and non-steroidal anti-inflammatory medicine (e.g. ibuprofen) or high dose salicylates (e.g. acetylsalicylic acid),
- ✓ immunosuppressants (medicines used to control your body's immune response) for the treatment of auto-immune disorders or following transplant surgery (e.g. ciclosporin, tacrolimus),
- ✓ tetracosactide (to treat Crohn's disease)
- ✓ gold salts, especially with intravenous administration (used to treat symptoms of rheumatoid arthritis),
- ✓ halofantrine (used to treat certain types of malaria),
- ✓ baclofen used to treat muscle stiffness in diseases such as multiple sclerosis,
- ✓ medicines to treat diabetes such as insulin or metformin,
- ✓ calcium including calcium supplements,
- ✓ stimulant laxatives (e.g. senna),
- ✓ medicines for the treatment of cancer,
- ✓ vincamine (used to treat symptomatic cognitive disorders in elderly including memory loss),
- ✓ medicines to treat mental health disorders such as depression, anxiety, schizophrenia…(e.g. tricyclic antidepressants, antipsychotics, imipramine-like antidepressants, neuroleptics),
- ✓ pentamidine (used to treat pneumonia),
- ✓ ritonavir, indinavir, nelfinavir (so called protease inhibitors used to treat HIV).
- ✓ hypericum perforatum (St. John's Wort),
- ✓ trimethoprim (for the treatment of infections),
- ✓ medicines used for the treatment of low blood pressure, shock or asthma (e.g. ephedrine, noradrenaline or adrenaline),
- ✓ nitroglycerin and other nitrates, or other vasodilators that may further reduce blood pressure.

Contact your doctor to re-evaluate your treatment if you are treated with a fluoroquinolone antibiotic and you are also on treatment with **Idagor** or an angiotensin receptor blocker for your hypertension.

Athletes should be aware that **Idagor** contains an active ingredient (indapamide) which is listed as a prohibited medicine for athletes to use (will give a positive test for prohibited substances).

Idagor with food and drink

Grapefruit juice and grapefruit should not be consumed by people who are taking **Idagor**. This is because grapefruit and grapefruit juice can lead to an increase in the blood levels of the active ingredient amlodipine, which can cause an unpredictable increase in the blood pressure lowering effect of **Idagor**.

Pregnancy and breastfeeding

You should not be treated with **Idagor** if you think you are pregnant, if you are pregnant or plan to become pregnant, as **Idagor** may cause serious harm to your unborn baby.

If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to become pregnant, ask your doctor or pharmacist for advice before taking **Idagor.**

Breastfeeding

You should not breastfeed your baby if you are on treatment with **Idagor** as harm to your baby cannot be excluded, and **Idagor** may suppress or decrease the volume of breastmilk secreted.

Driving and using machinery

Idagor may affect your ability to drive or use machines. You should not drive and use machines until you know how treatment with **Idagor** is affecting you. **Idagor** may cause a low blood pressure, dizziness, nausea, vision disturbances, fatigue, tiredness and headache.

Idagor contains sodium

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

3. How to take Idagor

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

Always take **Idagor** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

Swallow the tablet with a glass of water preferably in the morning and before a meal. Your doctor will decide on the correct dose for you. This will be one tablet once a day.

If you take more Idagor than you should

Taking too many tablets may cause you blood pressure to become low or even dangerously low sometimes associated with nausea, vomiting, cramps, dizziness, sleepiness, mental confusion, oliguria (passing less urine than is normal), anuria (no production or passing of urine). You may feel lightheaded, faint, or weak. If blood pressure drop is severe enough shock can occur. Your skin could feel cool and clammy and you could lose consciousness. Seek immediate medical care if you take too many **Idagor** tablets.

In the event of an overdosage, consult your doctor or pharmacist. If neither is available contact the nearest hospital or poison centre.

If you forget to take Idagor

It is important to take your medicine every day as regular treatment is more effective. However, If you forget to take a dose of **Idagor**, take the next dose at the usual time.

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

If you stop taking Idagor

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

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Idagor can have side effects.

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

Stop taking Idagor and see a doctor immediately, if you experience any of the following side effects:

- sudden wheeziness, chest pain, shortness of breath, or difficulty in breathing (bronchospasm)
- swelling of eyelids, face or lips,
- swelling of the mouth, tongue and throat, which causes great difficulty breathing,
- severe skin reactions including 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, toxic epidermal necrolysis) or other allergic reactions,
- severe dizziness or fainting,
- heart attack, unusual fast or abnormal heart beat, or life-threatening irregular beat.
- inflamed pancreas which may cause severe abdominal and back pain accompanied with feeling very unwell.

These are serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

***Frequent* side effects:**

Headache, dizziness, palpitations (awareness of your heartbeat), flushing, vertigo, pins and needles, vision disturbances (including double vision), tinnitus (sensation of noises in the ears), light-headedness due to low blood pressure, cough, shortness of breath, gastro-intestinal disorders (nausea, vomiting, abdominal pain, taste disturbances, dyspepsia or difficulty of digestion, diarrhoea, constipation), allergic reactions (such as skin rashes, itching), cramps, feeling of tiredness, somnolence, ankle swelling (oedema).

***Less frequent* side effects:**

Mood swings, anxiety, depression, sleep disturbances, trembling, hives, fainting, loss of pain sensation, rhinitis (blocked up or runny nose), altered bowel habits, hair loss, purpura (red pinpoints on skin), skin discoloration, itchy skin, sweating, chest pain, joint or muscle pain, back pain, pain, feeling unwell (malaise), kidney problems, disorder in passing urine, increased need to urinate at night, increased number of times of passing urine, inability to obtain an erection, fever or high temperature, discomfort or enlargement of the breasts in men, weight increase or decrease, increase in some white blood cells, high potassium levels in the blood, hypoglycaemia (very low blood sugar level), low sodium levels in the blood, rapid heartbeat, vasculitis (inflammation of blood vessels), photosensitivity reactions (change in skin appearance) after exposure to the sun or artificial UVA, blister clusters over the skin, swelling of hands, ankles or feet, blood creatinine increased and blood urea increase, fall, dry mouth.

Confusion, changes in laboratory parameters: Increased level of liver enzymes, high level of serum bilirubin.

Decreased numbers of white blood cells, decrease in the number of platelets (which causes easy bruising and nasal bleeding), anaemia (decrease in red blood cells), cardiovascular disorders (irregular heartbeat, angina pectoris (pains to the chest, jaw and back , brought on by physical effort, and due to problems with the blood flow to the heart), stroke), eosinophilic pneumonia (a rare type of pneumonia), swelling of the gums, severe skin reactions including intense skin rash,

reddening of the skin over your whole body, severe itching, blistering, peeling and swelling of the skin, erythema multiforme (a skin rash which often starts with red itchy patches on your face, arms or legs), bleeding, tender or enlarged gums, abnormal liver function, inflammation of the liver (hepatitis), severe kidney problems, yellowing of the skin (jaundice), abdominal bloating (gastritis), disorder of the nerves which can cause weakness, tingling or numbness, increased muscle tension, hyperglycaemia, high level of calcium in the blood, cerebrovascular accident possibly secondary to excessive low blood pressure.

Hepatic encephalopathy (disease of the brain caused by liver illness), abnormal ECG heart tracing, low potassium levels in the blood, if you suffer from systemic lupus erythematous (a type of collagen disease), this might get worse.

Short sightedness (myopia), vision blurred,

Trembling, rigid posture, mask like face, slow movements and a shuffling, unbalanced walk.

Discoloration, numbness and pain in fingers or toes (Raynaud's phenomenon).

Changes in laboratory parameters (blood tests) can occur. Your doctor may request blood tests to monitor your condition.

Concentrated urine (dark in colour), feel or are sick, have muscle cramps, confusion and fits which may be due to inappropriate ADH (anti-diuretic hormone) secretion which can occur with ACE-inhibitors. If you have these symptoms contact your doctor as soon as possible.

If you notice any side effects not mentioned in this leaflet, please inform 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 **Idagor**.

5. How to store Idagor

Store at or below 30 °C.

Store all medicine out of reach of children.

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).

Idagor does not require any special storage conditions.

6. Content of the pack and other information

What Idagor contains

- The active substances are perindopril arginine, indapamide and amlodipine.

  One film-coated tablet of:

  - **Idagor 5/1,25/5 mg** contains 3,395 mg perindopril equivalent to 5mg perindopril arginine, 1,25 mg indapamide and 6,935mg amlodipine besilate equivalent to 5 mg of amlodipine,
  - **Idagor 5/1,25/10 mg** contains 3,395 mg perindopril equivalent to 5mg perindopril arginine, 1,25 mg indapamide and 13,870mg amlodipine besilate equivalent to 10 mg of amlodipine,
  - **Idagor 10/2,5/5 mg** contains 6,790 mg perindopril equivalent to 10 mg perindopril arginine, 2,5 mg indapamide and 6,935mg amlodipine besilate equivalent to 5 mg of amlodipine,
  - **Idagor 10/2,5/10 mg** contains 6,790 mg perindopril equivalent to 10 mg perindopril arginine, 2,5 mg indapamide and 13,870 mg amlodipine besilate equivalent to 10 mg of amlodipine.

- The other ingredients are:

- Tablet core: Calcium carbonate starch compound: Calcium carbonate 90 %, Pregelatinised maize starch 10 %, cellulose microcrystalline (E460), croscarmellose sodium (E468), magnesium stearate (E572), colloidal anhydrous silica, pregelatinised starch.
- Tablet film-coating: Glycerol(E422), hypromellose 6mPa.s (E464), macrogol 6 000, magnesium stearate (E572), titanium dioxide (E171).

What Idagor looks like and contents of the pack

Idagor 5/1,25/5 mg are white, oblong, film-coated tablet, 9,75 mm long and 5,16 mm wide, engraved with on one face and  on the other face.

Idagor 5/1,25/10 mg are white, oblong, film-coated tablet, 10,7 mm Long and 5,66 mm wide, engraved with  on one face and  on the other face.

Idagor 10/2,5/5 mg are white, oblong, film-coated tablet, 11,5 mm long and 6,09 mm wide, engraved with on one face and on the other face.

Idagor 10/2,5/10 mg are white, oblong, film-coated tablet, 12,2 mm long and 6,46 mm, engraved with on one face and on the other face.

Tablet container of 30 film-coated tablets white polypropylene tablet container and a white opaque stopper containing a desiccant gel placed into a carton.

Holder of Certificate of Registration

Servier Laboratories South Africa (Pty) Ltd

Building Number 4

Country Club Estate

21 Woodlands Drive

Woodmead

2191

This leaflet was last revised in

24 November 2020

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