Front Side

435 mm

370 mm

SCHEDULING STATUS : S3

1. NAME OF THE MEDICINE

TROBET 75, 150 and 300 film-coated tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TROBET 75: Each film coated tablet contains 75 mg irbesartan.
TROBET 150: Each film coated tablet contains 150 mg irbesartan.
TROBET 300: Each film coated tablet contains 300 mg irbesartan.
Excipients with known effect:
Contains sugar: lactose monohydrate
TROBET 75 contains sugar (0,75 mg lactose monohydrate)
TROBET 150 contains sugar (1,5 mg lactose monohydrate)
TROBET 300 contains sugar (3 mg lactose monohydrate)

3. PHARMACEUTICAL FORM

Film-coated tablet.
TROBET 75
White to off-white, oval shaped, film coated tablets debossed with "ML 94" on one side and plain on other side.
TROBET 150
White to off-white, oval shaped, film coated tablets debossed with "ML 95" on one side and plain on other side.
TROBET 300
White to off-white, oval shaped, film coated tablets debossed with "ML 96" on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
TROBET is indicated for the treatment of essential hypertension. It may be used either alone or in combination with other antihypertensive medicines.
TROBET is indicated for the treatment of diabetic nephropathy with an elevated serum creatinine and proteinuria (> 300 mg/day) in patients with type 2 diabetes and hypertension.

4.2 Posology and method of administration
Posology
The usual recommended initial and maintenance dose is 150 mg once daily, with or without food.
In patients insufficiently controlled with 150 mg once daily, the dose of **TROBET** may be increased to 300 mg, or other antihypertensive medicines may be added.
In patients with hypertension and type 2 diabetic renal disease, 300 mg of **TROBET** once daily is the preferred maintenance dose.

Special populations
Elderly patients and patients with Renal or Hepatic impairment
No dosage reduction is generally necessary in the elderly or in patients with impaired renal function or impaired hepatic function (mild to moderate degree).
Patients with intravascular volume Depletion
See section 4.4: 'Intravascular volume depletion'.
Paediatric population
Safety and efficacy in paediatric patients have not been established.

Method of administration
For oral use

4.3 Contraindications
TROBET is contraindicated in patients who have the following:

- Hypersensitivity to irbesartan or to any of the ingredients of **TROBET**.
- A history of angioedema related to previous therapy with angiotensin receptor blockers (ARBs) or angiotensin converting enzyme inhibitors (ACEIs): these patients must never again be given these medicines.
- Hereditary or idiopathic angioedema.
- Hypertrophic obstructive cardiomyopathy (HOCM).
- Severe renal function impairment (creatinine clearance less than 30 mL/min).
- Moderate to severe renal impairment, and concomitantly using fluoroquinolones.
- Bilateral renal artery stenosis.
- Renal artery stenosis in patients with single kidney, or a transplanted kidney.
- Aortic stenosis.
- Concomitant therapy with potassium-sparing diuretics, such as spironolactone, triamterene, amiloride.
- Porphyria.
- Lithium therapy: concomitant administration with **TROBET** may lead to toxic blood concentrations of lithium (see sections 4.4 and 4.5).
- Pregnancy and lactation (see sections 4.4 and 4.5).
- The concomitant use of **TROBET** with aliskiren-containing products (see sections 4.4 and 4.5).

4.4 Special warnings and precautions for use

Should a woman pregnant while receiving **TROBET**, the treatment should be stopped promptly and switched to different class of antihypertensive medicine (see sections 4.3 and 4.6).

Intravascular volume depletion
TROBET has been associated with hypotension in hypertensive patients without other co-morbid conditions. Symptomatic hypotension, especially after the first dose, may occur in patients who are volume and/or sodium depleted by vigorous diuretic therapy, dietary salt restriction, diarrhoea, or vomiting. Such conditions should be corrected before the administration of **TROBET** or a lower starting dose (**TROBET 75**) should be considered (see section 4.2).

Renal impairment and kidney transplantation
When **TROBET** is used in patients with impaired renal function, a periodic monitoring of potassium and creatinine serum levels is recommended (see section 4.5). As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. There is no experience regarding the administration of **TROBET** in patients with a recent kidney transplantation.

Renovascular hypertension
There is an increased risk of severe hypotension and renal insufficiency when patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney are treated with medicines that affect the renin-angiotensin-aldosterone system. While this is not documented with **TROBET**, a similar effect should be anticipated with angiotensin-II receptor antagonists. The use of **TROBET** in patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney is contraindicated (see section 4.3).

Fluoroquinolones and ARBs
Concomitant use of fluoroquinolones and ARBs such as **TROBET** may precipitate acute kidney injury in patients, especially those with moderate to severe renal impairment and elderly patients (see section 4.3). Renal function should be assessed before initiating treatment and monitored during treatment with fluoroquinolones or ARBs such as **TROBET** whether used separately and/or concomitantly.

Lithium
The combination of lithium and **TROBET** is contraindicated (see sections 4.3 and 4.5).

Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy
Special caution is indicated in patients suffering from aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy (see section 4.3).

Dual blockade of the renin-angiotensin-aldosterone system (RAAS)
There is evidence that the concomitant use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren increases the risk of hypotension, hyperkalaemia and decreased renal function (including acute renal failure). Dual blockade of RAAS through the combined use of ACE-inhibitors or angiotensin II receptor blockers such as **TROBET** is therefore not recommended (see section 4.5). ACE-inhibitors and angiotensin II receptor blockers should not be used concomitantly in patients with diabetic nephropathy.
TROBET should not be used concomitantly with aliskiren (see section 4.3).

Hyperkalaemia
Hyperkalaemia may occur during the treatment with **TROBET**, especially in the presence of renal impairment, overt proteinuria due to diabetic renal disease, and/or heart failure. Close monitoring of serum potassium in patients at risk is recommended (see section 4.5).

Primary aldosteronism
Patients with primary aldosteronism generally will not respond to antihypertensive medicines acting through inhibition of the renin-angiotensin system. Therefore, the use of **TROBET** is not recommended.

General
In patients whose vascular tone and renal function depend predominantly on the activity of the renin-angiotensin-aldosterone system (e.g. patients with severe congestive heart failure or underlying renal disease, including renal artery stenosis), treatment with angiotensin converting enzyme inhibitors or angiotensin-II receptor antagonists that affect this system has been associated with acute hypotension, uraemia, oliguria, or acute renal failure (see section 4.5). Excessive blood pressure decreases in patients with ischaemic cardiopathy or ischaemic cardiovascular disease could result in a myocardial infarction or stroke.

Lactose
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction
Fluoroquinolones
Concomitant use of ARBs as in **TROBET** and fluoroquinolones may precipitate acute kidney injury. The mechanism of the possible interaction between the different classes of medicines, over and above different mechanisms of kidney damage, is unknown (see section 4.3).

Potassium supplements and potassium-sparing diuretics
Based on experience with the use of other medicines that affect the renin-angiotensin system, concomitant use of potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium or other medicines that may increase serum potassium levels (e.g. heparin) may lead to increases in serum potassium and is, therefore, not recommended (see section 4.4). The use of potassium-sparing diuretics with **TROBET** is contraindicated (see section 4.3).

Lithium
Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors. Similar effects have been very reported with **TROBET** so far. Therefore, this combination is contraindicated (see section 4.3).

Non-steroidal anti-inflammatory drugs
When angiotensin II antagonists are administered simultaneously with nonsteroidal anti-inflammatory drugs (NSAIDs) (i.e. selective COX-2 inhibitors, acetylsalicylic acid (> 3 g/day) and non-selective NSAIDs), attenuation of the antihypertensive effect may occur.
Concomitant use of angiotensin II antagonists and NSAIDs may lead to an increased risk of worsening of renal function, including possible acute renal failure, and an increase in serum potassium, especially in patients with poor pre-existing renal function. These effects may be reversible. The combination should be administered with caution, especially in the elderly, volume-depleted (including those on diuretic therapy) or with compromised renal function. Patients should be adequately hydrated and consideration should be given to monitoring renal function after initiation of concomitant therapy, and periodically thereafter.

Diuretics and other antihypertensive medicines
Other antihypertensive medicines may increase the hypotensive effects of irbesartan; however **TROBET** has been safely administered with other antihypertensive medicines, such as beta-blockers, long-acting calcium channel blockers, and thiazide diuretics. Prior treatment with high dose diuretics may result in volume depletion and a risk of hypotension when initiating therapy with **TROBET** (see section 4.4).

Dual blockade of the RAAS with ARBs and ACE-inhibitors
Clinical trial data has shown that dual blockade of the renin-angiotensin-aldosterone system through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is associated with a higher frequency of adverse events, such as hypotension, hyperkalaemia and decreased renal function (including acute renal failure) compared to the use of a single RAAS-acting medicine (see section 4.4).

Additional information on TROBET interactions
The pharmacokinetics of **TROBET** is not affected by hydrochlorothiazide or nifedipine. **TROBET** is mainly metabolised by CYP2C9 and to a lesser extent by glucuronidation. No significant pharmacokinetic or pharmacodynamic interactions are observed when **TROBET** is coadministered with warfarin, a medicine metabolised by CYP2C9.
The effects of CYP2C9 inducers such as rifampicin on the pharmacokinetics of **TROBET** have not been evaluated. The pharmacokinetics of digoxin and simvastatin are not altered by coadministration of **TROBET**.

4.6 Fertility, pregnancy and lactation
Women of childbearing potential
Women of childbearing age should ensure effective contraception.

Pregnancy
Safety in pregnancy has not been established (see sections 4.3 and 4.4). When pregnancy is planned or confirmed, **TROBET** should be discontinued.
Medicines affecting the renin-angiotensin system, such as **TROBET**, can cause embryonal toxicity, foetal and neonatal morbidity and mortality when administered in pregnant women.
Patients planning pregnancy should be changed to alternative antihypertensive treatments, which have an established safety profile for use in pregnancy.
Breastfeeding
Safety in lactation has not been established. It is unknown whether irbesartan or its metabolites are excreted in human milk.
Available pharmacodynamics/toxicological data in rats have shown excretion of irbesartan or its metabolites in milk.

Fertility
TROBET had no effect upon fertility of treated rats and their offspring up to the dose levels inducing the first signs of parental toxicity.

4.7 Effects on ability to drive and use machines
TROBET may cause dizziness and fatigue which may affect the ability to drive and use machines. Caution is advised before driving or operating machinery until the effects of **TROBET** are known.
4.8 Undesirable effects
The following adverse reactions have been reported during clinical trials in patients with hypertension.

Nervous system disorders
Frequent: dizziness, headache
Cardiac disorders
Less frequent: tachycardia
Vascular disorders
Less frequent: flushing
Respiratory, thoracic and mediastinal disorders
Less frequent: cough
Gastrointestinal disorders
Frequent: nausea, vomiting
Less frequent: diarrhoea, dyspepsia/heartburn
Hepatobiliary disorders
Less frequent: jaundice
Reproductive system and breast disorders
Less frequent: sexual dysfunction
General disorders and administration site conditions
Frequent: fatigue
Less frequent: chest pain
Investigations
No clinically significant changes in laboratory test parameters occurred in controlled clinical studies of hypertension.
No special monitoring of laboratory parameters is necessary for patients with essential hypertension receiving therapy with **TROBET**.
Frequency unknown: oedema.
The following adverse reactions have been reported during clinical trials in patients with hypertension and type 2 diabetic renal disease.
Nervous system disorders
Frequent: dizziness, orthostatic dizziness
Vascular disorders
Frequent: orthostatic hypotension
Musculoskeletal and connective tissue disorders
Frequent: musculoskeletal pain
Investigations
Frequent: hyperkalaemia, increased plasma creatine kinase[1], decrease in haemoglobin[2]
[1] None of these increases were associated with identifiable clinical musculoskeletal events.
[2] In hypertensive patients with advanced diabetic renal disease treated with irbesartan. The decrease in haemoglobin was not clinically significant.
The following adverse reactions have been reported during post-marketing experience.
Blood and lymphatic system disorders
Frequency unknown: thrombocytopenia
Immune system disorders
Frequency unknown: hypersensitivity reactions (such as angioedema, rash, urticaria, anaphylactic reaction, anaphylactic shock)
Metabolism and nutrition disorders
Frequency unknown: hyperkalaemia
Nervous system disorders
Frequency unknown: vertigo, headache
Ear and labyrith disorders
Frequency unknown: tinnitus
Gastrointestinal disorders
Frequency unknown: dysgusesia
Hepatobiliary disorders
Frequency unknown: abnormal liver function, jaundice, hepatitis
Skin and subcutaneous tissue disorders
Frequency unknown: leukocytoclastic vasculitis
Musculoskeletal and connective tissue disorders
Frequency unknown: arthralgia, myalgia (in some cases associated with increased plasma creatine kinase levels), muscle cramps
Renal and urinary disorders
Frequency unknown: impaired renal function including cases of renal failure of patients at risk (see section 4.4)
General disorders and administration site conditions
Frequency unknown: asthenia.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of **TROBET** is important. It allows continued monitoring of the benefit/risk balance of **TROBET**. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the **"6.04 Adverse Drug Reactions Reporting Form"**, found online under SAHPRA's publications:https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose
Experience in adults exposed to doses of up to 900 mg/day for 8 weeks revealed no toxicity. The most likely manifestations of overdose are expected to be hypotension and tachycardia; bradycardia might also occur from overdose.
No specific information is available on the treatment of overdose with **TROBET**. The patient should be closely monitored, and the treatment should be symptomatic and supportive. Suggested measures include induction of emesis. Activated charcoal may be useful in the treatment of overdose. **TROBET** is not removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Category and class: A7.1.3 Other hypotensives
Pharmacotherapeutic group: Angiotensin-II antagonists , plain.
ATC code: C09CA04
Mechanism of action
Irbesartan is a specific antagonist of angiotensin-II receptors (AT, subtype), known as an angiotensin receptor blocker (ARB). Angiotensin-II is an important component of the renin-angiotensin system (RAS) and is involved in the pathophysiology of hypertension and in sodium homeostasis.
Irbesartan blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin-II by selective antagonism of the angiotensin-II (AT, subtype) receptors localised on vascular smooth muscle cells and in the adrenal cortex. It has no agonist activity at the AT, receptor and much greater affinity (more than 8500-fold) for the AT, receptor than for the AT_2 receptor (a receptor that has not been shown to be associated with cardiovascular homeostasis).
Irbesartan does not inhibit enzymes involved in the renin-angiotensin system (i.e. renin, angiotensin converting enzyme (ACE)), or affect other hormone receptors or ion channels involved in the cardiovascular regulation of blood pressure and sodium homeostasis.
Irbesartan blockade of AT, receptors interrupts the feedback loop within the renin-angiotensin system, resulting in increases in plasma renin levels and angiotensin-II levels. Aldosterone plasma concentrations decline following irbesartan administration. However, serum potassium levels are not significantly affected (mean increase of < 0,1 mmol/L) at the recommended doses. Irbesartan has no notable effects on serum triglycerides, cholesterol, or glucose concentrations. There is no effect on serum uric acid or urinary uric acid excretion.

5.2 Pharmacokinetic properties
Absorption
Irbesartan is orally active and does not require biotransformation for its activity. After oral administration, irbesartan is well absorbed: studies of absolute bioavailability gave values of approximately 60 – 80 %. Concomitant food intake does not significantly influence the bioavailability of irbesartan. Peak plasma concentration occurs at 1,5 – 2 hours after oral administration.
Distribution
Plasma protein binding is approximately 96 %, with negligible binding to cellular blood components. The volume of distribution is 53 – 93 litres.
Biotransformation
Following oral or intravenous administration of ^{14}C irbesartan, 80 – 85 % of the circulating plasma radioactivity is attributable to unchanged irbesartan. Irbesartan is metabolised by the liver via glucuronide conjugation and oxidation. The major circulating metabolite is irbesartan glucuronide (approximately 6 %). Irbesartan undergoes oxidation primarily by the cytochrome P450 enzyme CYP2C9; isoenzyme CYP3A4 has negligible effect. It is not metabolised by, nor does it substantially induce or inhibit most isoenzymes commonly associated with metabolism of medicines (i.e. 1A1, 1A2, 2A6, 2B6, 2D6 or 2E1). Irbesartan does not induce or inhibit isoenzyme 3A4.
Elimination
Irbesartan and its metabolites are eliminated by both biliary and renal pathways. After either oral or IV administration of ^{14}C irbesartan, about 20 % of the radioactivity is recovered in the urine, and the remainder in the faeces. Less than 2 % of the dose is excreted in the urine as unchanged irbesartan.
Linearity/non-linearity
Irbesartan exhibits linear and dose proportional pharmacokinetics over the therapeutic dose range. Peak plasma concentrations are attained at 1,5 – 2 hours after oral administration. The total body and renal clearance are 157 –176 and 3 – 3,5 mL/min, respectively. The terminal elimination half-life of irbesartan is 11 – 15 hours.
Steady-state plasma concentrations are attained within 3 days after initiation of a once-daily dosing regimen. Limited accumulation of irbesartan (< 20 %) is observed in plasma upon repeated once-daily dosing.
Special populations
Race
In black and white normotensive patients, the plasma AUC and $t_{1/2}$ of irbesartan are approximately 20 – 25 % greater in blacks than in whites; the peak plasma concentrations (C_{max}) of irbesartan are essentially equivalent.
Gender
In male and female hypertensive subjects, higher (11 – 44 %) plasma concentrations of irbesartan were observed in females than in males, although, following multiple dosing, males and females did not show differences in either accumulation or elimination half-life. No gender-specific differences in clinical effect have been observed
Elderly patients
In elderly (male and female) normotensive subjects (65 – 80 years) with clinically normal renal and hepatic function, the plasma AUC and peak plasma concentrations (C_{max}) of irbesartan are approximately 20 – 50 % greater than those observed in younger subjects (18 – 40 years).
Regardless of age, the elimination half-life is comparable. No significant age-related differences in clinical effect have been observed.
Renal impairment
In patients with renal impairment (regardless of degree) or those undergoing haemodialysis, the pharmacokinetic parameters of irbesartan are not significantly altered. Irbesartan is not removed by haemodialysis.
Hepatic impairment
In patients with hepatic insufficiency due to mild or moderate cirrhosis, the pharmacokinetic parameters of irbesartan are not significantly altered.

5.3. Preclinical safety data
No further information of relevance available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Carboxy methylcellulose calcium, colloidal silicon dioxide, povidone, sodium starch glycolate (Type A), purified talc, magnesium stearate and film-coating containing: hypromellose, lactose monohydrate, titanium dioxide (Color Index No. 77891) and polyethylene glycol 3000.

6.2 Incompatibilities
Not applicable

6.3 Shelf life
60 months from the manufacturing date for container pack.
36 months from the manufacturing date for blister pack.

6.4 Special precautions for storage
Store at or below 25 °C. Protect from light.
Keep the blisters in the carton until required for use.
Keep the HDPE container tightly closed.
Store in the original package in order to protect from light and moisture.
KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container
1) Blister Pack:
Tablets are packed in Clear film 300 µ PVC/25 µ PE/90 µ PVdC as the forming material and 25 µ Aluminium preprinted foil/ 6-8 gsm heat seal lacquered as the lidding material, packed in a pre-printed carton.
Pack size include 10, 28 or 30 tablets.

2) HDPE Container Pack:
Tablets are packed in 60 ml white round HDPE container with 33-400 mm neck finish which are closed with 33 mm child resistant closure with pulp and heat seal liner and packed in outer carton.
Pack size include 28 or 30 tablets
Not all packs and pack sizes are necessarily marketed.

6.6 Special precautions for disposal and other handling
No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Macleods Pharmaceuticals SA (Pty) Ltd
Office block 1, Bassonia Estate Office Park (East),
1 Cussonia Drive, Bassonia Rock, Ext. 12,
Alberton, South Africa.

8. REGISTRATION NUMBERS

TROBET 75: 46/7.1.3/0251
TROBET 150: 46/7.1.3/0252
TROBET 300: 46/7.1.3/0253

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30 November 2021

10. DATE OF REVISION OF THE TEXT

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PATIENT INFORMATION LEAFLET

SCHEDULING STATUS S3

TROBET 75, 150 and 300 film-coated tablets
Irbesartan
Excipients with known effect
Contains Sugar *(Lactose monohydrate)*
TROBET 75 contains sugar *(0,75 mg lactose monohydrate)*
TROBET 150 contains sugar *(1,5 mg lactose monohydrate)*
TROBET 300 contains sugar *(3 mg lactose monohydrate)*

Read all of this leaflet carefully before you start taking TROBET

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

TROBET
75/150/300
film-coated tablets
PM03937101

Front Side

435 mm

370 mm

1. What TROBET is and what it is used for

TROBET contains the active ingredient irbesartan, which belongs to a group of medicines called angiotensin-II receptor blockers (ARBs). It is used to treat high blood pressure (essential hypertension) and for the protection of the kidney in patients with high blood pressure, type 2 diabetes and laboratory evidence of impaired kidney function.
Your doctor may prescribe you **TROBET** either alone or in combination of other medicines.

2. What you need to know before you take TROBET

Do not take TROBET

- If you are hypersensitive (allergic) to irbesartan, or any of the other ingredients of **TROBET** listed in section 6 of this leaflet.
- If you have a history of angioedema (swelling around your face, throat or tongue) related to previous therapy with ARBs or angiotensin converting enzyme inhibitors (ACEIs) (used to treat high blood pressure).
- If you have hereditary angioedema (swelling around your face, throat or tongue).
- If you have hypertrophic obstructive cardiomyopathy (HOCM) (a heart disease characterised by the obstruction of blood flow and thickening of heart tissue).
- If you have severe kidney impairment.
- If you have kidney impairment and are using fluoroquinolones (used to treat bacterial infections).
- If you have renal artery stenosis (kidney problems with reduced blood supply to your kidney) or a transplanted kidney.
- If you have aortic stenosis (a decrease in blood supply flow through the aortic artery).
- If you are taking potassium-sparing diuretics (such as spironolactone, triamterene or amiloride).
- If you have porphyria.
- If you are taking lithium.
- If you are pregnant or breastfeeding.
- If you are taking medicines containing aliskiren (used to treat high blood pressure).

Warnings and precautions
Tell your doctor or health care provider before taking **TROBET**:

- If you get excessive vomiting or diarrhoea (leading to salt/volume depletion).
- If you suffer from kidney problems.
- If you are 65 years or older.
- If you suffer from heart problems.
- If you are taking medicines to lower blood pressure (such as an ACE inhibitor).
- If you have diabetic kidney disease. Your doctor may perform regular blood tests, especially to measure the levels of potassium in your blood in the event of poor kidney function.

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

Children and adolescents
TROBET should not be used in children and adolescents as the safety and efficacy have not been established.

Other medicines and TROBET
Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)
Tell your doctor if you are using other medicines to reduce your blood pressure. Your doctor may adjust your dose or take other precautions.
Do not take **TROBET** with fluoroquinolones (used to treat bacterial infections), such as levofloxacin, ciprofloxacin or moxifloxacin.
You may need to have your blood checked regularly if you take:

- Potassium supplements or medicines that may increase potassium levels in the blood (such as heparin),
- Medicines containing lithium.
- Non-steroidal anti-inflammatory drugs (NSAIDs) (used to treat pain, fever and inflammation).
- Diuretic medicines ('water pills' used to get rid of excess water).

TROBET with food, drink and alcohol
No information of relevance available.

Pregnancy and breastfeeding
If you are taking **TROBET**, you should use effective contraception.
If you are pregnant or breastfeeding, think you might be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before taking **TROBET**.
Your doctor will change your treatment with **TROBET** to an alternative therapy which is safe to use during pregnancy and breastfeeding.
You should not use TROBET if you are pregnant or breast-feeding (see Do not take TROBET).

Driving and using machines
Your ability to drive and use machines may be affected by side effects, such as dizziness and tiredness. Do not drive a vehicle or operate machinery until you know how **TROBET** affects you.
TROBET contains sugar (lactose monohydrate)
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take TROBET

Do not share medicines prescribed for you with any other person.
Always take **TROBET** exactly as your doctor or pharmacist has told you. You should check with your doctor or pharmacist if you are not sure.
The usual dose is 150 mg once a day.
Your doctor may decide to increase your daily dose to 300 mg depending on your blood pressure.
Your doctor will tell you how long your treatment with **TROBET** will last. Do not stop treatment early because your blood pressure may increase again.
If you have the impression that the effect of **TROBET** is too strong or too weak, tell your doctor or pharmacist.

If you take more TROBET than you should
In the event of overdosage, consult your doctor or pharmacist without delay. If neither is available, contact the nearest hospital or poison centre.
If you forget to take TROBET
If you forget to take a dose, take it as soon as you remember unless it is nearly time to take your next dose. Do not take a double dose to make up for a forgotten dose.

4. Possible side effects

TROBET can have side effects.
Not all side effects reported for **TROBET** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking **TROBET**, please consult your health care provider for advice.
If any of the following happens, stop taking **TROBET** and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of your hands, feet, ankles, face, lips and 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 **TROBET**. 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:

- yellowing of the eyes or skin, also called jaundice or hepatitis,
- decreased kidney function or kidney failure (causing drowsiness, shortness of breath, fatigue, confusion, nausea, fits, passing less urine than is normal for you),
- too high levels of potassium in your blood (causing abnormal or slow heart rate, low blood pressure, cramps, weakness),
- bleeding or bruising more easily than normal,
- changes in the way your heart beats,
- leukocytoclastic vasculitis (causing rash, joint pains and increasing size of lymph nodes).

These are all serious side effects. You may need urgent medical attention.
Tell your doctor if you notice any of the following:
Frequent side effects:

- headache or dizziness,
- nausea (feeling sick) or vomiting (being sick),
- feeling tired,
- dizziness or light-headedness when getting up from a lying or sitting position,
- muscle pain,
- increases in blood levels of creatine kinase (enzyme that measures the muscle and heart function),
- decrease in level of haemoglobin (protein in red blood cells).

Less frequent side effects:

- changes in liver function,
- changes in sexual function,
- flushing,
- cough,
- diarrhoea,
- indigestion or heartburn,
- chest pain.

The following side-effects have been reported with unknown frequency:

- vertigo (sensation of spinning or swaying) or tinnitus (ringing in the ears),
- pain in a joint,
- pain in a muscle or group of muscles or muscle cramps,
- distortion of the sense of taste,
- abnormal physical weakness or lack of energy.

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 or pharmacist. 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 **TROBET**.

5. How to store TROBET

- Store at or below 25 °C.
- Keep the blister strip(s) in the outer carton until required for use.
- STORE ALL MEDICINES OUT OF REACH OF CHILDREN.
- Do not use after the expiry date printed on the carton.
- 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 TROBET contains
The active substance in **TROBET** is irbesartan.
TROBET 75: Each film-coated tablet contains 75 mg of irbesartan.
TROBET 150: Each film-coated tablet contains 150 mg of irbesartan.
TROBET 300: Each film-coated tablet contains 300 mg of irbesartan.
The other ingredients in **TROBET** are:
Carboxy methylcellulose calcium, colloidal silicon dioxide, povidone, sodium starch glycolate (Type A), purified talc, magnesium stearate and film-coating containing hypromellose, lactose monohydrate, titanium dioxide (Color Index No. 77891) and polyethylene glycol 3000.

What TROBET looks like and contents of the pack
TROBET 75:
White to off-white, oval shaped, film coated tablets debossed with "ML 94" on one side and plain on other side.
TROBET 150:
White to off-white, oval shaped, film coated tablets debossed with "ML 95" on one side and plain on other side.
TROBET 300:
White to off-white, oval shaped, film coated tablets debossed with "ML 96" on one side and plain on other side.
1) Blister Pack:
Tablets are packed in Clear film 300 µ PVC/25 µ PE/90 µ PVdC as the forming material and 25 µ Aluminium preprinted foil/ 6-8 gsm heat seal lacquered as the lidding material, packed in a pre-printed carton.
Pack size include 10, 28 or 30 tablets.

2) HDPE Container Pack:
Tablets are packed in 60 ml white round HDPE container with 33-400 mm neck finish which are closed with 33 mm child resistant closure with pulp and heat seal liner and packed in outer carton.
Pack size include 28 or 30 tablets
Not all packs and pack sizes are necessarily marketed.

Holder of certificate of registration
MACLEODS PHARMACEUTICALS SA (PTY) LTD
Office block 1, Bassonia Estate Office Park (East),
1 Cussonia Drive, Bassonia Rock, Ext. 12,
Alberton, South Africa.

This leaflet was last revised in
Date of first authorisation: 30 November 2021
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Registration numbers
TROBET 75: 46/7.1.3/0251
TROBET 150: 46/7.1.3/0252
TROBET 300: 46/7.1.3/0253

PASIËNTINLIGTINGSTUK

SKEDULERINGSTATUS: S3

TROBET 75, 150 en 300 filmbedekte tablette
Irbesartan
Bestanddele met 'n bekende effek
Bevat suiker (*Laktosemonohidraat*)
TROBET 75 bevat suiker (*0,75 mg laktosemonohidraat*)
TROBET 150 bevat suiker (*1,5 mg laktosemonohidraat*)
TROBET 300 bevat suiker (*3 mg laktosemonohidraat*)

Lees hierdie inligtingstuk sorgvuldig voordat jy TROBET begin neem

- Hou hierdie inligtingstuk. Dit mag nodig wees dat jy dit weer moet lees.
- Vra asseblief jou dokter, apteker, verpleegkundige of ander gesondheidsorgverskaffer indien jy verdere vrae het.
- **TROBET** is vir jou persoonlik voorgeskryf, en jy moet nie jou medisyne met ander persone deel nie. Dit mag skadelik vir hulle wees, selfs al is hul simptome dieselfde as joune.

Wat in hierdie inligtingstuk is

1. Wat **TROBET** is en waarvoor dit gebruik word
2. Wat jy behoort te weet voordat jy **TROBET** neem
3. Hoe om **TROBET** te neem
4. Moontlike newe-effekte
5. Hoe om **TROBET** te bewaar
6. Inhoud van die pak en ander inligting

1. Wat TROBET is en waarvoor dit gebruik word

TROBET bevat die aktiewe bestanddeel irbesartan, wat aan 'n groep medisyne behoort wat angiotensien II reseptor blokkeerders (ARB's) genoem word. Dit word gebruik om hoë bloeddruk (essensiële hipertensie) te behandel en vir die beskerming van die nier in pasiënte met hoë bloeddruk, tipe 2 diabetes en laboratorium bewyse van ingekorte nierfunksie.
Jou dokter kan **TROBET** aan jou voorskryf óf **alleen** óf in kombinasie met ander medisyne.

2. Wat jy behoort te weet voordat jy TROBET neem

Moet nie TROBET neem:

- indien jy hipersensitief (allergies) vir irbesartan, of enige van die ander bestanddele van **TROBET**, gelys in afdeling 6 van hierdie inligtingstuk, is nie.
- indien jy 'n geskiedenis van angioödeem het (swelling rondom jou gesig, keel of tong), want verband hou met vorige behandeling met ARB's of angiotensien omskakelings ensiem inhibeerders (ACEI's) (gebruik om hoë bloeddruk te behandel).
- as jy oorerflike angioödeem het (swelling rondom jou gesig, keel of tong).
- indien jy hipertrofiese obstruktiewe kardiomiopatie (HOKM) het ('n hartsiekte wat gekenmerk word deur die obstruksie van bloedvloei en verdikking van hartweefsel).
- as jy ernstige nierversaking het.
- indien jy nierinkorting het en fluorokinolone gebruik (wat gebruik word om bakteriële infeksies te behandel).
- as jy nier slagaarstenose het (nierprobleme met verminderde bloedtoevoer na jou nier) of 'n oorgeplante nier.
- indien jy aortastenose het ('n vermindering in bloedtoevoer vloei deur die aortaslagaar).
- as jy kaliumbesparende diuretika (soos spironolaktoon, triamtereen of amiloried) neem.
- indien jy porfirie het.
- indien jy litium neem.
- indien jy swanger is of borsvoed.
- indien jy medisyne gebruik wat aliskiren bevat (wat gebruik word om hoë bloeddruk te behandel).

Waarskuwings en voorsorgmaatreëls
Vertel jou dokter of gesondheidsorgverskaffer voordat jy **TROBET** neem:

- indien jy oormatige braking of diaree kry (wat tot sout-/volume uitputting).
- indien jy aan nierprobleme ly.
- as jy 65 jaar of ouer is.
- indien jy aan hartprobleme ly.
- as jy medisyne neem om bloeddruk te verlaag (soos ACE-inhibeerder).
- indien jy diabetiese niersiekte het. Jou dokter kan gereeld bloedtoetse uitvoer, veral om die vlakke van kalium in jou bloed te bepaal in die geval van swak nierfunksie.

Jou dokter kan jou nierfunksie, bloeddruk en die hoeveelheid elektroliete (soos kalium) in jou bloed met gereelde tussenposes nagaan.

Kinders en adolessente
TROBET moet nie in kinders en adolessente gebruik word nie, aangesien die veiligheid en doeltreffendheid nie vasgestel is nie.

Ander medisyne en TROBET
Vertel altyd vir jou gesondheidsorgverskaffer indien jy enige ander medisyne neem. (Dit sluit alle komplementêre of tradisionele medisyne in).
Vertel jou dokter as jy ander medisyne gebruik om jou bloeddruk te verlaag. Jou dokter kan jou dosering aanpas of ander voorsorgmaatreëls tref.
Moet nie **TROBET** saam met fluorokinolone (wat gebruik word om bakteriële infeksies te behandel), soos levofloksasien, siprofloksasien of moksifloksasien, neem nie.
Jy moet dalk jou bloed gereeld laat ondersoek indien jy die volgende neem:

- Kaliumaanvullings of medisyne wat kaliumvlakke in die bloed kan verhoog (soos heparien).
- Medisyne wat litium bevat.
- Nie-steroïdale anti-inflammatoriese medisyne (NSAIM's) (wat gebruik word om pyn, koors en inflammasie, te behandel).
- Diuretiese medisyne ('waterpille' wat gebruik word om van oortollige water ontslae te raak).

TROBET met voedsel, drank en alkohol
Geen relevante inligting beskikbaar nie.

Swangerskap en borsvoeding
Indien jy **TROBET** neem, moet jy effektiewe voorbehoedmiddel gebruik.
Indien jy swanger is of borsvoed, dink dat jy moontlik swanger kan wees of beplan om 'n baba te hê, raadpleeg asseblief jou dokter, apteker of ander gesondheidsorgverskaffer vir advies voordat jy **TROBET** neem.
Jou dokter sal jou behandeling met **TROBET** verander na 'n alternatiewe behandeling wat veilig is om te gebruik gedurende swangerskap en borsvoeding.
Jy moet nie TROBET gebruik indien jy swanger is of borsvoed nie (sien Moet nie TROBET neem).

Bestuur en gebruik van masjinerie
Jou vermoë om te bestuur en masjinerie te gebruik kan geaffekteer word deur newe-effekte, soos duiseligheid en moegheid. Moet nie 'n voertuig bestuur of masjinerie gebruik totdat jy weet hoe **TROBET** jou affekteer nie.
TROBET bevat suiker (laktosemonohidraat)
Indien jy deur jou dokter ingelig is dat jy 'n onverdraagsaamheid teenoor sommige suikers het, kontak jou dokter voordat jy hierdie medisyne gebruik.

3. Hoe om TROBET te neem

Moet nie medisyne wat vir jou voorgeskryf is met enige ander persoon deel nie
Neem altyd **TROBET** presies soos jou dokter of apteker vir jou gesê het. Vra jou dokter of apteker indien jy nie seker is nie.
Die aanbevole dosis is 150 mg een keer per dag.
Jou dokter kan besluit om jou daaglikse dosis te verhoog tot 300 mg, afhangende van jou bloeddruk.
Jou dokter sal jou vertel hoe lank jou behandeling met **TROBET** sal duur. Moet nie vroeër met die behandeling ophou nie, aangesien jou bloeddruk weer kan styg.
Indien jy onder die indruk is dat die effek van **TROBET** te sterk of te swak is, vertel jou dokter of apteker.

Indien jy meer TROBET geneem het as wat jy behoort te neem
In die geval van oordosering, raadpleeg jou dokter of apteker sonder versuim. Indien nie een beskikbaar is nie, kontak die naaste hospitaal of giftbeheersentrum.
Indien jy vergeet om TROBET te neem
Indien jy vergeet om 'n dosis te neem, neem dit so gou as wat jy onthou, tensy dit amper tyd is om jou volgende dosis te neem. Moet nie 'n dubbele dosis neem om vir 'n vergete individuele dosis op te maak nie.

4. Moontlike newe-effekte

TROBET kan newe-effekte hê.
Nie al die newe-effekte wat vir **TROBET** aangemeld is, is in hierdie inligtingstuk ingesluit nie. Sou jou algemene gesondheid verslegt of jy enige onaangename effekte ervaar terwyl jy **TROBET** neem, raadpleeg asseblief jou gesondheidsorgverskaffer vir advies.
Indien enige van die volgende gebeur, hou op om **TROBET** te gebruik en vertel jou dokter onmiddellik of gaan na die ongevalle afdeling van jou naaste hospitaal:

- swelling van jou hande, voete, enkels, gesig, lippe en mond of keel, wat dit moeilik kan maak om te sluk of asem te haal,
- uitslag of jeuk
- flou word.

Hierdie is alles baie ernstige newe-effekte. Indien jy dit het, het jy moontlik 'n ernstige reaksie op **TROBET** gehad. Jy mag dalk dringende mediese aandag of hospitalisasie benodig.
Vertel vir jou dokter onmiddellik of gaan na die ongevalle afdeling van jou naaste hospitaal indien jy enige van die volgende opmerk:

- geelwording van die oë of vel, ook genoem geelsug of hepatitis,
- verminderde nierfunksie of nierversaking (wat lomerigheid, kortasem, moegheid, verwarring, naarheid, aanvalle veroorsaak, minder urineer as wat jy normaalweg doen),
- te hoë kaliumvlakke in jou bloed (wat abnormale of stadige harttempo, lae bloeddruk, krampe, swakheid veroorsaak),
- bloeding of kneusing makliker as normaalweg,
- veranderinge in die manier waarin jou hart klop,
- leukositoklastiese vaskulitis (wat uitslag, gewrigspyne en toenemende grootte van limfkliere veroorsaak).

Hierdie is alles ernstige newe-effekte. Jy mag moontlik dringende mediese aandag nodig hê.
Vertel vir jou dokter indien jy enige van die volgende opmerk:
Gereelde newe-effekte:

- hoofpyn of duiseligheid,
- naarheid (siek voel) of braking (siek wees),
- voel moeg,
- duiseligheid of lighoofdigheid wanneer jy opstaan vanuit 'n lêende of sittende posisie,
- spierpyn,
- verhoging in bloedvlakke van kreatienkinase (ensieme wat die spier- en hartfunksie meet),
- afname in hemoglobienvlak (proteïen in rooibloedselle).

Minder gereelde newe-effekte:

- veranderinge in lewerfunksie,
- veranderinge in seksuele funksie,
- blosing,
- hoes,
- diaree,
- slegte spysvertering of sooibrand,
- borskaspyn.

Die volgende newe-effekte is met onbekende frekwensie aangemeld:

- vertigo (sensasie van spin of tol) of tinnitus (gesuis in die ore),
- pyn in 'n gewrig,
- pyn in 'n spier of groep van spiere of spierkrampe,
- vervorming van die smaaksin,
- abnormale fisiese swakheid of gebrek aan energie.

Stel asseblief jou dokter of apteker in kennis, indien jy enige newe-effekte opmerk wat nie in hierdie inligtingstuk genoem word nie.

Aanmelding van newe-effekte
Indien jy newe-effekte kry praat met jou dokter of apteker. Dit sluit enige moontlike newe-effekte in wat nie in hierdie inligtingsblad genoem is nie. Jy kan ook newe-effekte aan SAHPRA rapporteer via die **"6.04 Adverse Drug Reaction Reporting Form"**, wat aanlyn gevind kan word onder SAHPRA se publikasies:https://www.sahpra.org.za/Publications/Index/8.
Deur newe-effekte aan te meld kan jy help om meer inligting beskikbaar te stel aangaande die veiligheid van **TROBET**.

5. Hoe om TROBET te bewaar

- Bewaar by of benede 25°C.
- Hou die stulpstrook(e) in die buitenste karton totdat dit benodig word vir gebruik.
- BEWAAR ALLE MEDISYNE BUITE BEREIK VAN KINDERS
- Moet nie gebruik na die vervaldatum wat op die karton gedruk is nie.
- Neem alle ongebruikte medisyne terug na jou apteker.
- Moet nie ongebruikte medisyne in afvoerpype of rioolstelsels (bv. toilette) gooi nie.

6. Inhoud van die pak en ander inligting

Wat TROBET bevat
Die aktiewe bestanddeel in **TROBET** is irbesartan.
TROBET 75: Elke filmbedekte tablet bevat 75 mg irbesartan.
TROBET 150: Elke filmbedekte tablet bevat 150 mg irbesartan.
TROBET 300: Elke filmbedekte tablet bevat 300 mg irbesartan.
Die ander bestanddele in **TROBET** is:
Kalsiumkarboksie metielsellulose, kolloïdale silikondioksied, povidoon, natriumstyselglikolaat (Tipe A), gesuiwerde talk, magnesiumstearaat en filmbedekking wat hipromellose, laktosemonohidraat, titaandioksied (Kleurindeks Nr. 77891) en polietileenglikol 3 000 bevat.

Hoe TROBET lyk en Inhoud van die pak
TROBET 75:
Wit tot naaswit, ovaalvormige, filmbedekte tablette, met "ML 94" aan die een kant gedruk en glad aan die ander kant.
TROBET 150:
Wit tot naaswit, ovaalvormige, filmbedekte tablette, met "ML 95" aan die een kant gedruk en glad aan die ander kant.
TROBET 300:
Wit tot naaswit, ovaalvormige, filmbedekte tablette, met "ML 96" gedruk aan die een kant en glad aan die ander kant.
1) Stulpverpakking:
Tablette word verpak in deurskynige film 300 µ PVC/25 µ PE/90 µ PVdC as die vormingsmateriaal en 25 µ aluminium voorafgedrukte foelie/6-8 gsm lakverniste hittesêel as die dekmateriaal, verpak in 'n voorafgedrukte karton.
Verpakkingsgroottes sluit 10, 28 of 30 tablette in.
2) HDPE houer verpakking:
Tablette word in 60 ml wit ronde HDPE houer met 33-400 mm nek afwerking verpak, wat met 33 mm kinderbestande sluiting met pulp en hittesêlvoering toegemaak is, en in buitenste karton verpak is.
Verkpakkingsgroottes sluit 28 of 30 tablette in.
Nie alle verpakkings en verpakkingsgroottes word noodwendig bemark nie.

Houer van die Registrasiesertifikaat
MACLEODS PHARMACEUTICALS SA (Edms) Bpk
Kantoorblok 1, Bassonia Estate Kantoorpark (Oos),
Cussonia Weg 1, Bassonia Rock, Uitbr. 12,
Alberton, Suid Afrika

Hierdie inligtingstuk was herslen in
Datum van eerste magtiging: 30 November 2021.
Datum van hersiening: Word met hersiening deur SAHPRA toegeken.

Registrasienommers
TROBET 75:46/7.1.3/0251
TROBET 150:46/7.1.3/0252
TROBET 300:46/7.1.3/0253

PACKAGING RESEARCH & DEVELOPMENT

MACLEODS

Restricted Circulation

(Front Page)

ARTWORK / PRINTPROOF APPROVAL FORM

1. Product: TROBET 75/150/300 (IrbesartanTablets 75/150/300 mg)	
2. Country: South Africa (Private Market)	3. Packaging component: Patient Information
4. No. of Colours: 1 Colour	5. Pantone Shade No.: Black
6. Specification: 40 gsm bible paper	
7. Machine Layout No.: NA	8. Dimensions: 435 (L) x 370 (W) mm
9. Design / Style: Booklet	10. Item code No.: PM03937101
11. Artwork has been made: Actual Size	12. Pharma code No.: 31833 std
13. Barcode/NDC No: NA	14. Supersedes Item code No: NA
15. Revision no: 00	16. A/W File name: Y:\Irbesartan\SA Private Market\Irbesartan Tablets 75, 150 and 300 PI & PIL - PM03937101.cdr
Approved By:	17. Location: Daman

PRD	M.A. HOLDER	MEDICAL/RAD	QC	PRODN	QA
25-08-2022	Vanita Rajool	25/08/22	25/08/22	26/08/22	26/08/22 Yeadav 26/08/22

Note: 1. To follow overleaf checklist for approval of Artwork / Print proof.

Instructions to Vendor :

1. Before processing, please ensure First pull out / Commercial supply should match with approved Artwork with respect to Design, Size, Fonts & Text.
2. Print proof to represent full printing area with Station Numbers.

FRM/CQA/021/04-02

Reason for revision :	Item code	Artwork Release Date	Artwork Implementation Date
1) New Artwork for South Africa Private Market	PM03937101		