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Wayne Mantz

SCHEDULING STATUS
S3

PROPRIETARY NAME AND DOSAGE FORM

CO-NORMOTEN 50/12.5 (Tablet)
CO-NORMOTEN 100/25 (Tablet)

COMPOSITION

Each **CO-NORMOTEN 50/12.5** tablet contains 50 mg losartan potassium and 12,5 mg hydrochlorothiazide.
Each **CO-NORMOTEN 100/25** tablet contains 100 mg losartan potassium and 25 mg hydrochlorothiazide.

Each tablet also contains the following inactive ingredients:
Microcrystalline cellulose, lactose monohydrate, pregelatinised maize starch, sodium starch glycolate Type A, magnesium stearate, opadry white with titanium dioxide.

PHARMACOLOGICAL CLASSIFICATION

A 7.1.3 Other hypotensives

PHARMACOLOGICAL ACTION
Pharmacodynamics

CO-NORMOTEN (losartan potassium-hydrochlorothiazide) combines an angiotensin II receptor (type AT_1) antagonist and a diuretic, hydrochlorothiazide.
Losartan
Angiotensin II, a potent vasoconstrictor, is the primary active hormone of the renin-angiotensin system, and a major determinant of the pathophysiology of hypertension. Angiotensin II binds to the AT_1 receptor found in many tissues (e.g. vascular smooth muscle, adrenal gland, kidneys and the heart) and elicits several important biological actions, including vasoconstriction and the release of aldosterone. Angiotensin II also stimulates smooth muscle cell proliferation. Losartan is a synthetic, orally active compound which binds selectively to the AT_1 receptor. Both losartan and its pharmacologically active carboxylic acid metabolite (E-3174) block the actions of angiotensin II, regardless of the source of synthesis. Losartan binds selectively to the AT_1 receptor and does not bind to or block other hormone receptors or ion channels important in cardiovascular regulation. Losartan does not inhibit ACE (kininase II), the enzyme that degrades bradykinin.
Hydrochlorothiazide
The mechanism of the antihypertensive effect of thiazides is unknown. Thiazides do not usually affect normal blood pressure. Hydrochlorothiazide is a diuretic and antihypertensive agent. It affects the distal renal tubular mechanism of electrolyte reabsorption. Hydrochlorothiazide increases excretion of sodium and chloride in approximately equivalent amounts. Natriuresis may be accompanied by some loss of potassium, magnesium and bicarbonate. After oral use, diuresis begins within 2 hours, peaks in about 4 hours and lasts about 6 to 12 hours.
Losartan and hydrochlorothiazide
Losartan and hydrochlorothiazide are additive in their antihypertensive efficacy.

Pharmacokinetics
__Losartan__
Absorption
Following oral administration, losartan undergoes first-pass metabolism, forming an active carboxylic acid metabolite and other inactive metabolites. The systemic bioavailability of losartan tablets is approximately 33 %. Mean peak concentrations of losartan and its active metabolite are reached in 1 hour and in 3 – 4 hours, respectively. There is no clinically significant effect on the plasma concentration profile of losartan when administered with a standardised meal.
Distribution
Both losartan and its active metabolite are > 99 % bound to plasma proteins, primarily albumin. The volume of distribution of losartan is 34 litres. Studies in rats indicate that losartan crosses the blood-brain barrier poorly, if at all.
Metabolism
About 14 % of an intravenously- or orally-administered dose of losartan is converted to its active metabolite.
Elimination
Plasma clearance of losartan and its active metabolite is about 600 ml/min and 50 ml/min, respectively. Renal clearance of losartan and its active metabolite is about 74 ml/min and 26 ml/min, respectively. When losartan potassium is administered orally, about 4 % of the dose is excreted unchanged in the urine, and about 6 % of the dose is excreted in the urine as active metabolite. The pharmacokinetics of losartan and its active metabolite are linear with oral losartan potassium doses up to 200 mg. Following oral administration, plasma concentrations of losartan and its active metabolite decline polyexponentially with a terminal half-life of about 2 hours and 6 – 9 hours, respectively. Both biliary and urinary excretion contribute to the elimination of losartan and its metabolites. Following an oral dose of ^{14}C-labelled losartan in man, about 35 % of radioactivity is recovered in the urine and 58 % in the faeces. Following oral administration in patients with mild to moderate alcoholic cirrhosis of the liver, plasma concentrations of losartan and its active metabolite were, respectively, 5-fold and 1,7-fold greater than those seen in young male volunteers.
Neither losartan nor the metabolite can be removed by haemodialysis.

__Hydrochlorothiazide__
When plasma levels have been followed for at least 24 hours, the plasma half-life has been observed to vary between 5,6 and 14,8 hours. Hydrochlorothiazide is not metabolised but is eliminated rapidly by the kidney. At least 61 % of the oral dose is eliminated unchanged within 24 hours. Hydrochlorothiazide crosses the placental but not the blood-brain barrier.

__Losartan and hydrochlorothiazide__
In a pharmacokinetic interaction study, hydrochlorothiazide 12,5 mg did not alter the pharmacokinetics of losartan 50 mg and vice versa.

INDICATIONS

CO-NORMOTEN is indicated for the treatment of hypertension in patients established on treatment with identical doses of the individual agents.

CONTRA-INDICATIONS

- Hypersensitivity to any component of this product
- Hypersensitivity to other sulphonamide-derived medicines
- A history of angioedema related to previous therapy with angiotensin receptor blockers (ARBs) or with ACE inhibitors. 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)
- Anuria – Hydrochlorothiazide may aggravate renal dysfunction
- **CO-NORMOTEN** should not be given to patients with Addison's disease
- Aortic stenosis
- Bilateral renal artery stenosis
- Renal artery stenosis in patients with a single kidney
- Concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene and amiloride
- Porphyria
- Lithium therapy: Concomitant administration with **CO-NORMOTEN** may lead to toxic blood levels of lithium
- Pregnancy and lactation - Teratogenicity has been shown in experimental animals. When pregnancy is detected, **CO-NORMOTEN** should be discontinued as soon as possible. (see **PREGNANCY AND LACTATION**)
- Paediatric use - Safety and efficacy in children has not been established

WARNINGS AND SPECIAL PRECAUTIONS

Use with caution in:
- Hypotension after cardio-infarction.
- Patients who are sodium- or volume-depleted (e.g. those who have received high-dose diuretics). Thiazide diuretics may decrease urinary calcium excretion and may cause intermittent and slight elevation of serum calcium. Marked hypercalcaemia may be evidence of hidden hyperparathyroidism. **CO-NORMOTEN** should be discontinued before carrying out tests for parathyroid function.
- Symptomatic hypotension may occur following the initiation of therapy with **CO-NORMOTEN**.
- Sodium- or volume-depletion should be corrected before initiating therapy. See (**DOSAGE AND DIRECTIONS FOR USE**).
- Patients with electrolyte imbalances – The condition may be exacerbated. The correction of electrolyte imbalance prior to administration of **CO-NORMOTEN** is recommended.
- Periodic determination of serum electrolytes should be performed at appropriate intervals, as in any patient receiving a diuretic.
- Patients with impaired renal function. The area under the curve (AUC) may be increased by approximately 50 % in patients with moderate renal function impairment. In patients whose renal function is dependent on the renin-angiotensin system, especially those with congestive heart failure, there may be a risk of **CO-NORMOTEN** - induced renal failure. These changes in renal function may be reversible upon discontinuation of therapy.
- Patients with impaired hepatic function – Increased plasma concentrations of **CO-NORMOTEN** may occur. **CO-NORMOTEN** is not indicated since dose titration with losartan is required.
- Patients with diabetes mellitus or hyperglycaemia – Thiazide diuretics may exacerbate the condition.
- Dosage adjustments of antidiabetic medicines may be needed.
- Patients with allergy or bronchial asthma – Hypersensitivity reactions to hydrochlorothiazide may be more likely in these patients.
- Patients with gout or hyperuricaemia – The condition may be exacerbated by hydrochlorothiazide.
- Losartan, however, decreases uric acid which may attenuate the diuretic-induced hyperuricaemia.
- Systemic lupus erythematosus – Hydrochlorothiazide may exacerbate or activate systemic lupus erythematosus.
- Lapp lactase deficiency or glucose-galactose malabsorption. **CO-NORMOTEN** contains lactose. Patients with rare hereditary problems of galactose intolerance should not take **CO-NORMOTEN.**
- The risk of non-melanoma skin cancer (NMSC) is associated with exposure to increasing cumulative doses of hydrochlorothiazide. Studies have shown a cumulative dose-dependent association between hydrochlorothiazide and NMSC (basal cell carcinoma, squamous cell carcinoma), which could possibly be due to the photosensitizing actions of hydrochlorothiazide.

Effects on ability to drive and use machines
CO-NORMOTEN has the following side effects: dizziness, vertigo and transient blurred vision, that may affect the ability to drive and use machines. Tolerance to **CO-NORMOTEN** should be determined before undertaking tasks that require special attention.

INTERACTIONS

__Losartan__
No medication interactions of clinical significance have been identified. Compounds which have been studied in clinical pharmacokinetic trials include hydrochlorothiazide, digoxin, warfarin, cimetidine, phenobarbital and ketoconazole.
__Hydrochlorothiazide__
When administered concurrently the following medication may interact with thiazide diuretics:
Alcohol, barbiturates, or narcotics: potentiation of orthostatic hypotension may occur.
Antidiabetic medication: (oral agents and insulin): dosage adjustment of the antidiabetic medication may be required.
Other antihypertensive medication: additive effect or potentiation.
Cholestyramine and colestipol resins: absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins. Single doses of either cholestyramine or colestipol resins bind the hydrochlorothiazide and reduce its absorption from the gastrointestinal tract by up to 85 and 43 percent, respectively. **CO-NORMOTEN** should therefore be administered one hour before the intake of the resin.
Corticosteroids, ACTH: intensified electrolyte depletion, particularly hypokalaemia.
Pressor amines (e.g. norepinephrine): possible decreased response to pressor amines but not sufficient to preclude their use.
Skeletal muscle relaxants, nondepolarising: possible increased responsiveness to the muscle relaxant.
Lithium: should not be given with diuretics. Diuretic agents reduce the renal clearance of lithium and increase the risk of lithium toxicity. Refer to the package insert for lithium preparations before use of such preparations with **CO-NORMOTEN** (see **CONTRA-INDICATIONS**).
Non-steroidal anti-inflammatory medication: In some patients, the administration of a non-steroidal anti-inflammatory agent can reduce the diuretic, natriuretic and antihypertensive effects of loop, potassium-sparing and thiazide diuretics.

PREGNANCY AND LACTATION

CO-NORMOTEN is contra-indicated during pregnancy. See CONTRA-INDICATIONS. Women of childbearing age should ensure adequate contraception. Should a woman become pregnant while taking CO-NORMOTEN, the treatment should be discontinued promptly and switched to different medicine. Should a woman contemplate pregnancy, the doctor should consider alternative medication. CO-NORMOTEN is contra-indicated during lactation. See CONTRA-INDICATIONS.

DOSAGE AND DIRECTIONS FOR USE

Adults: The usual starting and maintenance dose of **CO-NORMOTEN 50/12.5** is one tablet once daily. For patients who do not respond adequately to **CO-NORMOTEN 50/12.5**, the dosage may be increased to two tablets once daily, or one **CO-NORMOTEN 100/25** tablet daily. No initial dosage adjustment is necessary for elderly patients. The maximum antihypertensive effect is attained within three weeks after initiation of therapy.
CO-NORMOTEN may be administered with other antihypertensive agents, particularly calcium channel blockers and beta-blockers.
CO-NORMOTEN may be administered with or without food.
CO-NORMOTEN should not be initiated in patients who are intravascularly volume depleted (e.g. those treated with high-dose diuretics). See **WARNINGS AND SPECIAL PRECAUTIONS**.

SIDE EFFECTS

__Side effects__
__Losartan__
Metabolic and nutritional disorders:
Less frequent: Hyperkalaemia
Nervous system disorders:
Frequent: Headache
Less frequent: Dizziness, fatigue, insomnia
Incidence unknown: Asthenia
Cardiac disorders:
Less frequent: Palpitations, tachycardia
Incidence unknown: Chest pain
Vascular disorders:
Less frequent: Orthostatic hypotension (dose-related), oedema
Respiratory, thoracic and mediastinal disorders:
Less frequent: Upper respiratory infection, nasal congestion, pharyngitis, sinus disorder, cough
Gastrointestinal disorders:
Less frequent: Diarrhoea
Incidence unknown: Abdominal pain, dyspepsia, nausea
Hepato-biliary disorders:
Less frequent: Elevations of alanine amino transferase (ALT)
Skin and subcutaneous tissue disorders:
Less frequent: Rash
Musculoskeletal, connective tissue and bone disorders:
Less frequent: Muscle cramps or pain, back pain
Renal and urinary disorders:
Incidence unknown: Impaired renal function
Immune disorders:
Less frequent: Angioedoema (involving swelling of the face, lips and/or tongue)
__Hydrochlorothiazide__
Blood and lymphatic system disorders:
Less frequent: Agranulocytosis, leukopenia, thrombocytopenia, aplastic anaemia, haemolytic anaemia
Metabolic and nutritional disorders:
Frequent: Electrolyte disturbances, hypokalaemia, hyponatraemia, hypochloraemia
Less frequent: Hyperuricaemia
Incidence unknown: Hyperglycaemia, glycosuria
Nervous system disorders:
Incidence unknown: Vertigo, paraesthesias, headache, weakness, restlessness
Eye disorders:
Incidence unknown: Xanthopsia, transient blurred vision
Vascular disorders:
Less frequent: Orthostatic hypotension
Gastrointestinal disorders:
Less frequent: Anorexia, gastric irritation, cramping, diarrhoea, nausea, vomiting, pancreatitis
Incidence unknown: Sialadenitis
Hepato-biliary disorders:
Less frequent: Cholecystitis
Musculoskeletal, connective tissue and bone disorders:
Incidence unknown: Muscle spasm
Renal and urinary disorders:
Incidence unknown: Renal dysfunction, interstitial nephritis, renal failure
Hypersensitivity:
Less frequent: Skin rash
Incidence unknown: Urticaria, purpura, necrotizing angiitis (vasculitis), (cutaneous vasculitis), fever, respiratory distress including pneumonitis and pulmonary oedema, anaphylactic reactions
Investigations:
Incidence unknown: Increases in cholesterol and triglyceride levels

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT
Losartan
Limited data are available in regard to overdosage in humans. The most likely manifestation of overdosage would be hypotension and tachycardia, bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted. Neither losartan nor the active metabolite can be removed by hemodialysis.
Hydrochlorothiazide
The most common signs and symptoms observed are those caused by electrolyte depletion (hypokalaemia, hypochloraemia, hyponatraemia) and dehydration resulting from excessive diuresis. If digoxin has also been administered, hypokalaemia may accentuate cardiac dysrhythmias. The degree to which hydrochlorothiazide is removed by haemodialysis has not been established.

IDENTIFICATION

CO-NORMOTEN 50/12.5: Light yellow coloured, oval shaped, biconvex film coated tablet with break line in both sides.
CO-NORMOTEN 100/25: Yellow coloured, oval shaped, biconvex film coated tablets with break line on both sides.

PRESENTATION
CO-NORMOTEN 50/12.5: 11.2 mm X 6.0 mm biconvex film coated tablets are packed in blister pack using a white opaque Triplex film sealed with printed aluminium lidding foil of 30 tablets. Each carton box contains 3 cards of blister and each card contains 10 tablets.

CO-NORMOTEN 100/25: 15.5 mm X 8.7 mm biconvex film coated tablets are packed in blister pack using a white opaque Triplex film sealed with printed aluminium lidding foil of 30 tablets. Each carton box contains 3 cards of blister and each card contains 10 tablets.

STORAGE INSTRUCTIONS

Store at or below 25 °C in a dry place. Keep the blisters in the outer carton until required for use. Keep out of reach of children.

REGISTRATION NUMBER
CO-NORMOTEN 50/12.5: A42/7.1.3/0857
CO-NORMOTEN 100/25: A42/7.1.3/0858

NAME AND BUSINESS ADDRESS OF THE APPLICANT

Trinity Pharma (Pty) Limited
Oval Business Park, Wanderers Building, Unit 1B, Office A
Cnr Sloane and Meadowbrook Close
Bryanston
2194

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HANDELSNAAM EN DOSEERVORM

CO-NORMOTEN 50/12.5 (Tablet)
CO-NORMOTEN 100/25 (Tablet)

SAMESTELLING

Elke **CO-NORMOTEN 50/12.5** tablet bevat 50 mg losartaankalium en 12,5 mg hidrochloortiasied.
Elke **CO-NORMOTEN 100/25** tablet bevat 100 mg losartaankalium en 25 mg hidrochloortiasied.

Elke tablet bevat ook die volgende onaktiewe bestanddele:
Mikrokristallyne sellulose, laktosemonohidraat, vooraf-gelatiniseerde mielie stysel, natrium styselglikolaat Tipe A, magnesiumstearaat, opadry wit met titaniumdioksied.

FARMAKOLOGIESE KLASSIFIKASIE

A 7.1.3 Ander hipotensiewe middels

FARMAKOLOGIESE WERKING
Farmakodinamika

CO-NORMOTEN (losartaankalium-hidrochloortiasied) is `n kombinasie van `n angiotensien II reseptorantagonis (tipe AT_1) en `n diuretikum, hidrochloortiasied.
Losartaan
Angiotensien II, `n kragtige vasokonstriktor, is die primêre aktiewe hormoon in die renien-angiotensien sisteem, wat `n sleutelrol in die patofisiologie van hipertensie speel. Angiotensien II bind aan die AT_1 reseptor wat in verskeie weefsels gevind kan word (bv. vaskulêre gladdespier, adrenale klier, niere en die hart) en ontlok vele belangrike biologiese aktiwiteite, insluitend vasokonstriksie en die vrystelling van aldosteroon. Angiotensien II stimuleer ook die vermeerdering van gladdespierselle. Losartaan is `n sintetiese, oraalaktiewe samestelling wat selektief bind aan AT_1 reseptors. Beide losartaan en sy farmakologiese aktiewe karboksielsuurmetaboliet (E-3174) blok die werking van angiotensien II, ongeag die bron van sintese. Losartaan bind selektief aan die AT_1 reseptor en bind of blok nie ander hormoonreseptors of ioonkanale belangrik in kardiovaskulêre regulering nie. Losartaan inhibeer nie AOE (kinase II), die ensiem wat bradikinien degradeer, nie.
Hidrochloortiasied
Die meganisme van die anti-hipertensiewe effek van tiasiedmiddels is onbekend. Tiasiedmiddels affekteer gewoonlik nie normale bloeddruk nie. Hidrochloortiasied is `n diuretikum asook `n anti-hipertensiewe middel. Dit affekteer die distale renale tubulêre meganisme van elektrolietherabsorpsie. Hidrochloortiasied verhoog die uitskeiding van natrium en chloried in ongeveer gelyke hoeveelhede. Urinêre uitskeiding van natrium mag met `n mate van kalium, magnesium en bikarbonaat verlies gepaard gaan. Diurese begin binne 2 uur na orale gebruik, bereik `n klimaks in ongeveer 4 uur en duur nagenoeg 6 tot 12 uur.
Losartaan en hidrochloortiasied
Die gesamentlike gebruik van losartaan en hidrochloortiasied het `n additiewe anti-hipertensiewe effek.

Farmakokinetika
__Losartaan__
Absorpsie
Na orale toedienning, ondergaan losartaan eerstedeurgangsmetabolisme, waardeur `n aktiewe karboksielsuurmetaboliet en `n ander onaktiewe metaboliet gevorm word. Die sistemiese biobeskikbaarheid van losartaan tablette is ongeveer 33 %. Die gemiddelde piekplasmakonsentrasies van losartaan en sy onaktiewe metaboliet word binne 1 uur en 3 – 4 ure onderskeidelik bereik. Daar is geen klinies beduidende effekte op die plasmakonsentrasieprofiel van losartaan wanneer dit met `n gestandardiseerde maaltyd toegedien word nie.
Verspreiding
Losartaan en sy aktiewe metaboliet is > 99 % plasmaproteïen gebonde, hoofsaaklik aan albumien. Die volume van verspreiding van losartaan is 34 liter. Studies in rotte toon dat losartaan die bloodbreinskans swak of selfs geensins kruis nie.
Metabolisme
Omtrent 14 % van `n intraveneuse of oraal toegediende losartaan dosis word omgeskakel na sy onaktiewe metaboliet.
Uitskeiding
Plasma opruiming van losartaan en sy aktiewe metaboliet is ongeveer 600 ml/min en 50 ml/min, onderskeidelik. Renale opruiming van losartaan en sy aktiewe metaboliet is ongeveer 74 ml/min en 26 ml/min, onderskeidelik. Wanneer losartaankalium oraal geneem word, word ongeveer 4 % van die dosis onveranderd in die uriene uitgeskei en ongeveer 6 % van die dosis in die uriene as aktiewe metaboliet uitgeskei. Die farmakokinetika van losartaan en sy aktiewe metaboliet is linieêr met orale losartaankalium dosisse tot en met 200 mg. Na orale toediening neem plasmakonsentrasies van losartaan en sy aktiewe metaboliet poli-eksponensiëel af met `n terminale halfleeftyd van ongeveer 2 ure en 6 – 9 ure, onderskeidelik. Beide biliêre en urinêre ekskresie dra by tot die uitskeiding van losartaan en sy aktiewe metaboliet. Na orale toediening van `n dosis ^{14}C-gemerkte losartaan in die mens, word ongeveer 35 % van die radio-aktiwiteit in die uriene herwin en ongeveer 58 % in die feses. Na orale toediening aan pasiënte met geringe tot matige alkoholiese sirrose van die lewer, was die plasmakonsentrasies van losartaan en sy aktiewe metaboliet onderskeidelik 5-voudig en 1,7-voudig meer as dié waargeneem in jong, manlike vrywilligers. Hemodialise verwyder nie losartaan of sy aktiewe metaboliet nie.

__Hidrochloortiasied__
Wanneer plasmavlakke waargeneem word oor `n tydperk van 24 uur, kan bevind word dat die plasmahalfleeftyd tussen 5,6 en 14,8 ure wissel. Hidrochloortiasied word nie gemetaboliseer nie, maar spoedig deur die niere verwyder. Minstens 61 % van `n orale dosis word onveranderd uitgeskei binne 24 uur. Hidrochloortiasied kruis the plasenta, maar nie die bloedbreinskans nie.

__Losartaan en hidrochloortiasied__
Tydens `n farmakokinetiese interaksiestudie, het hidrochloortiasied 12,5 mg nie die farmakokinetika van losartaan 50 mg gewysig nie en omgekeerd.

INDIKASIES

CO-NORMOTEN is aangedui vir die behandeling van hipertensie in pasiënte in wie behandeling op identiese dossise van die individuele middels gebasseer is.

KONTRA-INDIKASIES

- Hipersensitiwiteit vir enige van die komponente van hierdie produk
- Hipersensitiwiteit vir ander sulfoonamiedverwante medisyne
- `n Geskiedenis van angioedeem wat verwant is aan vorige terapie met angiotensien reseptorblokkers (ARBs) of AOE inhibeerders. Hierdie middels mag nooit weer aan hierdie pasiënte voorgeskryf word nie
- Oorerflike or idiopatiese angioedeem
- Hipertrofiese obstruktiewe kardiomiopatie (HOKM)
- Erge inkorting van nierfunksie (kreatinienopruiming minder as 30 ml/min)
- Anurie – Hidrochloortiasied mag nierdisfunksie vererger
- **CO-NORMOTEN** moet nie aan pasiënte met Addison se siekte gegee word nie
- Aortiese stenose
- Bilaterale renale arterie stenose
- Renale arterie stenose in pasiënte met `n enkele nier
- Gesamentlike toediening met kaliumsparende duiretikas soos spirinolaktoon, triamtereen en amiloried
- Porfirie
- Litium terapie: Gesamentlike toediening met **CO-NORMOTEN** mag tot tokiese bloedkonsentrasies van litium lei
- Swangerskap en laktasie – Teratogenisiteit is opgemerk in proefdiere. Indien swangerskap bevestig word, moet die gebruik van **CO-NORMOTEN** so vinnig as moontlik gestaak word (sien **SWANGERSKAP EN LAKTASIE**)
- Pediatriese gebruik – Veiligheid en effektiwiteit in kinders is nog nie vasgestel nie

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS
Gebruik met oorsig in:
- Hipotensie na kardiale infarksie.
- Pasiënte met natrium of volume uitputting (bv. dié wie hoë-dosis duiretikas ontvang het). Tiasied duiretikas mag die uitskeiding van urinêre kalsium verminder en mag afwisselende en geringe verhogings in serum kalsium veroorsaak. Opgemerkte hiperkalsemie mag dui op versteekte hiperparatiroïdisme. **CO-NORMOTEN** gebruik moet gestaak word voor daar paratiroïedfunksie toetse uitgevoer word.
- Simptomatiese hipotensie mag voorkom na aanvangsterapie met **CO-NORMOTEN**.
- Natrium- en volume uitputting moet reggestel word voor aanvangsterapie begin word (sien **DOSIS EN GEBRUIKSAANWYSINGS**).
- Pasiënte met elektrolietwanbalans – Die toestand mag vererger. Dit word aanbeveel dat elektrolietwanbalanse voor toedienning van **CO-NORMOTEN** reggestel word.
- Periodieke bepaling van serum elektrolietvlakke moet met toepaslike tussenposes uitgevoer word, soos in enige pasiënt wat `n duiretika ontvang.
- Pasiënte met ingekorte nierfunksie. Die area onder die kurwe (AOK) kan verminder met ongeveer 50 % in pasiënte met matige nierversaking. In pasiënte wie se nierfunksie afhanklik is van die renien-angiotensien sisteem, veral dié met kongestiewe hartversaking, mag die risiko loop om **CO-NORMOTEN** -geïnduseerde nierversaking te ontwikkel. Nierfunksie kan omgekeer word met die staking van terapie.
- Pasiënte met ingekorte lewerfunksie – Verhoogde plasmakonsentrasies van **CO-NORMOTEN** mag voorkom. **CO-NORMOTEN** word dus teenaangedui, aangesien dosistitrasie met losartaan vereis word.
- Pasiënte met diabetes mellitus of hiperglisemie – Tiasiedduiretikas mag die toestand vererger. Dosisaanpassings van anti-diabetiese medisyne mag nodig wees.
- Pasiënte met allergie of brongiale asma – Hipersensitiwiteitsreaksies teenoor hidrochloortiasied mag meer waarskynlik in hierdie pasiënte voorkom.
- Pasiënte met jig of hiperurisemie – Hierdie toestand mag vererger word deur hidrochloortiasied. Losartaan verlaag egter uriensuur wat die duiretika-geïnduseerde hiperurisemiese effek kan verswak.
- Sistemiese lupus eritematose – Hidrochloortiasied kan sistemiese lupus eritematose vererger of aktiveer.
- Lapp laktase tekort of glukose-galaktose wanabsorpsie. **CO-NORMOTEN** bevat laktose. Pasiënte met raar, oorerflike probleme van galaktose intoleransie moet nie **CO-NORMOTEN** neem nie.
- Daar bestaan 'n risiko van nie-melanoom velkanker (NMSC) wat geassosieer word met die blootstelling aan toenemende kumulatiewe dosisse van hidrochloortiasied. Studies het gewys dat 'n kumulatiewe dosisafhanklike assosiasie tussen hidrochloortiasied en NMSC (basale selkarsinoom, plaveiselselkarsinoom) ontstaan, wat moontlik te wyte is aan die fotosensitiserende aksies van hidrochloortiasied.

Uitwerking op die vermoë om voertuie te bestuur en masjinerie te gebruik
CO-NORMOTEN het die volgende newe-effekte: Duiseligheid, vertigo en kortstondige dowwe visie, wat die vermoë om te bestuur of masjinerie te gebruik, kan beïnvloed. Toleransie teenoor **CO-NORMOTEN** moet eers bepaal word voordat take uitgevoer word wat spesiale aandag vereis.

INTERAKSIES

__Losartaan__
Geen medisinale interaksies van kliniese belang is geïdentifiseer nie. Verbindings wat in kliniese farmakokinetiese toetse bestudeer is, sluit in hidrochloortiasied, digoksien, warfarien, simetidien, fenobarbital en ketokonasool.
__Hidrochloortiasied__
Wanneer gelyktydig toegedien word, kan die volgende medikasies met tiasieddiuretika reageer:
Alkohol, barbiturate, of narkotika: mag ortostatiese hipotensie potensieer.
Anti-diabetiese medikasie: (orale middels en insulien): dosisaanpassings van die anti-diabetiese medikasie mag nodig wees.
Ander anti-hipertensiewe medikasie: additiewe effek of potensiëring.
Cholestiramien en kolestipolharse: absorpsie van hidrochloortiasied word ingekort in die teenwoordigheid van anioniese uitruilingsharse. Enkel dosisse van cholestiramien of kolestipolharse bind aan hidrochloortiasied en verminder die absorpsie uit die spysverteringskanaal met 85 en 43 persent, onderskeidelik. **CO-NORMOTEN** moet dus een uur voor die inname van die hars toegedien word.
Kortikosteroïede, AKTH: verhoogde elektrolietuitputting, veral hipokalemie.
Pressor amiene (bv. norepinefrien): moontlike verlaagde reaksie op pressor amiene, maar nie voldoende om hul gebruik uit te sluit nie.
Gladdespierverslappers, nie-depolariserend: moontlike verhoogde reaksie teenoor die spierverslapper.
Litium: moet nie saam met diuretika gegee word nie. Diuretiese middels verminder die renale opruiming van litium en verhoog die risiko van litiumtoksisiteit. Verwys na die voubiljet van litiumpreparate voor die gebruik van sulke middels saam met **CO-NORMOTEN** (sien **KONTRA-INDIKASIES**).
Nie-steroïed anti-inflammatoriese middels: In sommige pasiënte kan die toediening van 'n nie-steroïed anti-inflammatoriese middel die diuretiese, natriuretiese en antihipertensiewe effekte van lus-, kaliumsparende- en tiasieddiuretika verminder.

SWANGERSKAP EN LAKTASIE

Die gebruik van CO-NORMOTEN is teenaangedui gedurende swangerskap (sien KONTRA-INDIKASIES). Vroue van vrugbare ouderdom moet voldoende kontrasepsie verseker. Indien 'n vrou sou swanger raak tydens die gebruik van CO-NORMOTEN, moet die behandeling dadelik gestaak word en die pasiënt oorgeskakel word na 'n alternatiewe geneesmiddel. Indien 'n vrou swangerskap oorweeg, moet die geneesheer alternatiewe medikasie oorweeg. CO-NORMOTEN is teenaangedui tydens laktasie (sien KONTRA-INDIKASIES).

DOSIS EN GEBRUIKSAANWYSINGS

Volwassenes: Die normale aanvangs- en instandhoudingsdosis is een **CO-NORMOTEN 50/12.5** tablet daagliks. Indien pasiënte nie voldoende reageer teenoor **CO-NORMOTEN 50/12.5**, kan die dosis verhoog word na twee tablette daagliks, of een **CO-NORMOTEN 100/25** tablet daagliks.
Geen aanvanklike dosisaanpassing is nodig vir bejaarde pasiënte nie. Die maksimum antihipertensiewe effek word binne drie weke na aanvang van terapie bereik. **CO-NORMOTEN** kan toegedien word saam met ander antihipertensiewe middels, veral kalsiumkanaalblokkers en beta-blokkers. **CO-NORMOTEN** kan met of sonder voedsel toegedien word. **CO-NORMOTEN** moet nie geïnisieer word in pasiënte wat aan intravaskulêre volume uitputting ly nie (bv. dié wat met hoë-dosis diuretika behandel word) (sien **WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS**).

NEWE-EFFEKTE

__Losartaan__
Metaboliese en voedingsversteurings:
Minder gereeld: Hiperkalemie
Senuweestelselversteurings:
Gereeld: Hoofpyn
Minder gereeld: Duiseligheid, moegheid, slaaploosheid
Voorkoms onbekend: Astenie
Kardiale versteurings:
Minder gereeld: Hartkloppings, tagikardie
Voorkoms onbekend: Borspyn
Vaskulêre versteurings:
Minder gereeld: Ortostatiese hipotensie (dosisverwant), edeem
Respiratoriese, torakale en mediastinale versteurings:
Minder gereeld: Boonste lugweginfeksie, nasale kongestie, faringitis, sinusversteuring, hoes
Gastroïntestinale versteurings:
Minder gereeld: Diaree
Voorkoms onbekend: Abdominale pyn, dispesie, naarheid
Hepatobiliêre versteurings:
Minder gereeld: Verhogings van alanien aminotransferase (ALT)
Vel- en subkutaneuse weefselversteurings:
Minder gereeld: Uitslag
Muskuloskeletale, bindweefsel- en beenversteurings:
Minder gereeld: Spierkrampe of pyn, rugpyn
Nier- en urinêre versteurings:
Voorkoms onbekend: Verswakte nierfunksie
Immuunversteurings:
Minder gereeld: Angio-edeem (met swelling van die gesig, lippe en/of tong)
__Hidrochloortiasied__
Bloed- en limfstelselversteurings:
Minder gereeld: Agranulositose, leukopenie, trombositopenie, aplastiese anemie, hemolitiese anemie
Metaboliese- en voedingsversteurings:
Gereeld: Elektrolietstoornisse, hipokalemie, hiponatremie, hipochloremie
Minder gereeld: Hiperurisemie
Voorkoms onbekend: Hiperglisemie, glikosurie
Senuweestelselversteurings:
Voorkoms onbekend: Vertigo, parestesie, hoofpyn, swakheid, rusteloosheid
Oogversteurings:
Voorkoms onbekend: Xanthopsie, kortstondige dowwe visie
Vaskulêre versteurings:
Minder gereeld: Ortostatiese hipotensie
Gastroïntestinale versteurings:
Minder gereeld: Anoreksia, maagirritasie, krampe, diaree, naarheid, braking, pankreatitis
Voorkoms onbekend: Sialadenitis
Hepatobiliêre versteurings:
Minder gereeld: Cholesistitis
Muskuloskeletale, bindweefsel- en beenversteurings:
Voorkoms onbekend: Spierkrampe
Nier- en urinêre versteurings:
Voorkoms onbekend: Nierdisfunksie, interstisiële nefritis, nierversaking
Hipersensitiwiteit:
Minder gereeld: Veluitslag
Voorkoms onbekend: Urtikaria, purpura, nekrotiserende angitis (vaskulitis), (kutaneuse vaskulitis), koors, respiratoriese nood insluitend pneumonitis en pulmonêre edeem, anafilaktiese reaksies
Spesiale ondersoeke:
Voorkoms onbekend: Verhogings in cholesterol en trigliseriedvlakke

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN
Losartaan
Beperkte data is beskikbaar ten opsigte van oordosering by mense. Die mees waarskynlike manifestasie van oordosering sou hipotensie en tagikardie wees. Bradikardie kan voorkom as gevolg van parasimpatiese (vagale) stimulasie. Indien simptomatiese hipotensie sou voorkom, moet ondersteunende maatreëls ingestel word. Hemodialise verwyder nie losartaan of sy aktiewe metaboliet nie.
Hidrochloortiasied
Die mees algemene tekens en simptome wat waargeneem kan word is dié wat veroorsaak word deur elektrolietuitputting (hipokalemie, hipochloremie, hiponatremie) en dehidrasie as gevolg van oormatige diuresis. Indien digoksien gelyktydig toegedien is, kan hipokalemie hartaritmië beklemtoon. Die mate waartoe hidrochloortiasied deur hemodialise verwyder kan word, is nie vasgestel nie.

IDENTIFIKASIE

CO-NORMOTEN 50/12.5: Liggeelkleurige, ovaalvormige, bikonvekse filmbedekte tablet met `n breeklyn aan beide kante.
CO-NORMOTEN 100/25: Geelkleurige, ovaalvormige, bikonvekse filmbedekte tablet met `n breeklyn aan beide kante.

AANBIEDING
CO-NORMOTEN 50/12.5: 11.2 mm X 6.0 mm bikonveks filmbedekte tablette word in stulpverpakkings verpak en met 'n wit, ondeursigtige Triplex-film verseël met 'n gedrukte aluminium verseëlingsfoelie van 30 tablette. Elke kartondoos bevat 3 stulpverpakkingskaarte en elke kaart bevat 10 tablette.

CO-NORMOTEN 100/25: 15.5 mm X 8.7 mm bikonveks filmbedekte tablette word in stulpverpakkings verpak en met 'n wit, ondeursigtige Triplex-film verseël met 'n gedrukte aluminium verseëlingsfoelie van 30 tablette. Elke kartondoos bevat 3 stulpverpakkingskaarte en elke kaart bevat 10 tablette.

BERGINGSINSTRUKSIES

Bewaar by of benede 25 °C in `n droë plek.
Hou die stulpverpakkings in die buitenste kartondoos totdat dit benodig word vir gebruik.
Hou buite bereik van kinders.

REGISTRASIENOMMERS
CO-NORMOTEN 50/12.5: A42/7.1.3/0857
CO-NORMOTEN 100/25: A42/7.1.3/0858

NAAM EN BESIGHEIDSADRES VAN DIE APPLIKANT

Trinity Pharma (Edms) Beperk
Oval Besigheids Park, Wanderers Gebou, Eenheid 1B, Kantoor A
H/v Sloane en Meadowbrook Straat
Bryanston
2194

DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET
30 September 2016

300 x 450 mm
F/B

NAME OF MEDICINAL PRODUCT

CO-NORMOTEN 50/12.5 (Tablet)
CO-NORMOTEN 100/25 (Tablet)

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

SCHEDULING STATUS
S3

WHAT CO-NORMOTEN CONTAINS
CO-NORMOTEN 50/12.5 are tablets containing 50 mg of losartan potassium and 12,5 mg of hydrochlorothiazide as the active ingredients.

CO-NORMOTEN 100/25 are film coated tablets containing 100 mg of losartan potassium and 25 mg of hydrochlorothiazide as the active ingredients.

In addition, CO-NORMOTEN contains the following inactive ingredients:
Microcrystalline cellulose, lactose monohydrate, pregelatinised maize starch, sodium starch glycolate Type A, magnesium stearate, Opadry white with titanium dioxide.

WHAT CO-NORMOTEN IS USED FOR
CO-NORMOTEN tablets contain a combination of angiotensin II receptor antagonist (losartan) and a diuretic (hydrochlorothiazide). Losartan and hydrochlorothiazide work together to lower blood pressure. Your doctor has prescribed **CO-NORMOTEN** because you have a condition known as hypertension or high blood pressure.

BEFORE YOU TAKE CO-NORMOTEN
Use in children
There is no experience with the use of **CO-NORMOTEN** in children. Therefore, **CO-NORMOTEN** should not be given to children.

Use in the elderly
Most older patients require the same dose as younger patients.

Do not take CO-NORMOTEN:
- If you are allergic to any of the ingredients in this medicine.
- If you are allergic to other sulphonamide-derived medicines (ask your doctor if you are not sure what sulphonamide medicines are).
- If you have a history of swelling under the skin particularly on the facial area related to previous treatment with an angiotensin receptor blocker. This condition of swelling could be hereditary or may occur without any particular reason, if this is the case do not take **CO-NORMOTEN.**
- If you have severe kidney problems or are not passing urine.
- If you have porphyria.
- If you have heart problems.
- If you are taking potassium sparing diuretics (water tablets).
- If you are on lithium therapy, taking **CO-NORMOTEN** together with lithium could lead to toxic levels of lithium.
- If you have Addison's disease.
- If you have narrowing of the arteries to both kidneys or if you have a single kidney narrowing of the artery to that kidney.
- If you are not sure whether you should start taking **CO-NORMOTEN**, contact your doctor.

Take special care with CO-NORMOTEN:
- If you have electrolyte imbalances, it is recommended that before you start taking **CO-NORMOTEN** the imbalance is corrected.
- If you have impaired kidney or liver function. Your doctor may change your medication or adjust the dose you are taking.
- If you are diabetic.
- If you suffer from allergies or asthma, inform your doctor as you are more likely to be hypersensitive to the hydrochlorothiazide in **CO-NORMOTEN.**
- If you suffer from gout or high levels of uric acid.
- If you have lupus erythematosus.
- Tell your doctor or pharmacist about any medical problems you have or have had, and about any allergies. Tell your doctor if you have recently suffered from excessive vomiting or diarrhoea.
- Before surgery and anaesthesia (even at the dentist's office), tell the doctor or dentist that you are taking **CO-NORMOTEN** as there may be a sudden fall in blood pressure associated with the anaesthesia.
- There is a risk of developing non-melanoma skin cancer (NMSC) when cumulative doses of hydrochlorothiazide is taken.

Taking CO-NORMOTEN with food and drink:
CO-NORMOTEN may be taken with or without food.

Pregnancy and Breast-feeding:
You should not use **CO-NORMOTEN** while you are pregnant or breast-feeding. If you are pregnant or become pregnant while taking **CO-NORMOTEN**, stop taking **CO-NORMOTEN** and tell your doctor immediately.

Driving and using machinery:
You should not perform tasks which may require special attention (for example, driving an automobile or operating dangerous machinery) until you know how you tolerate your medicine.

Important information about some of the ingredients of CO-NORMOTEN:
CO-NORMOTEN contains lactose which is a type of sugar. If you have been told by your doctor that you cannot tolerate or digest some sugars (have an intolerance to sugars), talk to your doctor before taking **CO-NORMOTEN.**

Taking other medicines with CO-NORMOTEN:
If you are taking other medicines on a regular basis, including complementary or traditional medicines, the use of **CO-NORMOTEN** with these medicines may cause undesirable interactions. Please consult your doctor, pharmacist or other healthcare professional, for advice. If you are taking other medicines on a regular basis, concomitant use of **CO-NORMOTEN** may cause undesirable interactions. Please consult your doctor or pharmacist. You should tell your doctor about all medicines that you are taking, including those obtained without a prescription. It is especially important for your doctor to know if you are taking other medicines, including medicines that are used to reduce blood pressure, other diuretics (water tablets), medications to treat diabetes including insulin, resins which reduce high cholesterol, muscle relaxants, cold and flu medicines, steroids, certain pain and arthritis medicines, or lithium (a medicine used to treat a certain kind of depression), sedatives, tranquilizers, narcotics, alcohol and analgesics may increase the blood pressure-lowering effect of **CO-NORMOTEN**, so tell your doctor if you take any of these medicines.

HOW TO TAKE CO-NORMOTEN
Take **CO-NORMOTEN** every day, exactly as your doctor has instructed. It is important to continue taking **CO-NORMOTEN** for as long as your doctor prescribes it in order to maintain smooth control of your blood pressure. The usual dose of **CO-NORMOTEN** for most patients is 1 tablet of **CO-NORMOTEN 50/12.5** per day to control blood pressure over the 24 hour period. In some patients, your doctor may increase the dose to 2 tablets of **CO-NORMOTEN 50/12.5** per day or 1 tablet of **CO-NORMOTEN 100/25** tablet per day.

CO-NORMOTEN can be taken with or without food. For convenience and to help you remember, try to take **CO-NORMOTEN** at the same time each day.

If you take more of CO-NORMOTEN than you should:
In case of an overdose, contact your doctor or pharmacist immediately so that medical attention may be given promptly. If neither is available, seek help at the nearest hospital or poison control centre.

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

POSSIBLE SIDE-EFFECTS
CO-NORMOTEN can have side-effects.
Not all side-effects reported for CO-NORMOTEN are included in this leaflet. Should your general health worsen while taking CO-NORMOTEN, please consult your doctor, pharmacist or other health care professional for advice.
If any of the side-effects occur you must contact your doctor immediately or go to the nearest hospital: Swelling underneath the surface of the skin, swelling of your lips, throat or tongue, difficulty breathing, noticing that your skin or eyes are a yellow colour (jaundice) and severe stomach pain.
Other side-effects that may occur include:
- Unable to sleep, headache, dizziness
- Cough, upper airway infection, congestion in the nose, sinusitis, sinus disorder
- Diarrhoea, abdominal pain, nausea, indigestion
- Muscle pain or cramps, leg pain, back pain
- Weakness, tiredness, chest pain
- Increased potassium levels (which can cause an abnormal heart rhythm)
- Blurred vision, worsening eyesight
- Low blood pressure, which may be associated with changes in posture (feeling light headed or weak when you stand up), chest pain, palpitations
- Inflammation of the pancreas
- Hives, itching, inflammation of the skin, rash, redness of the skin, flushing, sweating

Tell your doctor or pharmacist promptly about these or any other unusual symptoms.

STORAGE AND DISPOSING OF CO-NORMOTEN
Do not use this medicine after the expiry date stated on the outer carton or the blister strip inside the carton. Store at or below 25 °C in a dry place. In order to protect from the moisture do not store in the bathroom. Keep the blisters in the outer carton until required for use. Do not share medicines prescribed for you, with others. Keep all medicines out of the reach and sight of children.

PRESENTATION OF CO-NORMOTEN
CO-NORMOTEN 50/12.5: 11.2 mm X 6.0 mm biconvex film coated tablets are packed in blister pack using a white opaque Triplex film sealed with printed aluminium lidding foil of 30 tablets. Each carton box contains 3 cards of blister and each card contains 10 tablets.

CO-NORMOTEN 100/25: 15.5 mm X 8.7 mm biconvex film coated tablets are packed in blister pack using a white opaque Triplex film sealed with printed aluminium lidding foil of 30 tablets. Each carton box contains 3 cards of blister and each card contains 10 tablets.

IDENTIFCATION OF CO-NORMOTEN
CO-NORMOTEN 50/12.5: Light yellow coloured, oval shaped, biconvex film coated tablet with break line on both sides.
CO-NORMOTEN 100/25: Yellow coloured, oval shaped, biconvex film coated tablets with break line on both sides.

REGISTRATION NUMBER
CO-NORMOTEN 50/12.5: A42/7.1.3/0857
CO-NORMOTEN 100/25: A42/7.1.3/0858

NAME AND BUSINESS ADDRESS OF THE APPLICANT
Trinity Pharma (Pty) Ltd.
Oval Business Park, Wanderers Building, Unit 1B, Office A
Cnr Sloane and Meadowbrook Close
Bryanston
2194

DATE OF PUBLICATION
30 September 2016

GENEESMIDDELNAAM

CO-NORMOTEN 50/12.5 (Tablet)
CO-NORMOTEN 100/25 (Tablet)

Lees hierdie pamflet sorgvuldig deur voordat jy CO-NORMOTEN begin gebruik
Bewaar hierdie pamflet. Dit mag nodig wees om dit later weer te lees. Indien jy enige verdere vrae het, raadpleeg asseblief jou dokter of apteker. **CO-NORMOTEN** is vir jou persoonlik voorgeskryf en moenie met ander persone gedeel word nie. Dit mag skadelik vir hul wees, selfs al het hulle dieselfde simptome as jy.

SKEDULERINGSTATUS
S3

WAT CO-NORMOTEN BEVAT
CO-NORMOTEN 50/12.5 is tablette wat 50 mg losartaankalium en 12,5 mg hidrochloortiasied bevat as die aktiewe bestanddele.

CO-NORMOTEN 100/25 is tablette wat 100 mg losartaankalium en 25 mg hidrochloortiasied bevat as die aktiewe bestanddele.

Daarbenewens, bevat CO-NORMOTEN die volgende onaktiewe bestanddele:
Mikrokristallyne sellulose, laktosemonohidraat, vooraf-gelatiniseerde mielie stysel mielieblom, natriumstyselglikolaat Tipe A, magnesiumstearaat, opadry wit met titaniumdioksied.

WAARVOOR CO-NORMOTEN GEBRUIK WORD
CO-NORMOTEN tablette bevat 'n kombinasie van `n angiotensien II reseptorantagonis (losartaan) en 'n waterpil (hidrochloortiasied). Losartaan en hidrochloortiasied werk saam om jou bloeddruk te verlaag. Jou dokter het **CO-NORMOTEN** vir jou voorgeskryf, want jy ly aan 'n toestand wat bekend staan as hipertensie of hoë bloeddruk.

VOORDAT JY CO-NORMOTEN GEBRUIK
Gebruik in kinders
Daar is geen ondervinding met die gebruik van **CO-NORMOTEN** in kinders nie. Daarom moet **CO-NORMOTEN** nie aan kinders gegee word nie.

Gebruik in bejaardes
Meeste ouer pasiënte benodig dieselfde dosis as jonger pasiënte.

Moenie CO-NORMOTEN gebruik:
- Indien jy allergies is vir enige van die bestanddele in hierdie medisyne.
- Indien jy allergies is vir ander sulfoonamiedverwante medisyne (vra jou dokter as jy nie seker is wat sulfoonamied medisyne is nie).
- Indien jy `n geskiedenis van swelling onder die vel het, veral op jou gesig, veral as dit verband hou met vorige gebruik van angiotensien reseptorblokkers. Hierdie kondisie kan oorerflik wees en mag enige tyd voorkom vir geen spesifieke rede. Indien dit die geval is, moet **CO-NORMOTEN** nie voorgeskryf word nie.
- Indien jy aan ernstige nierprobleme ly of sukkel om te urineer.
- Indien jy aan porfirie ly.
- Indien jy hartprobleme het.
- Indien jy kaliumsparende waterpille gebruik.
- Indien jy litiumterpaie ontvang. Toksiese vlakke van litium mag voorkom indien **CO-NORMOTEN** en litium saam geneem word.
- Indien jy aan Addison se siekte ly.
- Indien jou arterieë na albei niere vernou is, of indien u `n enkele vernouing van die slagaar na die nier het.
- Indien jy nie seker is of jy **CO-NORMOTEN** moet neem nie, raadpleeg asseblief jou dokter.

Neem spesiale sorg met CO-NORMOTEN:
- Indien jy `n elektrolietwanbalans het, word dit aanbeveel dat jy eers die wanbalans regstel voordat jy **CO-NORMOTEN** begin gebruik.
- Indien jy verswakte nier- of lewerfunksies het. Jou dokter kan jou medikasie verander of jou dosis aanpas.
- Indien jy `n diabeet is.
- Indien jy aan allergieë of asma ly moet jy jou dokter inlig, aangesien jy meer geneig kan wees om hipersensitief teenoor hidrochloortiasied in **CO-NORMOTEN** te wees.
- Indien jy ly aan jig of hoë vlakke van uriensuur.
- Indien jy aan lupus eritematose ly.
- Stel jou dokter of apteker in kennis van enige mediese problem wat jy het of gehad het ten op sigte van enige allergieë. Stel jou dokter in kennis indien jy onlangs aan oormatige braking of diarree gely het.
- Stel die dokter of tandarts in kennis voor operasies en narkose (selfs by die tandarts) dat jy **CO-NORMOTEN** gebruik, aangesien daar `n skielike daling in bloeddruk mag voorkom met die toedienning van narkose.
- Daar is 'n risiko om nie-melanoom velkanker (NMSC) te ontwikkel wanneer kumulatiewe dossise van hidrochloortiasied geneem word.

Neem van CO-NORMOTEN met voedsel en vloeistowwe:
CO-NORMOTEN kan met of sonder voedsel geneem word.

Swangerskap en Borsvoeding:
Jy moet nie **CO-NORMOTEN** gebruik indien jy swanger is of borsvoed nie. Indien jy swanger is of swanger wil raak terwyl jy **CO-NORMOTEN** neem, moet jy dadelik ophou om **CO-NORMOTEN** te neem en dadelik jou dokter raadpleeg.

Bestuur en gebruik van masjinerie:
Moenie take uitvoer wat spesiale aandag vereis (byvoorbeeld bestuur van jou motor of die gebruik van gevaarlike masjinerie) totdat jy seker is hoe jy jou medisyne verdra nie.

Belangrike inligting oor die bestanddele in CO-NORMOTEN:
CO-NORMOTEN bevat laktose wat `n soort suiker is. Stel jou dokter in kennis dat jy sekere suikers nie kan verdra of verteer nie (onverdraagsaamheid teenoor suiker). Raadpleeg jou dokter voordat jy **CO-NORMOTEN** neem.

Neem van ander medisyne saam met CO-NORMOTEN:
Indien jy gereeld ander medisyne gebruik, insluitend aanvullings of tradisionele medisyne, kan die gelyktydige gebruik met **CO-NORMOTEN** en hierdie middels ongewenste interaksies voroorsaak. Raadpleeg asseblief jou dokter, apteker of gesondheidswerker vir advies. Stel jou dokter in kennis van enige medisyne wat jy tans neem, insluitend die wat sonder `n voorskrif verkry kan word. Dit is veral belangrik dat u dokter weet indien jy ander medisyne gebruik, insluitend medisyne wat gebruik word om jou bloeddruk te verlaag, ander waterpille, medikasie om diabetes te behandel (insluitend insulien), harse vir die behandeling van hoë cholesterol, spierverslappers, verkoue en griep medisyne, steroïedes, sekere tipes pyn- en artritis medikasies, litium (vir die behandeling van sekere soort depressie), slaapmiddels, kalmeermiddels, verdowingsmiddels, dwelmmiddels, alkohol en pynstillers wat die bloeddrukverlagende effek van **CO-NORMOTEN** kan verhoog. Stel jou dokter in kennis indien jy enige van die bogenoemde medikasies gebruik.

HOE OM CO-NORMOTEN TE NEEM
Neem **CO-NORMOTEN** elke dag, presies soos u dokter aan u verduidelik het. Dit is belangrik om aan te hou om **CO-NORMOTEN** te gebruik, so lank as wat u dokter dit voorskryf om jou bloeddruk optimaal te beheer. Die normale dosis **CO-NORMOTEN** vir meeste pasiënte is 1 tablet **CO-NORMOTEN 50/12.5** per dag om bloeddruk te beheer oor `n periode van 24 uur. In sommige pasiënte kan jou dokter die dosis verhoog tot 2 tablette **CO-NORMOTEN 50/12.5** per dag of 1 tablet **CO-NORMOTEN 100/25** per dag.

CO-NORMOTEN kan met of sonder voedsel geneem word. Vir gemaklikheids onthalwe en om jou te help onthou, probeer om **CO-NORMOTEN** op dieselfde tyd elke dag te neem.

Indien jy meer CO-NORMOTEN geneem het as wat jy moet:
In die geval van `n oordosis, kontak jou dokter of apteker onmiddellik sodat mediese hulp dadelik toegepas kan word. Indien beide nie beskikbaar is nie, soek hulp by die naaste hospitaal of gifbeheersentrum.

Indien jy vergeet het om CO-NORMOTEN te neem:
Probeer om **CO-NORMOTEN** daagliks te neem soos voorgeskryf. Indien jy egter `n dosis mis, moet jy nie `n ekstra dosis neem nie. Gaan slegs voort met jou normale skedule.

MOONTLIKE NEWE-EFFEKTE
CO-NORMOTEN kan newe-effekte hê.
Nie alle newe-effekte wat vir CO-NORMOTEN aangemeld is, word in hierdie pamflet ingesluit nie. Indien jou algemene gesondheid verswak wanneer jy CO-NORMOTEN neem, moet jy jou dokter, apteker of gesonheidswerker kontak vir advies.
Indien enige van die volgende newe-effekte voorkom, moet jy dadelik jou dokter kontak of na die naaste hospitaal toe gaan: Swelling onder die oppervlak van die vel, swelling van jou lippe, keel of tong, moeilike asemhaling, geel verkleuring (geelsug) van die vel of oë, erge maagpyn.
Ander newe-effekte wat mag voorkom, sluit in:
- Slaaploosheid, hoofpyn, duiseligheid
- Hoes, boonste lugweginfeksie, kongestie van die neus, sinusitis, sinusversteurings
- Diarree, maagpyn, naarheid, sooibrand
- Spierpyn en krampe, beenpyn, rugpyn
- Swakheid, moegheid, borspyn
- Verhoogde kaliumvlakke (wat abnormale hartritme kan veroorsaak)
- Dowwe visie, verswakte sig
- Lae bloeddruk, wat met verandering in postuur gepaard kan gaan (gevoel van lighoofdigheid, swakheid wanneer jy opstaan, borspyn, hartkloppings)
- Inflammasie van die pankreas
- Galbulte, jeuk, inflammasie van die vel, uitslag, rooiheid van die vel, gloede, sweet

Stel jou dokter of apteker dadelik in kennis indien jy enige van hierdie newe-effekte of ander ongewone simptome ervaar.

BEWARING EN WEGDOEN VAN CO-NORMOTEN
Moenie hierdie medisyne gebruik na die vervaldatum wat op die buitenste karton en op die stulpverpakking aangedui is nie.
Bewaar by of onder 25 °C in `n droë plek. Om die produk te beskerm teen vog, moet dit nie in die badkamer gestoor word nie. Hou die stulpverpakkings in die buitenste karton totdat dit benodig word vir gebruik. Moenie medisyne wat vir jou voorgeskryf is deel met ander nie. Hou alle medisyne buite die bereik en sig van kinders.

AANBIEDING VAN CO-NORMOTEN
CO-NORMOTEN 50/12.5: 11.2 mm X 6.0 mm bikonveks filmbedekte tablette word in stulpverpakkings verpak en met 'n wit, ondeursigtige Triplex-film verseël met 'n gedrukte aluminium verseëlingsfoelie van 30 tablette. Elke kartondoos bevat 3 stulpverpakkingskaarte en elke kaart bevat 10 tablette.

CO-NORMOTEN 100/25: 15.5 mm X 8.7 mm bikonveks filmbedekte tablette word in stulpverpakkings verpak en met 'n wit, ondeursigtige Triplex-film verseël met 'n gedrukte aluminium verseëlingsfoelie van 30 tablette. Elke kartondoos bevat 3 stulpverpakkingskaarte en elke kaart bevat 10 tablette.

IDENTIFIKASIE VAN CO-NORMOTEN
CO-NORMOTEN 50/12.5:
Liggeelkleurige, ovaalvormige, bikonvekse filmbedekte tablet met `n breeklyn aan beide kante.
CO-NORMOTEN 100/25:
Geelkleurige, ovaalvormige, bikonvekse filmbedekte tablet met `n breeklyn aan beide kante.

REGISTRASIENOMMERS
CO-NORMOTEN 50/12.5: A42/7.1.3/0857
CO-NORMOTEN 100/25: A42/7.1.3/0858

NAAM EN BESIGHEIDSADRES VAN DIE APPLIKANT
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