Front Side

435 mm

400 mm

SCHEDULING STATUS: S3

1. NAME OF THE MEDICINE

TROBET CO 150/12,5 (film-coated tablet)
TROBET CO 300/12,5 (film-coated tablet)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

TROBET CO 150/12,5
Each film-coated tablet contains 150 mg Irbesartan and 12,5 mg hydrochlorothiazide
TROBET CO 150/12,5 contains sugar (2,16 mg lactose monohydrate)
TROBET CO 300/12,5
Each film-coated tablet contains 300 mg Irbesartan and 12,5 mg hydrochlorothiazide
TROBET CO 300/12,5 contains sugar (4,32 mg lactose monohydrate)
Excipients:
For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Film-coated tablet.
TROBET CO 150/12,5
Peach colored, oval, film coated tablets debossed with "ML 34" on one side and plain on other side.
TROBET CO 300/12,5
Peach colored, oval, film coated tablets debossed with "ML 33" on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
TROBET CO is indicated for treatment of essential hypertension in patients stabilised on the individual components at the same dosages.

4.2 Posology and method of administration
Posology:
TROBET CO should be administered on a once-a-day schedule without regard to meals.
TROBET CO is indicated for use in patients who are adequately controlled on the individually components at the same dosages.
If blood pressure is not adequately controlled with **TROBET CO** alone, another antihypertensive medicine (e.g. beta-adrenergic blocking medicines, long-acting calcium channel blocking medicines) may be added.
Elderly patients and patients with renal or hepatic impairment:
No dosage reduction is generally necessary in the elderly or in patients with mild to moderate renal impairment (creatinine clearance >30 ml/min).
However due to the hydrochlorothiazide component, **TROBET CO** is contraindicated for patients with severe renal dysfunction. (Creatinine clearance < 30ml/min) (see section 4.4).
No dosage reduction is generally necessary in patients with mild to moderate hepatic impairment.
Due to the hydrochlorothiazide component **TROBET CO** should be used with caution in patients with severe hepatic impairment (see **Warnings and Special Precautions – Impaired Hepatic and Renal Function**).
Patients with intravascular volume depletion:
See section 4.4 - Hypotension-volume depleted patients

Method of administration:
Oral

4.3 Contraindications
TROBET CO is contraindicated in:
- Hypersensitivity to irbesartan hydrochlorothiazide, sulphonamide derived medicines or any of the ingredients of **TROBET CO.**
- A history of angioedema related to previous therapy with ACE inhibitors or angiotensin receptor blockers (ARBs): 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).
- Bilateral renal artery stenosis.
- Renal artery stenosis in patients with a single kidney.
- Aortic stenosis.
- Concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene, amiloride (see Section 4.5).
- Porphyria.
- Thiazide diuretics in (fixed dose) combination with **TROBET CO** should not be given to patients with Addison's disease. This therapy is also contraindicated in patients with severe renal impairment or anuria, and in patients who show hypersensitivity to other sulphonamide-derived medicines.
- Lithium therapy: Concomitant administration with **TROBET CO** may lead to toxic blood concentrations of lithium (see section 4.5).
- Pregnancy and lactation (see section 4.6).
- The concomitant use of **TROBET CO** with aliskiren-containing products is contraindicated (see sections 4.4 and 4.5).

TROBET CO is contra-indicated in patients who are anuric.
Paediatric Use:
Safety and effectiveness in paediatric patients have not been established.

4.4 Special warnings and precautions for use
Should a woman become pregnant while receiving **TROBET CO**, the treatment should be stopped promptly and switched to a different class of antihypertensive medicine (see sections 4.3 and 4.6).
Hydrochlorothiazide crosses the placental barrier and appears in cord blood. The routine use of diuretics in otherwise healthy pregnant women is not recommended and exposes mother and foetus to unnecessary hazard, including foetal and neonatal jaundice, thrombocytopenia and possibly other adverse reaction which have occurred in the adult.

Hypotension-Volume depleted patients:
TROBET CO has been associated with hypotension in hypertensive patients without other co-morbid conditions. Symptomatic hypotension may be expected to occur in sodium/volume depleted patients such as those treated vigorously with diuretic and/or salt restriction, or on haemodialysis. Volume and/or sodium depletion should be corrected before initiating therapy with **TROBET CO** Hydrochlorothiazide may potentiate the action of other antihypertensive medicines (see section 4.5).

Dual blockade of the renin-angiotensin-aldosterone system (RAAS):
There is evidence that the concomitant use of ACE-inhibitors, angiotensin II receptor blockers (ARBs) or aliskiren-containing medicines may increase the risk of hypotension, hyperkalaemia and decreases renal function (including acute renal failure). Dual blockade of RAAS through the combined use of **TROBET CO** and aliskiren-containing medicines is therefore contraindicated (see section 4.3). **TROBET CO** should not be used concomitantly with aliskiren-containing medicines (see section 4.3).

Renal artery stenosis- 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 angiotensin converting enzyme inhibitors or angiotensin-II receptor antagonists such as **TROBET CO.**
As a consequence of inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible individuals. In patients whose renal function depends on the activity of the renin-angiotensin-aldosterone system (e.g. hypertensive patients with renal artery stenosis in one or both kidneys, or patients with severe congestive heart failure), treatment with other medicines that affect this system has been associated with oliguria and/or progressive uraemia and (rarely) with acute renal failure and/or death. The possibility of a similar effect occurring with use of an angiotensin II receptor antagonist cannot be excluded.
The antihypertensive effects of hydrochlorothiazide may be increased in the postsympathectomy patient.

Impaired renal function:
TROBET CO is not recommended for patients with severe renal disease (creatinine clearance <30 ml/min) (see section 4.3 – anuric patients).
Hydrochlorothiazide-associated precipitation of uraemia may occur in patients with impaired renal function.
When **TROBET CO** is used in patients with impaired renal function, a periodic monitoring of potassium, creatinine and uric acid serum levels is recommended. There is no experience regarding the administration of **TROBET CO** in patients with a recent kidney transplantation.
No dosage adjustment is necessary in patients with renal impairment whose creatinine clearance is ≥ 30 ml/min. However, in patients with mild to moderate renal impairment (creatinine clearance ≥ 30 ml/min but < 60 ml/min) **TROBET CO** should be administered with caution

Impaired hepatic function:
TROBET CO should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations in fluid and electrolyte balance may precipitate hepatic coma.

Electrolyte and metabolic imbalances:
Hydrochlorothiazide can cause fluid or electrolyte imbalance (hypokalaemia, hyponatraemia and hypochloraemic alkalosis). Chloride deficit is generally mild and usually does not require treatment.
Calcium excretion is decreased by hydrochlorothiazide which may cause intermittent and slight elevation of serum calcium. Marked hypercalcaemia suggests the possibility of hyperparathyroidism. Hydrochlorothiazide should be discontinued before carrying out tests for parathyroid function.
Hydrochlorothiazide been shown to increase the urinary excretion of magnesium which may result in hypomagnesaemia.
Hyperuricaemia may occur, and an acute attack of gout may be precipitated in certain patients receiving hydrochlorothiazide therapy.
Hypokalaemia may develop with the use of hydrochlorothiazide. The risk of hypokalaemia is greatest in patients with cirrhosis of the liver, in patients experiencing brisk diuresis, in patients who are receiving inadequate oral intake of electrolytes and in patients receiving concomitant therapy with corticosteroids or ACTH. Conversely, due to the irbesartan component of **TROBET CO** hyperkalaemia might occur, especially in the presence of renal impairment and/or heart failure, and diabetes mellitus. Adequate monitoring of serum potassium in patients at risk is recommended.
There is no evidence that irbesartan would reduce or prevent diuretic-induced hyponatraemia.
Insulin requirement in diabetic patients may be increased and latent diabetes mellitus may become manifest during hydrochlorothiazide administration. Increases in cholesterol and triglyceride levels have been associated with hydrochlorothiazide diuretic therapy.
Monitoring of laboratory parameters may be necessary in patients at risk for electrolyte and metabolic disturbances.

Systemic Lupus Erythematosus:
Exacerbation or activation of systemic lupus erythematosus has been reported with the use of hydrochlorothiazide

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

Use in the elderly:
In clinical studies there was no age-related difference in efficacy or safety profile of irbesartan.

Anti-doping test:
Hydrochlorothiazide contained in **TROBET CO** could produce a positive analytic result in an anti-doping test.

Acute Myopia and Secondary Acute Angle-Closure Glaucoma:
Sulphonamide medicines or sulphonamide derivative medicines including hydrochlorothiazide, can cause an idiosyncratic reaction, resulting in transient myopia and acute angle-closure glaucoma. Symptoms include acute onset of decreased visual acuity or ocular pain and typically occur within hours to weeks of medicine initiation. Untreated acute angle-closure glaucoma can lead to permanent vision loss.
The primary treatment is to discontinue **TROBET CO** intake as rapidly as possible. Prompt medical or surgical treatments may need to be considered if the intraocular pressure remains uncontrolled. Risk factors for developing acute angleclosure glaucoma may include a history of sulphonamide or penicillin allergy.

General:
As with any antihypertensive medicine, excessive blood pressure decrease in patients with ischaemic cardiopathy or ischaemic cardiovascular disease could result in a myocardial infarction or stroke.
Hypersensitivity reactions to hydrochlorothiazide may occur in patients with or without a history of allergy or bronchial asthma, but are more likely in patients with such a history.
Cases of photosensitivity reactions have been reported with hydrochlorothiazide. If photosensitivity reaction occurs during treatment, it is recommended to stop the treatment. If a re-administration is deemed necessary, it is recommended to protect exposed areas to the sun or to artificial UVA.

Lactose:
TROBET CO 150/12,5 contains 2,16 mg of lactose in each tablet.
TROBET CO 300/12,5 contains 4,32 mg of lactose in each tablet.
Lactose is a source of glucose and galactose. If you have one of the rare genetic disorders galactosaemia, or glucose-galactose intolerance or congenital lactase deficiency you must talk to your doctor or pharmacist before taking this medicine.
The small amount of lactose in each dose is unlikely to cause symptoms in adults with lactose intolerance.

4.5 Interaction with other medicines and other forms of interaction
Dual blockade of the RAAS with ARBs, ACE inhibitors, or aliskiren-containing medicines:
Clinical trial data has shown that dual blockade of the renin-angiotensin-aldosterone-system (RAAS) through the combined use of ACE inhibitors, angiotensin II receptor blockers or aliskiren-containing medicines is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function (see sections 4.3 and 4.4).

Lithium:
Diuretic medicines reduce the renal clearance of lithium and increase the risk of lithium toxicity. Co-administration with **TROBET CO** should be approached with caution and the frequent monitoring of serum lithium levels is recommended.

Other antihypertensive medicines:
The antihypertensive effect of **TROBET CO** may be increased with the concomitant use of other antihypertensive medicines. Prior treatment with high dose diuretics may result in volume depletion and a risk of hypotension when initiating therapy with irbesartan with or without hydrochlorothiazide unless the volume depletion is corrected first (see section 4.4).

Based on *in vitro* data no interaction should be expected to occur with medicines whose metabolism is dependent upon cytochrome P450 isoenzymes 1A1, 1A2, 2A6, 2B6, 2D6, 2E1 or 3A4.
Irbesartan is primarily metabolised by 2C9, however, during clinical interactions studies, no significant pharmacodynamics interactions were observed when irbesartan was co administered with warfarin (a medicine metabolised by 2C9). Irbesartan does not affect the pharmacokinetics of digoxin. The pharmacokinetics of irbesartan is not affected by coadministration with nifedipine or hydrochlorothiazide.

Medicines affecting potassium:
Based on experience with 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 sodium) may lead to increase in serum potassium.

Non-steroidal anti-inflammatory drugs:
When **TROBET CO** is administered simultaneously with nonsteroidal anti- inflammatory drugs (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 **TROBET CO** 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. The combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring renal function after initiation of concomitant therapy, and periodically thereafter.

Additional information on hydrochlorothiazide interactions: when administered concurrently the following medicines may interact with hydrochlorothiazide:

Alcohol, barbiturates or narcotics - potentiation of hydrochlorothiazide diuretic-induced orthostatic hypotension may occur.

Antidiabetic medicines (oral medicines and insulin) - hydrochlorothiazide may elevate blood glucose levels, thus dosage adjustments of antidiabetic medicines may be necessary.

Antigout medicine - dosage adjustment of antigout medicine may be needed, since hydrochlorothiazide may raise the blood level of uric acid.

Digoxin and other antidysrythmic medicines (e.g. sotalol) - diuretic induced hypokalaemia may accentuate cardiac dysrhythmias.

Calcium salts - hydrochlorothiazide may increase serum calcium levels due to decreased excretion. If calcium is prescribed, serum calcium level should be monitored and calcium dosage adjusted accordingly.

Cholestyramine resin and colestipol hydrochloride - may delay or decrease absorption of hydrochlorothiazide. **TROBET CO** tablets should be taken at least one hour before or 4 hours after these medicines.

Inhibitors of Endogenous Prostaglandin Synthesis (i.e. non-steroidal anti-inflammatory medicines) - in some patients the use of medicines can reduce the effects of hydrochlorothiazide.

Other diuretics and antihypertensive medicines - The hydrochlorothiazide component of **TROBET CO** may potentiate the actions of antihypertensive medicines, especially ganglionic or peripheral adrenergic blocking medicines. Hydrochlorothiazide may interact with diazoxide; blood glucose, serum uric acid levels and blood pressure should be monitored.

Medicines used during surgery - The effects of non-depolarising muscle relaxants, pre-anaesthics and anaesthics used in surgery (e.g. tubocurarine) may be potentiated by hydrochlorothiazide; dosage adjustment may be required

Corticosteroids, ACTH - electrolyte depletion, particularly hypokalaemia, may be increased.

Pressor amines (e.g. noradrenaline) - the effect of pressor amines may be decreased, but not sufficiently to preclude their use.

Carbamazepine: concomitant use of carbamazepine and hydrochlorothiazide has been associated with the risk of symptomatic hyponatraemia. Electrolytes should be monitored during concomitant use, if possible, another class of diuretics should be used.

Other interactions: anticholinergic medicines (e.g. atropine, biperiden) may increase the bioavailability of hydrochlorothiazide by decreasing gastrointestinal motility and stomach emptying rate. Hydrochlorothiazide may increase the risk of adverse effects caused by amantadine. Hydrochlorothiazide may reduce the renal excretion of cytotoxic medicines (e.g. cyclophosphamide, methotrexate) and potentiate their myelosuppressive effects.

4.6 Fertility, pregnancy and lactation
Pregnancy:
Safety in pregnancy and lactation has not been established (see **CONTRA-INDICATIONS**). When pregnancy is detected or confirmed **TROBET CO** should be discontinued. Medicines affecting the renin-angiotensin system, such as **TROBET CO** can cause embryonal toxicity, foetal and neonatal morbidity and mortality when administered to pregnant women. Women of childbearing age should ensure effective contraception.

Lactation:
Safety has not been established.

4.7 Effects on ability to drive and use machines
TROBET CO is unlikely to affect the ability to drive and use machines. When driving vehicles or operating machines, it should be taken into account that occasionally dizziness or weariness may occur during treatment of hypertension.

4.8 Undesirable effects
Irbesartan:
Headache, dizziness, fatigue, nausea, vomiting, oedema.
Other side effects: Chest pain, cough, diarrhoea, dyspepsia, sexual dysfunction, tachycardia and dizziness (orthostatic).
Hydrochlorothiazide:
Other clinical adverse events reported with use of hydrochlorothiazide alone include: anorexia, gastric irritation, diarrhoea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, sialadenitis, vertigo, paraesthesia, xanthopsia, leucopenia, neutropenia/agranulocytosis, thrombocytopenia, aplastic anaemia, haemolytic anaemia, photosensitivity reactions, fever, urticaria, necrotising angiitis (vasculitis, cutaneous vasculitis) respiratory distress (including pneumonitis and pulmonary oedema), anaphylactic reactions, toxic epidermal necrolysis, hyperglycaemia, glycosuria, hyperuricaemia, electrolyte imbalance (including hyponatraemia and hypokalaemia), renal dysfunction, interstitial nephritis, muscle spasm, weakness, restlessness, transient blurred vision.

Laboratory Test abnormalities:
No clinically significantly changes in laboratory test parameters occurred in controlled clinical studies. No special monitoring of laboratory parameters is necessary.

Irbesartan/hydrochlorothiazide combination:

Table 1: Adverse Reactions in Placebo-Controlled Trials and Spontaneous Reports*

System	Frequency	Undesirable effects
Investigations:	Frequent:	increases in blood urea, creatinine and creatine kinase
	Less frequent:	decreases in serum potassium and sodium
Cardiac disorders:	Less frequent:	syncope, hypotension, tachycardia, oedema
Nervous system disorders:	Frequent:	dizziness
	Less frequent:	orthostatic dizziness, headache
Ear and labyrinth disorders:	Less frequent:	tinnitus
Respiratory, thoracic and mediastinal disorders:	Less frequent:	cough
Gastrointestinal disorders:	Frequent:	nausea/vomiting
	Less frequent:	diarrhoea, dyspepsia, dysgeusia
Renal and urinary disorders:	Frequent:	abnormal urination
	Less frequent:	impaired renal function including isolated cases of renal failure in patients at risk
Metabolism and nutrition disorders:	Less frequent:	hyperkalaemia
Vascular disorders:	Less frequent:	flushing
General disorders and administration site conditions:	Frequent:	fatigue
Immune system disorders:	Less frequent:	cases of hypersensitivity reactions such as angioedema, rash, urticaria
Hepatobiliary disorders:	Less frequent:	jaundice hepatitis, abnormal liver function
Reproductive system and breast disorders:	Less frequent:	sexual dysfunction, libido changes

Additional information on individual components: in addition to the adverse reactions listed above for the combination product, other adverse reactions previously reported with one of the individual components may be potential adverse reactions with **TROBET CO.** Tables 2 and 3 below detail the adverse reactions reported with the individual components of **TROBET CO.**

Table 2: Adverse reactions reported with the use of **irbesartan** alone

System	Frequency	Undesirable effects
Nervous system disorders	Frequent: Less frequent	Dizziness headache, orthostatic dizziness
Cardiac disorders	Less frequent:	Tachycardia
Respiratory, thoracic and mediastinal disorders	Less frequent	Cough
Gastrointestinal disorders	Frequent: Less frequent:	nausea, vomiting diarrhoea, dyspepsia
Reproductive system and breast disorders	Less frequent	sexual dysfunction
General disorders and administration site conditions:	Frequent: Less frequent:	Fatigue chest pain, oedema

Table 3: Adverse reactions reported with the use of hydrochlorothiazide alone

System	Frequency	Undesirable effects
Investigations:	Less frequent:	electrolyte imbalance (including hypokalaemia and hyponatraemia, see WARNINGS AND SPECIAL PRECAUTIONS), hyperuricaemia, glycosuria, hyperglycaemia, increases in cholesterol and triglycerides
Cardiac disorders:	Less frequent:	cardiac dysrhythmias
Blood and lymphatic system disorders:	Less frequent:	aplastic anaemia, bone marrow depression, neutropenia/agranulocytosis, haemolytic anaemia, leucopenia, thrombocytopenia
Nervous system disorders:	Less frequent:	vertigo, paraesthesia, light-headedness, restlessness
Eye disorders:	Less frequent:	transient blurred vision, xanthopsia
Respiratory, thoracic and mediastinal disorders:	Less frequent:	respiratory distress (including pneumonitis and pulmonary oedema)
Gastrointestinal disorders:	Less frequent:	pancreatitis, anorexia, diarrhoea, constipation, gastric irritation, sialadenitis, loss of appetite
Renal and urinary disorders:	Less frequent:	interstitial nephritis, renal dysfunction
Skin and subcutaneous tissue disorders:	Less frequent:	anaphylactic reactions, toxic epidermal necrolysis, necrotising angiitis (vasculitis, cutaneous vasculitis), cutaneous lupus erythematosus-like reactions, reactivation of cutaneous lupus erythematosus, photosensitivity reactions, rash, urticaria
Musculoskeletal and connective tissue disorders:	Less frequent:	weakness, muscle spasm
Vascular disorders:	Less frequent:	postural hypotension
General disorders and administration site conditions:	Less frequent:	fever
Hepatobiliary disorders:	Less frequent:	jaundice (intrahepatic cholestatic jaundice)
Psychiatric disorders:	Less frequent:	depression, sleep disturbances

The dose dependent adverse events of hydrochlorothiazide (particularly electrolyte disturbances) may increase when titrating the hydrochlorothiazide.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. 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://sahpra.org.za/wp-content/uploads/2020/01/6.4_ARF1_v5.1_27Jan2020.pdf

4.9 Overdose
No specific information is available on the treatment of over dosage with **TROBET CO.** The patient should be closely monitored and treatment should be symptomatic and supportive. Irbesartan is not removed from the body by haemodialysis.
The most common signs and symptoms observed in adults expose to hydrochlorothiazide and those caused by electrolyte depletion (hypokalaemia, hypochloraemia, hyponatraemia) and dehydration resulting from excessive diuresis. If digoxin or other antidysrythmic medicines (e.g. sotalol) has also been administered, hypokalaemia may accentuate cardiac dysrhythmias.
The degree to which hydrochlorothiazide is removed by haemodialysis has not been established.

5. PHARMACOLOGICAL PROPERTIES

Pharmaceutical groups: A7.1.3 – Vascular medicines - Other hypotensives.
ATC code: C09DA04.
5.1 Pharmacodynamic properties
Irbesartan is a specific antagonist of angiotensin II receptor (AT1 subtype). Angiotensin II is an important component of the renin-angiotensin system 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 antagonist of the angiotensin II (AT1 subtype) receptors localised on vascular smooth muscle cells and in the adrenal cortex. It has no agonist activity at the AT1 receptor and much greater affinity (more than 8 500 fold) for the AT1 receptor than for the AT2 receptor (a receptor that has not been shown to be associated with cardiovascular homeostasis).
Irbesartan does not inhibit enzyme 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 AT1 receptors interrupts the feedback loop within the renin-angiotensin system, resulting in increases in plasma renin levels and angiotensin II levels. Aldosterone plasma concentration declines following irbesartan administration, however, serum potassium levels are not significantly affected (mean increase of <0,1 mEq/l at the recommended doses. Irbesartan has no notable effect on serum triglycerides, cholesterol or glucose concentrations. There is no effect on serum or urinary acid excretion.

Hydrochlorothiazide is a benzothiadiazine diuretic with diuretic, natruretic and antihypertensive effects. The mechanism of antihypertensive effect of hydrochlorothiazide is not fully known. Hydrochlorothiazide affects the renal tubular mechanism of electrolyte reabsorption, increasing excretion of sodium and chloride in approximately equivalent amounts. Natriuresis causes a secondary loss of potassium and bicarbonate.
5.2 Pharmacokinetic properties
Concomitant administration of hydrochlorothiazide and irbesartan has no effect on the pharmacokinetics of irbesartan. Irbesartan and hydrochlorothiazide are orally active medicines and do not require biotransformation for their activity.
Absorption
Irbesartan
Following oral administration of **TROBET CO** the absolute bioavailability is 60-80 %.
Peak plasma concentration occurs at 1,5 to 2 hours after oral administration of irbesartan.
Hydrochlorothiazide
Following oral administration of **TROBET CO** the absolute bioavailability 50 to 80 % for Peak plasma concentration occurs at 1 to 1,5 hours after oral administration for hydrochlorothiazide.
Distribution
Irbesartan
Irbesartan is 90 % protein bound in plasma and has negligible binding to cellular components of blood.
Hydrochlorothiazide
The volume of distribution is 53 to 93 litres. Hydrochlorothiazide is 68 % protein bound in plasma and its apparent volume of distribution is 3,6–7,8 litres/kg.
Linearity/non-linearity
Irbesartan
Irbesartan exhibits linear pharmacokinetics over the therapeutic dose range Steady-state plasma concentrations are attained within 3 days after initiation of a once daily dosing regimen. Limited accumulation (<20 %) is observed in plasma upon repeated once-daily dosing.
Biotransformation
Irbesartan
In plasma, unchanged irbesartan accounts for 80 to 85 % of the circulating radioactivity following oral or intravenous administration of ^{14}C irbesartan.
Irbesartan is metabolised by the liver via glucuronide conjugation and oxidation, the major circulation metabolite is irbesartan glucuronide (~6 %). Irbesartan undergoes oxidation primarily by the cytochrome P450 isoenzyme2C9; isoenzyme 3A4 has negligible effect. It is not metabolised by, nor does it substantially induce or inhibit most isoenzyme commonly associate with medicine metabolism (i.e. 1A1, 1A2, 2A6, 2B6, 2D6, 2E1). Irbesartan does not induce or inhibit isoenzyme 3A4.

Hydrochlorothiazide
Hydrochlorothiazide is not metabolised and is eliminated by the kidney.

Elimination
Irbesartan
Irbesartan and its metabolites are excreted by both biliary and renal routes. About 20 % of administered radioactive after an oral or intravenous dose of ^{14}C irbesartan is recovered in urine with the remainder in faeces. Less than 2 % of dose is excreted in urine as unchanged irbesartan. The terminal elimination half-life ($t_{1/2}$) of irbesartan is 11 to 15 hours. The total body clearance of intravenously administered irbesartan is 157 to 176 ml/min, of which 3,0 to 3,5 ml/min is renal clearance.
Hydrochlorothiazide
The mean plasma half-life of hydrochlorothiazide reportedly ranges from 5 to 15 hours.
Special populations
Elderly
Irbesartan
In elderly (male and female) normotensive subjects (65 to 80 years) with clinically normal renal and hepatic function, the plasma AUC and peak plasma concentration (C_{max}) of irbesartan are approximately 20 to 50 % greater than those observe in younger subjects (18 to 40 years). Regardless of age the elimination half-life is comparable. No significant age related differences in clinical effect have been observed.
Hydrochlorothiazide
The area under the plasma concentration time curve (AUC) for hydrochlorothiazide was elevated in the elderly group following multiple dosing consistent with previously published data.

Race
Irbesartan
In black and white normotensive subjects, the plasma AUC and $t_{1/2}$ of irbesartan are approximately 20 to 25 % greater in black than in whites; the peak plasma concentration (C_{max}) of irbesartan are essentially equivalent.

Renal impairment
Irbesartan
In patients with renal impairment (regardless of degree) and in haemodialysis patients, the pharmacokinetics of irbesartan are not significantly altered. Irbesartan is not removed by haemodialysis.
Hydrochlorothiazide
In patients with severe renal impairment (creatinine clearance <30 ml/min), the elimination half-life of hydrochlorothiazide was increased in 21 hours.

Hepatic impairment
Irbesartan
In patients with hepatic insufficiency due to mild to moderate cirrhosis, the pharmacokinetics of irbesartan is not significantly altered.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Carboxymethylcellulose calcium, colloidal silicon dioxide, povidone, sodium starch glycolate Type A, talc, magnesium stearate, coating containing hypromellose, lactose monohydrate, titanium dioxide (colour index no. 77891), polyethylene glycol, yellow iron oxide (colour index no.: 77492), red iron oxide (colour index no.: 77491).
Contains sugar (lactose).

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 white Opaque film 300 micron PVC/25 micron PE/90 micron PVdC as the forming material and 25 micron Aluminium foil coated with 6-8 gsm heat seal lacquerodas the lidding material, packed in a pre-printed carton.
Pack size include 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 NUMBER(S)

TROBET CO 150/12,5 : 46/7.1.3/0831
TROBET CO 300/12,5 : 46/7.1.3/0832

9. DATE OF FIRST AUTHORSATION/RENEWAL OF THE AUTHORISATION

14 December 2021

10. DATE OF REVISION OF THE TEXT

–

TROBET CO
150/12.5, 300/12,5
film-coated tablets
PM03937601

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS S3

TROBET CO 150/12,5 (Film-coated tablet)
TROBET CO 300/12,5 (Film-coated tablet)
Irbesartan 150 mg, 300 mg and Hydrochlorothiazide 12,5 mg
Contains Sugar (Lactose monohydrate)

Read all of this leaflet carefully before you start taking TROBET CO
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **TROBET 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.

Front Side

435 mm

400 mm

What is in this leaflet

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

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

TROBET CO is used in the treatment of high blood pressure (hypertension).
TROBET CO belongs to a group of medicine known as angiotensin-II receptor antagonist. Angiotensin II is a substance produced in the body which binds to receptor in blood vessels causing them to tighten this result in an increase in blood pressure. **TROBET CO** prevents the binding of angiotensin II to these receptors causing the blood vessels to relax and the blood pressure to lower.
Hydrochlorothiazide is one of a group of medicines (so called thiazide diuretics) that causes increased urine output and so causes a lowering of blood pressure.
The two actives in **TROBET CO** work together to lower blood pressure further than if either was given alone.

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

Do not take TROBET CO:

- If you are allergic to irbesartan, hydrochlorothiazide, sulphonamide derived medicines or any of the ingredients of **TROBET CO.**
- If you have had angioedema previously (swelling of the face, lips, mouth, tongue or throat with or without difficulty in swallowing or breathing) while taking an ACE inhibitor or angiotensin receptor blocker such as irbesartan. You must never again be given these medicines.
- If you have inherited or idiopathic (unknown cause) type angioedema.
- If you have hypertrophic obstructive cardiomyopathy; a heart disorder in which the walls of the ventricles lower heart chambers thicken (hypertrophy) and become stiff and the thickened muscle blocks the flow of blood out of the heart.
- If you have severe kidney disease and have difficulty in producing urine.
- If you have narrowing of the blood vessels to both kidneys or to a single functioning kidney.
- If you have aortic stenosis; a narrowing of the aortic valve opening between the ventricle (large pumping chamber of the heart) and the aorta (the main artery leading away from the heart).
- If you are taking diuretics (water pills) that cause your body to retain your potassium such as spironolactone, triamterene and amiloride.
- If you have porphyria.
- If you have Addison's disease.
- If you are taking medicines containing lithium.
- If you are or think you may be pregnant.
- If you are planning to become pregnant.
- If you are breastfeeding.
- If you are taking medicines that contain aliskiren which is used to treat high blood pressure.

If any of the above apply to you, inform your doctor or pharmacist first and ask for their advice.
TROBET CO should not be given to children.

Warnings and precautions
Take special care with **TROBET CO**:
There are certain conditions, which you may have or have had, which require special care before or while taking **TROBET CO.** Therefore, before taking **TROBET CO**, you should tell your doctor:

- If you had excessive vomiting or diarrhoea leading to an extreme loss of fluid and/or salt in your body, or if you receive diuretics (medicines that increase the amount of water that you pass out through your kidneys) or are under dietary salt restriction leading to an extreme loss of fluid and salt in your body or are on haemodialysis – treatment with **TROBET CO** could lead to low blood pressure. Your doctor will treat you first for the loss of fluid and salts from your body or start you on a lower dose of **TROBET CO.**
- If you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren and an ACE inhibitor (e.g. enalapril, lisinopril, ramipril), **TROBET CO** should not be taken together with other medicines containing aliskiren and medicines known as ACE-inhibitors to reduce blood pressure as the concomitant use increases the risk of low blood pressure, high potassium levels in the blood and reduced kidney function.
- If you have congestive heart failure (disease of the heart with shortness of breath, and swelling of the feet or legs due to fluid build) or if you have high blood pressure with narrowing of the blood vessels to both kidneys or to a single functioning kidney, treatment with **TROBET CO** could lead to reduced volume of urine, high levels of urea in the blood and with acute kidney failure and or death.
- If you suffer from kidney disease or had a kidney transplant.
- If you suffer from liver disease.
- If you suffer from heart problems.
- If you have primary aldosteronism (a type of hormonal disorder that leads to high blood pressure) as **TROBET CO** is not recommended in treating patients with this disorder.
- If you suffer from lupus erythematosus (also known as lupus or SLE).
- If you are to go under any surgery or receive anesthetics, you should make sure the doctor knows that you are taking **TROBET CO.**
- If you suffer from high blood pressure and Type 2 diabetes with kidney disease, blood tests may show an increased level of potassium. When you take **TROBET CO**, your doctor may perform regular blood tests, especially for measuring blood potassium level in case of poor kidney function.
- Your doctor may check your kidney function, blood pressure, and the amount of electrolytes (e.g. potassium, calcium, sodium, magnesium) in your blood at regular intervals.
- If you are diabetic, your insulin requirement may increase or latent diabetes may become activated. Uric acid levels and triglyceride levels in the blood may be increased.
- You may have changes in your vision or pain in one or both of your eyes while taking **TROBET CO.** This could be a sign that you are developing glaucoma (increased pressure in your eye(s)). You should discontinue **TROBET CO** treatment and seek medical attention.
- You may experience an increased sensitivity of the skin to the sun with symptoms of sunburn (such as redness, itching, swelling, blistering) occurring more quickly than normal.
- The hydrochlorothiazide contained in **TROBET CO** could produce a positive result in an anti-doping test.
- An acute attack of gout may be precipitated in certain patients receiving **TROBET CO.**
- **TROBET CO** can be taken if you are elderly.

Children and adolescents
TROBET CO is not for patients who are under 18 years.

Other medicines and TROBET CO
Inform your doctor if you are taking any of the following medicines:

- Medicines containing lithium (used for some types of psychiatric illnesses).
- Certain type of pain killers called non-steroidal anti-inflammatory medicines (NSAIDs) such as ibuprofen, diclofenac and COX-2 inhibitors such as celecoxib.
- Medicines that increase the amount of potassium in your blood. These include potassium supplements or salt substitutes containing potassium, potassium-sparing diuretic medicines ("water pills") (e.g. spironolactone, triamterene, amiloride) and heparin (blood thinner).
- If you are taking any of the following medicines used to treat high blood pressure:
  - an ACE inhibitor (for example enalapril, lisinopril, ramipril), in particular if you have diabetes-related kidney problems.
  - Aliskiren containing medicines
- Other diuretics (water tablets), laxatives, carbenoxolone (for ulcers, penicillin G sodium and amphotericin (for infections)
- Medicines for diabetes (oral antidiabetic medicines and insulin)
- Medicines for the treatment of gout
- Medicines to control heart rhythm (e.g. digoxin, sotalol)
- Calcium salts
- Cholestyramine resin and colestipol hydrochloride (for lowering blood cholesterol levels) – **TROBET CO** should be taken at least one hour before or 4 hours after these medicines.
- Medicines used during surgery (e.g. tubocurarine)
- Steroid medicines
- Noradrenaline (for low blood pressure)
- Carbamazepine (for epilepsy)
- Atropine (lowers heart rate, reduce salivation and secretions from the lungs)
- Biperiden and amantadine (for Parkinson's)
- Cyclophosphamide and methotrexate (anticancer medicines).

TROBET CO with food and drink and alcohol:
TROBET CO can be taken with or without food. Do not drink any alcohol while taking **TROBET CO** as the alcohol together with **TROBET CO** will make you drowsy.

Pregnancy, breastfeeding and fertility
TROBET CO should not be used during pregnancy or if you are breastfeeding. You must tell your doctor if you think you are (or might become) pregnant. Your doctor will advise you to stop taking **TROBET CO** before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of **TROBET CO.** If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking **TROBET CO.**
Driving and using machines
Some people may feel dizzy and tired while taking **TROBET CO.** Cautioned is advised when operating hazardous machinery, including motor vehicles until you are reasonably certain that **TROBET CO** does not adversely affect you.
TROBET CO contains lactose.
If you have been told by your doctor that you have a rare hereditary problem of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption you should not use this medicine.
TROBET CO contains lactose which may have an effect on the control of your blood sugar if you have diabetes mellitus.

3. How to take TROBET CO

Do not share medicines prescribed for you with any other person.
Always take **TROBET CO** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.
If you have the impression that the effect **TROBET CO** is too stronger or too weak, talk to your doctor or pharmacist.
The recommended dose is one tablet a day.
The maximal blood pressure lowering effect should be reached within 6-8 weeks after beginning treatment in patients with high blood pressure.
TROBET CO can be taken with or without food. The tablet should be swallowed with a drink of water. You should try to take daily dose at about the same time each day. It is important that you continue to take **TROBET CO** until your doctor tells you otherwise.

If you take more TROBET 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.
If you forget to take TROBET CO
If you accidentally miss a daily dose, just take the next dose as normal. Do not take a double dose to make up for forgotten individual doses.
If you stop taking TROBET CO
Do not stop taking your tablets just because you feel better. It is important that you carry on taking **TROBET CO** for as long as your doctor tells you.

4. Possible side effects

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

- swelling of face, tongue, throat, hands, feet, lips or mouth which may cause difficulties in swallowing or breathing
- hives
- severe skin reactions that can include blistering of the skin.

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

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- Chest pain.
- Changes in the way your heart beats, for example, if you notice it beating faster.
- Less urine than is normal for you.
- Changes in how your liver is working, including inflammation of the liver (hepatitis) and jaundice.

You may notice tiredness, yellowing of your skin and the whites of your eyes and flu like symptoms, blood tests may reveal increased levels of liver enzymes in the blood.

- Severe abdominal pain with nausea and vomiting (signs of pancreatitis)
- Unusual bleeding or bruising (signs of thrombocytopenia)
- Pale skin, tiredness, breathlessness, dark urine (signs of low level of red blood cells also called haemolytic anaemia).
- Fever, sore throat or mouth ulcers due to infections (symptoms of low level of white blood cells also called leucopenia, agranulocytosis or neutropenia).
- Facial rash, joint pain, muscle disorder, fever (signs of lupus erythematosus or reactivation of a lupus erythematosus).

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:

- Dizziness.
- Nausea and vomiting.
- Abnormal urination.
- Tiredness.

Less frequent side effects:

- Headache.
- Spinning sensation, pins and needles.
- Restlessness, sleep disorders, depression.
- Blurred vision, yellowing of vision.
- Ringing in the ears.
- Low blood pressure when standing up from sitting or lying down; this may make you feel faint or dizzy.
- Low blood pressure, flushing, lightheadedness.
- Cough, lung problems including pneumonia or build-up of fluid in the lungs.
- Diarrhoea, constipation, stomach pain/cramp, upset stomach, altered sense of taste, loss of appetite, swollen and tender salivary glands.
- Muscle cramps, muscle pain, joint pain, swelling.
- Problems with sexual performance.
- An increased amount of potassium in your blood. If this is severe you may notice tiredness, weakness, an irregular heartbeat or pins and needles.
- Inflammation of small blood vessels mainly affecting the skin (a condition known as necrotising vasculitis), rash, itching, increased sensitivity of the skin to the sun.
- Oedema (swelling due to retained fluid).
- Fever, weakness.

Laboratory tests may show the following:

- Raised levels of an enzyme that measures the muscle and heart function (creatine kinase) or raised levels of substances that measure kidney function (blood urea, creatinine).
- Decreases in potassium and sodium.
- Decrease in number of white blood cells also called leucopenia, agranulocytosis or neutropenia.
- Decrease in number of red blood cells (also called haemolytic anaemia).
- Increased uric acid levels, blood sugar levels, blood cholesterol and triglyceride levels, sugar in the urine.

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 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://sahpra.org.za/wp-content/uploads/2020/01/6.04_ARF1_v5.1_27Jan2020.pdf By reporting side effects, you can help provide more information on the safety of **TROBET CO.**

5. How to store TROBET CO

Store at or below 25 °C (room temperature), Protect from light.
Store all medicines out of reach of children.
Store in the original package / container.
Keep the blisters in the carton until required for use.
Keep the HDPE containers tightly closed.
Do not store in a bathroom.
Do not use after the expiry date stated on the blister / label / carton / bottle.
Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of pack and other information

What TROBET CO contains

- The active substance is irbesartan 150 mg, 300 mg and Hydrochlorothiazide 12,5 mg
- The other ingredients are Carboxymethylcellulose calcium, colloidal silicon dioxide, povidone, sodium starch glycolate Type A, talc, magnesium stearate, coating containing hypromellose, lactose monohydrate, titanium dioxide (colour index no. 77891), polyethylene glycol, yellow iron oxide (colour index no.: 77492), red iron oxide (colour index no.: 77491)

What TROBET CO looks like and contents of the pack
TROBET CO 150/12,5:
Peach colored, oval, film coated tablets debossed with "ML 34" on one side and plain on other side.
TROBET CO 300/12,5:
Peach colored, oval, film coated tablets debossed with "ML 33" on one side and plain on other side.

1) Blister Pack:
Tablets are packed in white Opaque film 300 micron PVC/25 micron PE/90 micron PVdC as the forming material and 25 micron Aluminium foil coated with 6-8 gsm heat seal lacquered as the lidding material, packed in a pre-printed carton.
Pack size include 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 and Manufacturer
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
14 DECEMBER 2021

Registration number
TROBET CO 150/12,5: 46/7.1.3/0831
TROBET CO 300/12,5: 46/7.1.3/0832

Access to the corresponding Professional Information
The corresponding professional information can be accessed at https://www.macleodspharma.com/ or email macleodsrsa@macleodspharma.com or contact 011 682 1169.

PASIËNTINLIGTINGSTUK

SKEDULERINGSTATUS: S3

TROBET CO 150/12,5 (Filmbedekte tablet)
TROBET CO 300/12,5 (Filmbedekte tablet)
150 mg, 300 mg Irbesartan en 12,5 mg Hidrochloortiasied
Bevat suiker (Laktosemonohidraat)

Lees hierdie inligtingstuk sorgvuldig voordat jy TROBET CO begin neem

- Hou hierdie inligtingstuk. Dit mag nodig wees dat jy dit weer moet lees.
- Vra asseblief jou doktor of jou apteker indien jy verdere vrae het.
- **TROBET CO** 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 CO** is en waarvoor dit gebruik word
2. Wat jy behoort te weet voordat jy **TROBET CO** neem
3. Hoe om **TROBET CO** te neem
4. Moontlike newe-effekte
5. Hoe om **TROBET CO** te bewaar
6. Inhoud van die pak en ander inligting

1. Wat TROBET CO is en waarvoor dit gebruik word

TROBET CO word gebruik in die behandeling van hoë bloeddruk (hipertensie).
TROBET CO behoort aan 'n groep medisyne bekend as angiotensien II reseptor antagoniste.
Angiotensien II is 'n stof wat in die liggaam geproduseer word en aan reseptor in bloedvate bind, wat dan veroorsaak dat hulle saamtrek, wat lei tot 'n toename in bloeddruk. **TROBET CO** verhoed die binding van angiotensien II aan hierdie reseptore wat veroorsaak dat die bloedvate ontspan en die bloeddruk verlaag.
Hidrochloortiasied is een van 'n groep medisyne (sogenaamde tiasieddiuretika) wat verhoogde urienuitset veroorsaak en sodoende 'n verlaging in bloeddruk veroorsaak.
Die twee aktiewe bestanddele in **TROBET CO** werk saam om bloeddruk verder te verlaag as wanneer een van hulle alleen gegee word.

2. Wat jy behoort te weet voordat jy TROBET CO neem

Moet nie TROBET CO neem nie:

- indien jy allergies is vir irbesartan, hidrochloortiasied sulfonamied-afkomstige medisyne of enige van die bestanddele van **TROBET CO.**
- indien jy voorheen angioëdeem (swelling van die gesig, lippe, mond, tong of keel met of sonder probleme om te sluk of asem te haal) gehad het, terwyl jy 'n AOE-inhibeerder of angiotensienreseptor blokkeerder soos irbesartan geneem het. Jy moet nooit weer hierdie medisyne gegee word nie.
- indien jy oorerflike of idiopatiese (onbekende oorsaak) tipe angioëdeem het.
- indien jy hipertrofiese obstruktiewe kardiomiopatie het; 'n hart afwyking waarin die wande van die ventrikels se onderste hartkamers verdik (hipertrofie) en styf word en die verdikte spier die vloei van bloed uit die hart blokkeer.
- indien jy ernstige niersiekte het en sukkel om urine te produseer.
- indien jy vermoeng van die bloedvate in beide nierare of na 'n enkele funksionerende nier.
- indien jy aortastenose het; 'n vernouing van die aortaklep opening tussen die ventrikel (groot pompkamer van die hart) en die aorta (die hoofslagaar wat weg van die hart af lei).
- indien jy diuretika (waterpille) soos spironolaktoon, triamtereen en amiloried neem, wat veroorsaak dat jou liggaam jou kalium terughou.
- indien jy porfirie het.
- indien jy Addison se siekte het.
- indien jy medisyne neem wat litium bevat.
- indien jy swanger is of vermoed dat jy dalk swanger is.
- indien jy besig is om swanger te raak.
- indien jy borsvoed.
- indien jy medisyne neem wat aliskiren bevat wat gebruik word om hoë bloeddruk te behandel.

Indien enige van die bogenoemde op jou van toepassing is, stel eers jou dokter of apteker in kennis en vra hulle vir advies. **TROBET CO** moet nie aan kinders gegee word nie.

Waarskuwings en voorsorgmaatreëls
Wees veral versigtig met TROBET CO:
Daar is sekere toestande wat jy mag hê of gehad het, wat spesiale sorg vereis voor, of terwyl jy **TROBET CO** neem. Daarom, voordat jy **TROBET CO** neem, moet jy jou dokter vertel:

- indien jy oormatige braking of diarree gehad het wat gelei het tot 'n oormatige verlies van vloeistof en/of sout in jou liggaam, of indien jy diuretika ontvang (medisyne wat die hoeveelheid water wat jy deur jou niere uitskei, vermeerder) of onder soutbeperkende dieet is wat lei tot 'n oormatige verlies van vloeistof en sout in jou liggaam of op hemodialise is – behandeling met **TROBET CO** kan tot lae bloeddruk lei. Jou dokter sal jou eerstens behandel vir die verlies van vloeistof en soute uit jou liggaam of jou op 'n laer dosering van **TROBET CO** begin.
- indien jy diabetes of ingekorte nierfunksie het en jy behandel word met 'n bloeddrukverlagende middel wat aliskiren bevat en 'n ACE-inhibeerder (bv. enalapril, lisinopril, ramipril), **TROBET CO** moet nie saam met ander aliskiren bevattende medisyne en medisyne bekend as AOE-inhibeerders geneem word om bloeddruk te verlaag nie, aangesien die gesamentlike gebruik die risiko vir lae bloeddruk, hoë kaliumvlakke in die bloed en verminderde nierfunksie verhoog.
- indien jy kongestiewe hartversaking het (siekte van die hart met kortasem, en swelling van die voete of bene as gevolg van vloeistof wat opbou) of as jy hoë bloeddruk het met vernouing van die bloedvate na albei niere of na 'n enkele funksionerende nier, kan behandeling met **TROBET CO** lei tot verminderde volume van urine, hoë ureumvlakke in die bloed en met akute nierversaking en/of dood.
- indien jy aan niersiekte ly of 'n nieroorplanting gehad het.
- indien jy aan leversiekte ly.
- indien jy aan hartprobleme ly.
- indien jy primêre aldosteronisme het ('n tipe hormonale versteuring wat lei tot hoë bloeddruk) aangesien **TROBET CO** nie aanbeveel word vir die behandeling van pasiënte met hierdie versteuring nie.
- indien jy aan lupus eritematosus ly (ook bekend as lupus of SLE).
- indien jy onder enige operasie gaan of narkose ontvang, moet jy seker maak die dokter weet dat jy **TROBET CO** neem.
- indien jy aan hoë bloeddruk en Tipe 2-diabetes met niersiekte ly, kan bloedtoetse 'n verhoogde kaliumvlak toon. Wanneer jy **TROBET CO** neem, kan jou dokter gereelde bloedtoetse uitvoer, veral vir die bepaling van bloedkaliumvlakke in geval van swak nierfunksie.
- Jou dokter kan jou nierfunksie, bloeddruk en die hoeveelheid elektroliete (bv. kalium, kalsium, natrium, magnesium) in jou bloed met gereelde tussenposes nagaan.
- Indien jy diabeties is, kan jou insulienbehoefte toeneem of latente diabetes kan geaktiveer word. Cholesterol- en triglieselfdevlakke in die bloed kan verhoog word.
- Jy mag veranderinge in jou visie of pyn in een of albei van jou oë hê terwyl jy **TROBET CO** neem. Dit kan 'n teken wees dat jy gloukoom ontwikkel (verhoogde druk in jou oog(e)). Jy moet behandeling met **TROBET CO** staak en mediese hulp soek.
- Jy kan 'n verhoogde sensitiwiteit van die vel vir die son ervaar met simptome van sonbrand (soos rooiheid, jeuk, swelling, blase) wat vinniger as normaal verskyn.
- Die hidrochloortiasied vervat in **TROBET CO**, kan 'n positiewe resultaat in 'n anti-dwelm toets produseer.
- 'n Akute aanval van jig kan prasipiteer in sekere pasiënte wat **TROBET CO** ontvang.
- **TROBET CO** kan geneem word indien jy bejaard is.

Kinders en adolessente
TROBET CO is nie vir pasiënte wie jonger as 18 jaar is nie.

Ander medisyne en TROBET CO
Vertel vir jou dokter indien jy enige van die volgende medisyne neem:

- Litium bevattende medisyne (gebruik vir sommige tipes psigiatriese siektes).
- Sekere tipe pynstillers, naamlik nie-steroïdale anti-inflammatoriese middels (NSAIM's) soos ibuprofen, diklofenak en COX-2 inhibeerders soos selekoksib.
- Medisyne wat die hoeveelheid kalium in jou bloed vermeerder. Hierdie sluit kaliumaanvullings of kalium bevattende soutvervangers, kaliumbesparende diuretiese medisyne ("waterpille") (bv. spironolaktoon, triamtereen, amiloried) en heparien (bloedverdunner) in.
- Indien jy enige van die volgende medisyne neem wat gebruik word om hoë bloeddruk te behandel:
  - 'n AOE-inhibeerder (byvoorbeeld enalapril, lisinopril, ramipril), veral, indien jy diabetesverwante nierprobleme het.
  - Aliskiren bevattende medisyne
- Ander diuretika (watertablette), lakseermiddels, karbenoksoloon (vir meagsere), penisillien G natrium en amfoterisien (vir infeksies)
- Medisyne vir diabetes (orale antidiabetiese medisyne en insulien)
- Medisyne vir die behandeling van jig
- Medisyne om hartritme te beheer (bv. digoksien, sotalol)
- Kalsiumsoute
- Cholestiramienhars en kolestipolhidrochloried (vir die verlaging van bloedcholesterolvlakke) – **TROBET CO** moet ten minste een uur vóór of 4 uur ná hierdie medisyne geneem word.
- Medisyne wat tydens chirurgie gebruik word (bv. tubokurarien)
- Steroïedmedisyne
- Noradrenalien (vir lae bloeddruk)
- Karbamasepien (vir epilepsie)
- Atropien (verlaag harttempo, verminder speeksel afskeiding en afskeidings van die longe)
- Bipariden en amantadien (vir Parkinson se siekte)
- Sitoksofamied en metoreksaat (medisyne teen kanker).

TROBET CO met voedsel en drank en alkohol:
TROBET CO kan met of sonder kos geneem word. Moet nie enige alkohol drink terwyl jy **TROBET CO** neem nie, aangesien die alkohol saam met **TROBET CO** jou lomerig sal maak.

Swangerskap, borsvoeding en fertiliteit
TROBET CO moet nie gebruik word tydens swangerskap, of indien jy borsvoed nie. Jy moet jou dokter vertel as jy dink jy is swanger (of kan word). Jou dokter sal aanbeveel dat jy ophou om **TROBET CO** te neem voordat jy swanger word of sodra jy weet dat jy swanger is en sal jou aanraai om 'n ander medisyne in plaas van **TROBET CO** te neem. Indien jy swanger is of jou baba borsvoed, raadpleeg asseblief jou dokter, apteker of ander gesondheidsorgwerker vir advies voordat jy **TROBET CO** neem.
Bestuur en gebruik van masjinerie
Sommige mense kan duiselig en moeg voel terwyl hulle **TROBET CO** neem. Versigtigheid word aanbeveel wanneer gevaarlike masjinerie, insluitend motorvoertuie bestuur word totdat jy redelik seker is dat **TROBET CO** jou nie nadelig beïnvloed nie.
TROBET CO bevat laktose
Indien jy deur jou dokter ingelig is dat jy 'n seldsame oorerflike probleem van galaktose-intoleransie, Lapp-laktasetekort of glukose-galaktose-wanabsorpsie het, moet jy nie hierdie medisyne gebruik nie.
TROBET CO bevat laktose wat 'n uitwerking op die beheer van jou bloedsuiker kan hê indien jy diabetes mellitus het.

3. Hoe om TROBET CO te neem

Moet nie medisyne wat vir jou voorgeskryf is met enige ander persoon deel nie.
Neem altyd **TROBET CO** presies soos jou dokter jou beveel het. Vra jou dokter of apteker indien jy nie seker is nie.
Indien jy onder die indruk is dat die effek van **TROBET CO** te sterk of te swak is, praat met jou dokter of apteker.
Die aanbevole dosis is een tablet een keer per dag.
Die maksimum bloeddrukverlagende effek behoort binne 6-8 weke, na aanvang van behandeling in pasiënte met hoë bloeddruk, bereik te word.
TROBET CO kan met of sonder kos geneem word. Die tablet moet met 'n glas water geslukt word. Jy moet probeer om daaglikse doserings op ongeveer dieselfde tyd elke dag te neem. Dit is belangrik dat jy voortgaan om **TROBET CO** te neem totdat jou dokter jou anders vertel.

Indien jy meer TROBET CO geneem het as wat jy behoort te neem
In die geval van oordosering, raadpleeg jou dokter of apteker. Indien nie een beskikbaar is nie, kontak die naaste hospitaal of giftebeheersentrum.
Indien jy vergeet om TROBET CO te neem
Indien jy per ongeluk 'n dag se dosering oorslaan, neem net die volgende dosering soos normaal. Moet nie 'n dubbele dosis neem om vir vergete individuele dosisse op te maak nie.
Indien jy ophou om TROBET CO te neem
Moet nie ophou om jou tablette te neem net omdat jy beter voel nie. Dit is belangrik dat jy aanhou om **TROBET CO** te neem vir so lank as wat jou dokter jou sê.

4. Moontlike newe-effekte

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

- swelling van gesig, long, keel, hande, voete, lippe of mond, wat probleme kan veroorsaak om te sluk of asem te haal
- netelroos
- ernstige velreaksies wat blase van die vel kan insluit.

Hierdie is alles baie ernstige newe-effekte. Indien jy dit het, het jy moontlik 'n ernstige allergiese reaksie op **TROBET CO** gehad. Jy mag dalk dringende mediese aandag of hospitalisasie benodig.

Vertel jou dokter onmiddellik of gaan na die ongevalle afdeling van jou naaste hospitaal indien jy enige van die volgende opmerk:

- Borskaspyn.
- Veranderinge in die manier waarop jou hart klop, byvoorbeeld indien jy opmerk dat dit vinniger klop.
- Minder urinêre as wat vir jou normaal is.
- Veranderinge in hoe jou lewer werk, insluitend inflammasie van die lewer (hepatitis) en geelsug. Jy mag dalk moegheid, vergeling van jou vel en die wit van jou oë en griepagtige simptome opmerk, bloedtoetse kan verhoogde vlakke van leverensieme in die bloed toon.
- Erge bulkpyn met naarheid en braking (tekens van pankreatitis)
- Ongewone bloeding of kneusing (tekens van trombositopenie)
- Bleek vel, moegheid, kortasem, donker uriene (tekens van lae rooibloedselvlakke, ook bekend as hemolitiese anemie).
- Koors, seer keel of mondsere as gevolg van infeksies (simptome van lae witbloedselvlakke ook bekend as leukopenie, agranulositose of neutropenie).
- Gesigsuitslag, gewrigspyn, spier afwyking, koors (tekens van lupus eritemateuse of heraktivering van 'n lupus eritemateuse).

Hierdie is alles ernstige newe-effekte. Jy mag moontlik dringende mediese aandag nodig hê.

Vertel jou dokter indien jy enige van die volgende opmerk:
Gereelde newe-effekte:

- Duiseligheid.
- Naarheid en braking.
- Abnormale urinering.
- Moegheid.

Minder gereelde newe-effekte:

- Hoofpyn.
- Sensasie van draai, spelde en naalde.
- Rusteloosheid, slaap versteurings, depressie.
- Dowwe visie, vergeling van visie.
- Gesuis in die ore.
- Lae bloeddruk wanneer jy opstaan vanuit 'n sittende of liënde posisie; dit kan jou flou of duiselig laat voel.
- Lae bloeddruk, bloosing, ligkoppigheid.
- Hoes, longprobleme insluitend longontsteking of opbou van vloeistof in die longe.
- Diarree, hardlywigheid, maagpyn/kramp, ongemaklike maag, veranderde smaaksintuig, verlies van eetlus, geswelde en teer speekselkliere.
- Spierkrampe, spierpyn, gewrigspyn, swelling.
- Probleme met seksuele vermoë.
- 'n Verhoogde hoeveelheid van kalium in jou bloed. Indien dit ernstig is, kan jy moegheid, swakheid, 'n onreëlmatige hartslag of spelde en naalde opmerk.
- Ontsteking van klein bloedvate wat hoofsaaklik die vel affekteer ('n toestand bekend as nekrotiserende vaskulitis), uitslag, jeuk, verhoogde sensitiwiteit van die vel vir die son.
- Edeem (swelling as gevolg van teruggehoude vloeistof).
- Koors, swakheid.

Laboratoriumtoetse kan die volgende toon:

- Verhoogde vlakke van 'n ensiem wat die spier- en hartfunksie meet (kreatienkinase) of verhoogde vlakke van stowwe wat nierfunksie meet (bloedureum, kreatinien).
- Afnames in kalium en natrium.
- Afname in aantal witbloedselle wat ook leukopenie, agranulositose of neutropenie genoem word.
- Afname in aantal rooibloedselle (ook hemolitiese anemie genoem).
- Verhoogde uriensuurvlakke, bloedsuikervlakke, bloedcholesterol- en triglieriedvlakke, suiker in die urine.

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

Aanmelding van newe-effekte
Indien jy newe-effekte kry praat met jou dokter of apteker of verpleegkundige. Dit sluit enige moontlike newe-effekte in wat nie in hierdie inligtingstuk 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://sahpra.org.za/wp-content/uploads/2020/01/6.04_ARF1_v5.1_27Jan2020.pdf Deur newe-effekte aan te meld kan jy help om meer inligting beskikbaar te stel aangaande die veiligheid van **TROBET CO.**

5. Hoe om TROBET CO te bewaar

Bewaar by of benede 25°C (kamertemperatuur). Beskerm teen lig.
Bewaar alle medisyne buite bereik van kinders.
Bewaar in die oorspronklike verpakking/houer.
Hou die stuipstroke in die buitensie karton totdat dit benodig word vir gebruik.
Hou die HDPE houers dig gesluit.
Moet nie in 'n badkamer bêre nie.
Moet nie gebruik na die vervaldatum wat op die stuipstrook/etiket/karton/bottel aangebring 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 CO bevat

- Die aktiewe bestanddeel is 150 mg, 300 mg Irbesartan en 12,5 mg Hidrochloortiasied.
- Die ander bestanddele is Kalsiumkarboksiale metieselulose, kolloïdale silikondioksied, povidoon, natriumstyselglikolaat Tipe A, gesuiwerde talk, magnesiumstearaat, filmbedekking wat hipromelose, laktosemonohidraat, titaandioksied (kleurindeks nr. 77891), poliëtileenglikol, geel ystersoksied (kleurindeks nr. 77492), rooi ystersoksied (kleurindeks nr, 77491) bevat.

Hoe TROBET CO lyk en inhoud van die pak
TROBET CO 150/12,5:
Perskekleurige, ovaal, filmbedekte tablette, met "ML 34" op die een kant gedruk en glad aan die ander kant.
TROBET CO 300/12,5:
Perskekleurige, ovaal, filmbedekte tablette, met "ML 33" op die een kant gedruk en glad aan die ander kant.

1) Stuipverpakking:
Tablette word verpak in wit ondeursigtige film 300 mikron PVC/25 mikron PE/90 mikron PVdC as die vormingsmateriaal en 25 mikron aluminiumfoelie bedek met 6-8 gsm lakverniste hitteseël as die deksmateriaal, verpak in 'n vooraf gedrukte karton.
Verpakkingsgroottes sluit 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 hitteseëlvoering toegemaak is, en in buitensie karton verpak is.
Verpakkingsgroottes sluit 28 of 30 tablette in.
Nie alle verpakkings en verpakkingsgroottes word noodwendig bemark nie.

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

Hierdie inligtingstuk was hersien in
14 Desember 2021

Registrasienommers
TROBET CO 150/12,5: 46/7.1.3/0831
TROBET CO 300/12,5: 46/7.1.3/0832

Toegang tot die ooreenstemmende professionele inligting
Die ooreenstemmende professionele inligting kan verkry word by https://www.macleodspharma.com of stuur e-pos na macleodsrsa@macleodspharma.com of kontak 011 682 1169.

PACKAGING RESEARCH & DEVELOPMENT

MACLEODS

Restricted Circulation

(Front Page)

ARTWORK / PRINTPROOF APPROVAL FORM

1. Product: TROBET CO 150/12,5 & 300/12,5 (Irbesartan and Hydrochlorothiazide Tablet 150/12.5, 300/12,5 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 400 (W) mm
9. Design / Style: Booklet	10. Item code No.: PM03937601
11. Artwork has been made: Actual Size	12. Pharma code No.: 31840 mini
13. Barcode/NDC No: NA	14. Supersedes Item code No: NA
15. Revision no: 00	16. AW File name: Y:\Irbesartan and Hydrochlorothiazide\SA Private Market\Irbesartan and Hydrochlorothiazide Tablets PI & PIL - PM03937601.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	25/08/22	25/08/22 Cyadav 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	PM03937601		