REPREX
P1529149

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SKEDULERINGSTATUS

SUID-AFRIKA: S3

NAMIBIË: NS2

EIENDOMSNAAM (en doseervorm):

REPREX 2 mg (tablet)
REPREX 4 mg (tablet)
REPREX 8 mg (tablet)

SAMESTELLING:

REPREX 2 mg:
Elke onbedekte tablet bevat perindopril tert-butielamien 2 mg. Bevat suiker: 29.665 mg laktose.

REPREX 4 mg:
Elke onbedekte tablet bevat perindopril tert-butielamien 4 mg. Bevat suiker: 59.33 mg laktose.

REPREX 8 mg:
Elke onbedekte tablet bevat perindopril tert-butielamien 8 mg. Bevat suiker: 118.66 mg laktose.

Die ander bestanddele is mikrokristallyne sellulose, magnesiumstearaat en hidrofobiese anhidriese kolloïdale silika.

FARMAKOLOGIESE KLASSIFIKASIE:
A 7.1.3 Vaskulêre medisyne - ander hipotensiewe middels

FARMAKOLOGIESE WERKING:

Farmakodinamika
Perindopril is 'n spesifieke, nie-sulfhidriel mededingende angiotensien-I omskakelingsensiem (AOE) inhibeerder. Dit inhibeer die omskakeling van relatief onaktiewe angiotensien I na die aktiewe angiotensien II. Angiotensien II is 'n kragtige vasokonstriktor en stimuleer die vrystelling van aldosteroon. Verminderde angiotensien II vlakke het tot gevolg 'n afname in vasopressor aktiwiteit en 'n afname in aldosteroon afskeiding, wat kan lei tot klein toenames in serum kalium. Dit is ook van mening dat AOE - inhibisie die afbraking van bradikinien kan inhibeer wat lei tot verhoogde bradikinien vlakke. Perindopril werk deur sy aktiewe metaboliet, perindoprilat. Die ander metaboliete is farmakologies onaktief.

Farmakokinetika
Na orale toediening is die absorpsie van perindopril vinnig (piek konsentrasie binne 1 uur), en redelik volledig (plasma-beskikbaarheid bo 75 %). Die piek konsentrasie van die aktiewe metaboliet, perindoprilat, word bereik binne 3 tot 4 ure en piek farmakologiese aktiwiteit is verkry binne 4 tot 6 ure.

In terme van trog teenoor piek bloeddruk effek, wissel die trog effek tussen 75-100 % van die piek effek. Beide perindopril en perindoprilat het 'n lae volume van distribusie en plasmaproteïen binding is laag. Perindoprilat bind aan AOE by beide weefsel en plasmavlakke.

Afgesien van die aktiewe perindoprilat, gee perindopril aanleiding tot 5 metaboliete wat almal onaktief is. Perindopril word uitgeskei in die uriene en die halfleeftyd van sy vrye gedeelte is ongeveer een uur. Afbreking van die band tussen perindoprilat en die AOE lei tot 'n farmakodinamiese halfleeftyd van ongeveer 25 ure. By bejaardes, sowel as by pasiënte met hartversaking of nierversaking, is die eliminasie van perindoprilat stadiger. By sulke pasiënte moet dosering aanpassing toegepas word in verhouding tot die graad van vermindering in kreatinienopruiming.

Vermindering in bloeddruk by pasiënte wat behandel was met perindopril was vergesel deur 'n vermindering in die perifere weerstand met geen noemenswaardige veranderinge in glomerulêre filtrasie koers of hartklop.

'n Toename in die nakoming van groot arteries is ook waargeneem, wat dui op 'n direkte effek op arteriële gladdespier, in ooreenstemming met die resultate van dierestudies.

INDIKASIES:

REPREX tablette is aangedui by:
- Ligte tot matige hipertensie.
- Kongestiewe hartversaking nie voldoende beheer deur konvensionele terapie met diuretika en digitalis en by wie vasodilatasie aangedui word.

KONTRA-INDIKASIES:

REPREX tablette is teenaangedui by:
- Sensitiwiteit vir enige van die komponente van **REPREX**.
- 'n Geskiedenis van angio-edeem verwant aan vorige terapie met AOE inhibeerders of angiotensien reseptor blokkeerders (ARBs): Hierdie pasiënte moet nooit weer hierdie medisyne gegee word nie .
- Oorerflike of idiopatiese angio-edeem.
- Hipertrofiese obstruktiewe kardiomiopatie (HOKM).
- Ernstige nierfunksie-inkorting (kreatinienopruiming minder as 30 ml / min).
- Bilaterale renale arterie stenose.
- Renale arterie stenose by pasiënte met 'n enkele nier.
- Aortiese stenose.
- Gepaardgaande terapie met kalium sparende diuretika soos spironolaktoon, triamtereen, amiloried.
- Porfirie.
- Tiasied diuretika in (vastedosis) kombinasie met **REPREX** moet nie gegee word aan pasiënte met Addison se siekte nie. Hierdie terapie is teenaangedui by pasiënte met ernstige renale inkorting of anurie, en by pasiënte wat hipersensitiwiteit toon teenoor ander sulfonamied-verwante medisynes.
- Litiumterapie: Gepaardgaande toediening met **REPREX** kan lei tot toksiese bloedkonsentrasies van litium.
- Swangerskap en laktasie (sien **"WAARSKUWINGS EN SPESIALE VOORSORGSMAATREËLS"** en **"SWANGERSKAP EN LAKTASIE"**).
- Kinders: Die veiligheid van **REPREX** in kinders is nie vasgestel nie.

WAARSKUWINGS EN SPESIALE VOORSORGSMAATREËLS:

Indien 'n vrou swanger raak terwyl sy REPREX ontvang, moet die behandeling dadelik gestop word een oorgeskakel word na 'n ander klas van medisyne. Indien 'n vrou swangerskap oorweeg, moet die dokter alternatiewe medikasie oorweeg.
(Sien "KONTRA-INDIKASIES" en "SWANGERSKAP EN LAKTASIE").

Hipotensie:
AOE-inhibeerders, soos in **REPREX**, kan 'n daling in bloeddruk veroorsaak. Simptomatiese hipotensie is selde gesien by ongekompliseerde hipertensiewe pasiënte en is meer geneig om voor te kom by pasiënte wat reeds volume-uitgeput is, bv. deur diuretika-terapie, dieet sout beperking, dialise, diarree of braking, of wie ernstige renien-afhanklike hipertensie het. By pasiënte met simptomatiese hartversaking, met of sonder geassosieerde renale ontoereikendheid, was simptomatiese hipotensie waargeneem. Dit is mees waarskynlik om voor te kom by pasiënte met meer ernstige grade van hartversaking, soos weerspieël deur die gebruik van hoë dosisse van lus diuretikums, hiponatremie of funksionele renale inkorting. By pasiënte met 'n verhoogde risiko van simptomatiese hipotensie, moet aanvangs van terapie en dosisaanpassing noukeurig dopgehou word. Soortgelyke oorwegings geld vir pasiënte met isgemiese hart of serebrovaskulêre siekte by wie 'n oormatige daling in bloeddruk kan lei tot 'n miokardiale infarksie of serebrovaskulêre ongeluk. Indien hipotensie voorkom, behoort die pasiënt in die rugliggende posisie geplaas word en, indien nodig, 'n intraveneuse infusie van normale soutoplossing ontvang. 'n Verbygaande hipotensiewe reaksie is nie 'n kontra-indikasie vir verdere dosisse nie, wat gewoonlik gegee kan word sonder probleme, wanneer die bloeddruk verhoog het na volume uitbreiding.
By sommige pasiënte met kongestiewe hartversaking, wat normale of lae bloeddruk het, kan addisionele verlaging van sistemiese bloeddruk voorkom met **REPREX**. Indien hipotensie simptomaties word, kan 'n vermindering van die dosis of staking van **REPREX** nodig wees.

Aortiese-en mitrale klep stenose / hipertrofiese kardiomiopatie:
REPREX moet met omsigtigheid gegee word aan pasiënte met mitrale klep stenose en obstruksie in die uitvloei van die linker ventrikel, soos aortiese stenose of hipertrofiese kardiomiopatie (sien "**KONTRA-INDIKASIES**").

Ingekorte renale funksie:
In gevalle van renale inkorting (kreatinienopruiming <60 ml/min), moet die aanvanklike **REPREX** dosering aangepas word volgens die pasiënt se kreatinienopruiming en dan as 'n funksie van die pasiënt se reaksie op die behandeling (sien **"Nier ontoereikendheid"**). Roetine monitering van kalium en kreatinien is deel van die normale mediese praktyk vir hierdie pasiënte. By pasiënte met simptomatiese hartversaking, hipotensie na aanleiding van die aanvang van terapie met AOE-inhibeerders, soos in **REPREX** kan lei tot verdere inkorting in nierfunksie. Akute nierversaking is gerapporteer in die situasie.By pasiënte met bilaterale renale arterie stenose, of stenose van die arterie na 'n enkel nier, en wat met AOE-inhibeerders behandel is, soos in **REPREX**, kan verhogings in die bloed ureum en serum kreatinien voorkom (sien "**KONTRA-INDIKASIES**"). Dit is gewoonlik omkeerbaar by staking van terapie.

Dit is veral waarskynlik by pasiënte met renale inkorting. Indien renovaskulêre hipertensie ook teenwoordig is, is daar 'n verhoogde risiko van ernstige hipotensie en renale ontoereikendheid. By die pasiënte moet behandeling begin word onder streng mediese toesig met lae dosisse en sorgvuldige dosis titrasie. Aangesien behandeling met diuretika 'n bydraende faktor tot die bogenoemde kan wees, moet dit gestaak word en nierfunksie moet gemonitor word tydens die eerste weke van **REPREX** terapie. Sommige hipertensiewe pasiënte met geen skynbare bestaande nier vaskulêre siekte het toenames in bloed ureum en serum kreatinien ontwikkel, veral wanneer **REPREX** gelyktydig met 'n diuretika gegee was. Dit is meer waarskynlik om voor te kom by pasiënte met voorafbestaande nierinkorting. Dosering vermindering en / of staking van die diuretika en / of **REPREX** kan vereis word. By akute miokardiale infarksie, moet behandeling met **REPREX** nie geïnisieer word by pasiënte met bewyse van renale disfunksie (serum kreatinien-konsentrasies van meer as 177 mikromol/l of proteïenurie meer as 500 mg/24 ure). Indien renale disfunksie ontwikkel tydens behandeling (serum kreatinien konsentrasies van meer as 177 mikromol/l of verdubbeling van die pre-behandeling waarde) kan dit nodig wees om **REPREX** te onttrek (sien ook "**KONTRA-INDIKASIES**"). By akute miokardiale infarksie, kan pasiënte aanhoudende hipotensie en/of ingekorte nierfunksie ontwikkel.

Hemodialise pasiënte:
Anafilaktiese reaksies is aangemeld in pasiënte gedialiseer met hoë vloed membrane, en gelyktydig behandel met 'n AOE-inhibeerder, soos by **REPREX**. By hierdie pasiënte moet oorweging gegee word aan die gebruik van 'n ander soort dialise membraan of ander klas van antihipertensiewe agent.

Nieroorplanting:
Daar is geen ondervinding met betrekking tot die toediening van **REPREX** by pasiënte met 'n onlangse nieroorplanting nie.

Hipersensitiwiteit / angio-edeem:
Angio-edeem van die gesig, lippe, slymvliese, tong, glottis en / of larinks, en ledemate is aangemeld, by pasiënte wat behandel is met **REPREX** (sien "**KONTRA-INDIKASIES**"). Dit kan enige tyd voorkom gedurende behandeling. In sulke gevalle, moet **REPREX** onmiddellik gestaak word en geskikte monitering moet ingestel word en voortduur totdat die simptome heeltemal verdwyn het. In daardie gevalle waar die swelling beperk was tot die gesig en lippe, het die toestand gewoonlik sonder behandeling opgelos, alhoewel antihistamiene nuttig was in die verligting van simptome.
Angio-edeem geassosieer met laringeale edeem mag fataal wees. Waar daar betrokkenheid is van die tong, glottis of larinks, en waarskynlik is om lugweg obstruksie te veroorsaak, moet noodterapie onmiddellik toegedien word. Dit kan insluit die toediening van adrenalien en / of die instandhouding van die pasiënt se lugweg. Die pasiënt moet onder streng mediese toesig wees totdat die simptome verdwyn het. AOE-inhibeerders veroorsaak 'n hoër koers van angio-edeem by swart pasiënte as in ander etniese groepe.

Pasiënte met 'n geskiedenis van angio-edeem wat nie verband hou met AOE-inhibeerder terapie soos met **REPREX** kan 'n verhoogde risiko van angio-edeem hê tydens die ontvangs van 'n AOE-inhibeerder.

Anafilaktiese reaksies tydens lae-digtheid lipoproteïene (LDL) aferese:
Pasiënte wat AOE-inhibeerders ontvang soos in **REPREX** tydens lae-digtheid lipoproteïen (LDL) aferese met dekstraan sulfaat het selde lewensbedreigende anafilaktiese reaksies ondervind. Hierdie reaksies is vermy deur tydelike weerhouding van AOE-inhibeerders terapie voor elke aferese.

Anafilaktiese reaksies tydens desensitisasie:
Pasiënte wat AOE-inhibeerders soos in **REPREX** ontvang tydens desensitisasie behandeling (bv. hymenoptera gif) het anafilaktiese reaksies ondervind. Hierdie reaksies is vermy wanneer die AOE-inhibeerders tydelik teruggehou is, maar hulle het weer verskyn op die her-uitdaging.

Hepatiese versaking:

REPREX is geassosieer met 'n sindroom wat begin met cholestatiese geelsug en skielik vorder tot hepatiese nekrose en (soms) dood.
Die meganisme van hierdie sindroom is nie verstaan nie. Pasiënte wat AOE-inhibeerders ontvang wat geelsug of merkbare verhogings van hepatiese ensieme ontwikkel moet **REPREX** staak en toepaslike mediese opvolg ontvang.

Neutropenie / agranulositose / trombositopenie / anemie:
Neutropenie, agranulositose, trombositopenie en anemie is aangemeld by pasiënte wat AOE-inhibeerders soos in **REPREX** ontvang. By pasiënte met normale nierfunksie en geen ander kompliserende faktore, kom neutropenie selde voor.

REPREX moet met uiterste omsigtigheid gebruik word by pasiënte met kollageen vaskulêre siekte, immuunonderdrukkende terapie, behandeling met allopurinol of prokaïnamied, of 'n kombinasie van hierdie kompliserende faktore, veral as daar voorafbestaande ingekorte nierfunksie bestaan. Sommige van hierdie pasiënte ontwikkel ernstige infeksies, wat in 'n paar gevalle nie gereageer het op intensiewe antibiotiese terapie nie. Indien **REPREX** by sulke pasiënte gebruik is, is die periodieke monitering van die witbloedseltelling aangeraai en pasiënte moet opdrag gegee word om enige teken van infeksie te rapporteer.

Ras:
REPREX veroorsaak 'n hoër koers van angio-edeem by swart pasiënte as by ander etniese groepe. **REPREX** kan minder effektief wees in die verlaging van bloeddruk in swart mense as in ander etniese groepe, moontlik as gevolg van 'n hoër voorkoms van lae-renien vlakke in die swart hipertensiewe bevolking.

Hoes:
Hoes is gerapporteer met die gebruik van AOE-inhibeerders, soos in **REPREX**. Kenmerkend, is die hoes nie-produktief, aanhoudend en word opgelos na staking van terapie. **REPREX** geïnduseerde hoes moet in ag geneem word as deel van die differensiële diagnose van hoes.

Chirurgie / narkose:
By pasiënte wat groot operasies ondergaan of gedurende narkose met middels wat hipotensie produseer, kan **REPREX** angiotensien II-vorming blokkeer sekondêr tot kompenserende renien vrystelling. Die behandeling moet gestaak word een dag voor die chirurgie.

Indien hipotensie voorkom en is beskou om te wees as gevolg van hierdie meganisme, kan dit reggestel word deur volume uitbreiding.

Hiperkalemie:
Verhogings in serum kalium is waargeneem by sommige pasiënte wat behandel is met **REPREX.** Pasiënte wat 'n risiko het vir die ontwikkeling van hiperkalemie sluit dié in met renale ontoereikendheid, onbeheerde diabetes mellitus, of diegene wat meegaande kalium-sparende diuretika (sien "**KONTRA-INDIKASIES**"), kalium aanvullings of kalium- bevattende sout plaasvervangers gebruik; of die pasiënte wat ander medisyne geassosieer met toenames in serum kalium (bv. heparien) gebruik. As die gelyktydige gebruik van die bogenoemde middels noodsaaklik geag word, word gereelde monitering van serum kalium aanbeveel.

Diabetiese pasiënte:
By diabetiese pasiënte wat behandel is met mondelinge anti-diabetiese middels of insulien, moet glisemiese beheer noukeurig gemonitor word gedurende die eerste maand van behandeling met **REPREX** (sien "**INTERAKSIES**").

Litium:
Die kombinasie van litium en **REPREX** is oor die algemeen nie aanbeveel nie (sien "**KONTRA-INDIKASIES**" en "**INTERAKSIES**").

Kalium sparende diuretika, kalium aanvullings of kalium-bevattende sout plaasvervangers:
Die kombinasie van **REPREX** en kalium sparende diuretika (sien "**KONTRA-INDIKASIES**"), kalium aanvullings of kalium-bevattende sout plaasvervangers is oor die algemeen nie aanbeveel nie (sien "**INTERAKSIES**").

Kliniese laboratorium toets bevindings:

Aan die begin van behandeling, kan 'n daling in hemoglobien voorkom. 'n Styging in die plasma kalium is gerapporteer.

Spesiale populasies:
Dosering moet aangepas word by die bejaardes en by pasiënte met renale ontoereikendheid. (Sien "**DOSIS EN GEBRUIKSAANWYSINGS**").

REPREX bevat laktose en moet nie gegee word aan pasiënte met seldsame oorerflike probleme, of 'n geskiedenis van galaktose onverdraagsaamheid, Lapp laktase tekort of glukose-galaktose wanabsorpsie nie.

Bestuur en gebruik van masjinerie:
Versigtigheid wanneer bestuur of die uitvoer van take wat wakkerheid benodig, as gevolg van moontlike duiseligheid.

Uitwerking op die vermoë om te bestuur en masjinerie te gebruik:
Wanneer voertuie bestuur of masjinerie gebruik word, behoort dit in ag geneem word dat duiseligheid of moegheid soms kan voorkom.

INTERAKSIES:

Diuretika:
Pasiënte op diuretika, en veral diegene wat volume en/of sout arm is, kan oormatige verlaging in bloeddruk ervaar na die aanvang van terapie met **REPREX**. Die moontlikheid van hipotensiewe effekte kan verminder word deur die staking van die diuretika, en deur verhoging van volume of sout inname voor die inisiëring van terapie met lae en toenemende dosisse van perindopril.

Kalium sparende diuretika, kalium aanvullings of kalium-bevattende sout plaasvervangers, ander medisyne wat hiperkalemie kan veroorsaak:
Hiperkalemie kan voorkom by sommige pasiënte wat behandel is met **REPREX**. Kalium sparende diuretika (bv spironolaktoon, triamtereen of amiloried) (sien "**KONTRA-INDIKASIES**"), kalium aanvullings of kalium-bevattende sout plaasvervangers, kan lei tot aansienlike toenames in serum kalium. Daarom word die kombinasie van **REPREX** met die bogenoemde medisyne nie aanbeveel nie. As gelyktydige gebruik aangedui word as gevolg van bevestigde hipokalemie, moet hulle gebruik word met omsigtigheid en serum kalium moet gereeld gemonitor word.

'n Toegevoegde hiperkalemiese effek is moontlik by pasiënte wat AOE- inhibeerders ontvang, soos in **REPREX** met ander medisyne wat hiperkalemie kan veroorsaak (soos siklosporien), en serum kalium konsentrasies moet gemonitor word.

Litium:
Omkeerbare toenames in serum litium konsentrasies en toksisiteit is gerapporteer tydens die gelyktydige toediening van litium met **REPREX.**

Gelyktydige gebruik van tiasied diuretika, kan die risiko van litium toksisiteit verhoog en versterk die reeds verhoogde risiko van litium toksisiteit met AOE-inhibeerders. Kombinasie van **REPREX** met litium word nie aanbeveel nie (sien "**KONTRA-INDIKASIES**"), maar as die kombinasie noodsaaklik is, moet sorgvuldige monitering van serum litium vlakke uitgevoer word.

Nie-steroïedale anti-inflammatoriese middels (NSAIM's), insluitend aspirien ≥3 g / dag:
Die toediening van nie-steroïedale anti-inflammatoriese middels (NSAIM's) kan die antihipertensiewe effek van **REPREX** verminder.

Daarbenewens, oefen NSAIM's en AOE-inhibeerders 'n additiewe effek op die toename in serum kalium en kan lei tot 'n verswakking van nierfunksie.

Hierdie effekte is gewoonlik omkeerbaar. Akute nierversaking kan voorkom, veral by pasiënte met gekompromitteerde nierfunksie soos bejaarde of gedehidreerde pasiënte.

Antihipertensiewe middels en vasodilators:
Gelyktydige gebruik van hierdie middels kan die hipotensiewe gevolge van **REPREX** verhoog. Gelyktydige gebruik met nitrogliserien en ander nitrate, of ander vasodilators, kan bloeddruk verder verlaag.

Anti-diabetiese middels:
Epidemiologiese studies het voorgestel dat gelyktydige toediening van AOE-inhibeerders, soos in **REPREX** en anti-diabetiese medisynes (insuliene, orale hipoglisemiese middels) kan 'n verhoogde bloed-glukose verlaging effek veroorsaak met die risiko van hipoglisemie. Hierdie verskynsel blyk meer geneig te wees gedurende die eerste weke van die gekombineerde behandeling en in pasiënte met renale inkorting.

Asetielsalisielsuur, trombolitika, beta-blokkers en nitrate:
REPREX kan gelyktydig met asetielsalisielsuur (wanneer dit gebruik word as 'n trombolitikum), trombolitika, beta-blokkers en / of nitrate gebruik word.

Trisikliese antidepressante / antipsigotika / narkose:
Gelyktydige gebruik van sekere narkose medisynes, trisikliese antidepressante en antipsigotika met **REPREX** kan lei tot 'n verdere vermindering in bloeddruk.

Simpatomimeties:
Simpatomimetika kan die antihipertensiewe uitwerking van **REPREX** verminder.

SWANGERSKAP EN LAKTASIE:

Swangerskap:
REPREX is teenaangedui tydens swangerskap en laktasie. **REPREX** beweeg deur die plasenta en kan vermoed word om versteuring te veroorsaak in die fetus se bloeddruk regulerende meganismes. Oligohidramnios sowel as hipotensie, oligurie en anurie is gerapporteer in pasgeborenes na toediening van **REPREX** in die tweede en derde trimester. Gevalle van gebrekkige skedel verbening is waargeneem. Prematuriteit en lae geboortegewig kan voorkom.

Verder het die gebruik van **REPREX** tydens die eerste trimester van swangerskap verband gehou met 'n verhoogde risiko van geboorte defekte, in die besonder van die kardiovaskulêre en die sentrale senuweestelsel (sien "**KONTRA-INDIKASIES**" en "**WAARSKUWINGS EN SPESIALE VOORSORGSMAATREËLS**").

Laktasie:
Die veiligheid van **REPREX** gedurende laktasie is nie vasgestel nie en daarom moet moeders op **REPREX** nie hul babas borsvoed nie.

DOSIS EN GEBRUIKSAANWYSINGS:

Ligte tot matige hipertensie:
Die tablette moet geneem word voor etes.

Die aanbevole dosering is 4 mg mondelings geneem in die oggend voor ontbyt, wat verhoog kan word tot 'n enkel dosis van 8 mg indien nodig na een maand van behandeling.

By bejaarde pasiënte en by hartversaking moet aansienlik laer doserings gebruik word as gevolg van verswakte opruiming.
Insulien en nie-insulien afhanklike diabete kan behandel word met die gewone dosisse.

Kongestiewe hartversaking:
Die behandeling moet geïnisieer word onder streng mediese toesig. Aanvanklike dosis van 2 mg mondelings as 'n enkel dosis in die oggend, wat in die meeste gevalle tot 4 mg (sodra bloeddruk aanvaarbaarheid gedemonstreer is) verhoog kan word.

Gepaardgaande diuretika terapie by hipertensie:
Versigtigheid word aanbeveel by pasiënte wat tans met diuretikums behandel word. Aangesien die effekte van die AOE-inhibeerders gepotensieer kan word in 'n situasie waar hipovolemie kan voorkom, moet die diuretika terapie gestaak word voor die aanvang van terapie met **REPREX**. In die geval van kombinasie met 'n diuretikum is dit nie raadsaam om 'n kalium sout of 'n kalium sparende middel voor te skryf voor die bepaling van die bloed kalium nie, en aandag moet gegee word aan die moontlike oordosering van die diuretikum (sien **"KONTRA-INDIKASIES"** en **"INTERAKSIES"**).

Renale ontoereikendheid:
By pasiënte met renale ontoereikendheid (kreatinienopruiming 30 - 60 ml/min). moet die dosering van perindopril aangepas word met betrekking tot die erns van die ontoereikendheid. Die volgende doserings mag aanbeveel word:

Kreatinienopruiming	Aanbevole dosering
30 - 60 ml/min	2 mg per dag

REPREX is teenaangedui by pasiënte met 'n kreatinienopruiming minder as 30 ml/min.
Perindopril is dialiseerbaar (70 ml/min).

NEWE EFFEKTE:

Bloed en limfstelsel afwykings:
Minder dikwels: Afnames in hemoglobien, hematokrit, trombositopenie, leukopenie / neutropenie, agranulositose, pansitopenie. Gevalle by pasiënte met 'n aangebore tekort aan G-6PDH, van hemolitiese anemie word selde aangemeld.
Anemieë.

Psigiatriese afwykings:
Minder dikwels: Gemoed en/of slaapversteurings.

Senuweestelsel afwykings:
Dikwels: Hoofpyn, duiseligheid, vertigo, paraestesie.
Minder dikwels: Verwarring.

Oogafwykings:
Dikwels: Visuele versteurings.

Oor en labirint afwykings:
Dikwels: Tinnitus.

Kardio-vaskulêre afwykings:
Dikwels: Hipotensie en effekte wat verband hou met hipotensie.

Minder dikwels: Disritmieë, angina pectoris, miokardiale infarksie en beroerte, moontlik sekondêr tot oormatige hipotensie by hoë-risiko pasiënte, bv. by pasiënte met isgemiese hartsiekte of serebrovaskulêre siekte.
Die volgende newe effekte is aangemeld en die frekwensies is onbekend: Ortostatiese effekte (insluitend hipotensie), hartkloppings.

Respiratoriese, torakale en mediastinale afwykings:
Dikwels: Hoes, dispnee.
Minder dikwels: Brongospasma, eosinofiliese longontsteking en rinitis.

Gastroïntestinale afwykings:
Dikwels: Onspesifieke spysverteringstelsel afwykings, naarheid, braking, abdominale pyn, smaak versteuring, dispepsie, diarree en hardlywigheid.

Minder dikwels: Pankreatitis, droë mond.

Hepato-biliêre afwykings:
Minder dikwels: Lewersellulêre besering of cholestatiese geelsug, hepatitis, hetsy sitolities of cholestaties.

Vel en subkutane weefsel afwykings:
Dikwels: Uitslag, pruritus.
Minder dikwels: Angio-edeem van die gesig, lippe, slymvliese, tong, glottis en / of larinks, ledemate en urtikarie, erythema multiforme.

Muskuloskeletale, bindweefsel en been afwykings:
Dikwels: Spierkrampe.

Nier-en urinêre afwykings:
Minder dikwels: Renale ontoereikendheid, akute nierversaking.

Voortplantingstelsel en bors afwykings:
Minder dikwels: Impotensie.

Algemene afwykings:
Dikwels: Astenie.
Minder dikwels: Sweet.

Ondersoeke:
Minder dikwels: Verhoging van lewerensieme en serum bilirubien.
Die volgende newe effekte is aangemeld en die frekwensies is onbekend: In die teenwoordigheid van renale ontoereikendheid, ernstige hartversaking en renovaskulêre hipertensie, kan daar 'n toename in bloed ureum, plasma kreatinien en hiperkalemie wees, maar dit is omkeerbaar op die staking van die medikasie.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:

Die simptome wat verband hou met die oordosis van **REPREX** kan hipotensie, sirkulatoriese skok, elektroliet versteurings, nierversaking, hiperventilasie, tagikardie, hartkloppings, bradikardie, duiseligheid, angs en hoes insluit.

Die aanbevole behandeling van 'n oordosis is 'n binneaarse infusie van normale soutoplossing. Indien hipotensie voorkom, behoort die pasiënt in die skok posisie geplaas te word. As dit beskikbaar is, kan behandeling met angiotensien II infusie en / of binneaarse katesjolamiene ook oorweeg word.
REPREX kan verwyder word van die algemene sirkulasie deur hemodialise. Pasaangeër terapie is vir terapie-weerstandige bradikardie aangedui. Vitale tekens, serum elektroliete en kreatinien konsentrasies moet voortdurend gemonitor word. Verwagte simptome en tekens sal gekoppel word aan hipotensie. Verdere behandeling is simptomaties en ondersteunend.

IDENTIFIKASIE:

REPREX 2 mg: Wit tot naaswit gekleurde ronde bikonvekse onbedekte tablette, met debossellering "D" aan die een kant en "57" aan die ander kant.

REPREX 4 mg: Wit tot naaswit gekleurde kapsuulvormige onbedekte tablette, met debossellering "D" aan die een kant en "5" and "8" aan beide kante van die breeklyn aan die ander kant.

REPREX 8 mg: Wit tot naaswit gekleurde ronde onbedekte tablette, met debossellering "D" aan die een kant en "5" and "9" aan beide kante van die breeklyn aan die ander kant.

AANBIEDING:

REPREX 2 mg, REPREX 4 mg, en REPREX 8 mg:

Stolpverpakkings:
Tablette is verpak in stolpverpakkings (wat bestaan uit helder PVC film en silwerkleurige aluminium dekkingsfoelie). Elke stolpstrook bevat 10 tablette. Drie stolpstroke is verpak in 'n sak tesame met 'n silika jel sakkie.

<u>Pakgrootte:</u> 30s: Elke karton bevat 3 stolpstroke van 10 tablette elk.

BERGINGSAANWYSINGS:
Berg by of benede 25 °C in 'n droë plek.
Moet nie die stolpstroke verwyder uit die karton tot benodig.
HOU BUITE DIE BEREIK VAN KINDERS.

REGISTRASIENOMMER:

SUID-AFRIKA:
REPREX 2 mg: 43/7.1.3/1032
REPREX 4 mg: 43/7.1.3/1033
REPREX 8 mg: 43/7.1.3/1034

NAMIBIË:
REPREX 2 mg: 18/7.1.3/0095
REPREX 4 mg: 18/7.1.3/0096
REPREX 8 mg: 18/7.1.3/0097

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE:

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Suid-Afrika

DATUM VAN PUBLIKASIE VAN HIERDIE PROFESSIONELE INLIGTING:
Datum van registrasie:
30 September 2011
Datum van hersiening:
18 September 2021

SUID-AFRIKA: S3
NAMIBIË: NS2

REPREX 2 mg (tablet)
REPREX 4 mg (tablet)
REPREX 8 mg (tablet)
Perindopril tertbutielamien

Lees die hele brosjure sorgvuldig voordat u begin om REPREX te neem.
- Hou hierdie blaadjie. U mag dit moontlik weer wil lees.
- Indien u enige verdere vrae het, moet u asseblief u dokter of apteker raadpleeg.
- **REPREX** is vir u persoonlik voorgeskryf en u behoort nie u medisyne met ander mense te deel nie. Dit mag hulle skade aandoen, ookal het hulle dieselfde simptome as u.

1. WAT REPREX BEVAT

Die aktiewe bestanddeel is perindopriel.

REPREX 2 mg: Elke onbedekte tablet bevat 2 mg perindopril tertbutielamien. Bevat suiker: 29.665 mg laktose.

REPREX 4 mg: Elke onbedekte tablet bevat 4 mg perindopril tertbutielamien. Bevat suiker: 59.33 mg laktose.

REPREX 8 mg: Elke onbedekte tablet bevat 8 mg perindopril tertbutielamien. Bevat suiker: 118.66 mg laktose.
Die ander bestanddele is mikrokristallyne sellulose, magnesium stearaat en hidrofobiese anhidriese kolloïdale silika.

2. WAARVOOR REPREX GEBRUIK WORD

REPREX behoort aan 'n klas medisyne wat angiotensienomskakelings-ensieminhibeerders (AOE) genoem word. Dit werk deur sekere chemikalieë wat die bloedvate verstyf te verminder, sodat bloed meer egalig vloei en die hart die bloed meer effektief kan pomp.
REPREX word gebruik om hoë bloeddruk te behandel en word ook gebruik om kongestiewe hartversaking te behandel ('n kondisie waar die hart nie in staat is om genoeg bloed te pomp om aan die liggaam se vereistes te voorsien nie).

3. VOORDAT U REPREX NEEM

Moenie REPREX neem nie:
- As u al ooit 'n allergiese reaksie teen perindopril of enige bestanddeel van die produk gehad het.
- As u al ooit aan angioëdeem ('n kondisie wat moeite met sluk of asemhaling en pynlike swelling van die gesig, keel, tong, lippe, oë, hande, voete, enkels of onderbene veroorsaak) gely het verwanta an vorige terapie met AOE inhibeerders of angiotensien reseptor blokkeerders.
- As u aan oorerflike/idiopatiese (onbekende oorsaak) angioëdeem ly.
- As u aan hipertrofiese obstruktiewe kardiomiopatie (hartspiersiekte) ly.
- As u aan erge niersiekte ly.
- As u aan nierslagaarstenose (vernouing van die slagaar wat bloed aan die nier verskaf) ly.
- As u aan aortiese stenose ('n vernouing van die aortiese klep in die hart, wat die bloedvloei vanaf die hart na die hoofslagaar wat die hart verlaat vertraag) ly.
- As u diuretika neem (watertablette wat gebruik word om die hoeveelheid water in u liggaam te verminder) soos spironolaktoon, triamtereen, amiloried. Hierdie medisyne veroorsaak geen kaliumverlies nie
- As u 'n tiasieddiuretikum neem en aan Addison se siekte ly, of as u 'n tiasieddiuretikum neem en u ly aan 'n erge niersiekte, anurie (onvermoë van die niere om urien te vorm) of as u allergies teen enige "sulfa"-medisyne is.
- As u aan porfirie ly ('n oorerflike afwyking van bloedpigment-metabolisme).
- As u litium gebruik.
- As u swanger is of borsvoed (Sien "**Neem spesiale sorg met REPREX**" en "**Swangerskap en laktasie**").
- **REPREX** moet nie aan kinders gegee word nie.

REPREX kan u ongebore baba skade aandoen. As u swanger raak, moet u onmiddellik ophou om REPREX te neem. Raadpleeg u dokter oor ander medisyne om u bloeddruk te verlaag.

Neem spesiale sorg met REPREX:
- U behoort te weet dat die verlies van water uit u liggaam weens braking of diaree, dialise, die neem van diuretika (medisyne om die uitskeiding van urien te verhoog) en te min sout in u dieet 'n verlaging in bloeddruk kan veroorsaak wat tot lighoofdigheid en floute kan lei. Lae bloeddruk sal ook meer waarskynlik voorkom as u aan hartprobleme ly. As u 'n risiko van lae bloeddruk het, mag u dokter u terapie noukeurig moet monitor. Gaan lê as u flou of duiselig voel.
- As u swelling van die gesig om u lippe, tong of keel ontwikkel of moeite met sluk ondervind, behoort u onmiddellik u dokter te raadpleeg en ophou om **REPREX** te neem.
- As u bejaard is of aan 'n erge niersiekte ly, mag u dokter moontlik die dosis moet aanpas.
- **REPREX** is geassosieer met 'n afname in die aantal van 'n sekere tipe witbloedselle. 'n Afname in die aantal witbloedselle kom meer dikwels in mense met nierprobleme en kollageen vaskulêre siektes (siektes van die bindweefsel) voor. 'n Afname in die aantal witbloedselle veroorsaak 'n hoër risiko vir infeksies. Raadpleeg u dokter as u 'n koors, seer keel of ander tekens van 'n infeksie opdoen wat nie wil verdwyn nie.
- Moenie soutvervangers gebruik wat kalium, kaliumsupplemente of ander medisyne wat die bloedvlakke van kalium kan laat toeneem terwyl u **REPREX** gebruik nie, tensy deur u dokter voorgeskryf.
- U dokter mag u nierfunksie en kaliumvlakke in u bloed monitor. Moenie enige geskeduleerde doktersbesoeke oorslaan nie.
- 'n Aanhoudende droë hoes kan voorkom terwyl u **REPREX** gebruik.
- Om seker te maak dat hierdie medikasie help, sal u bloeddruk op 'n gereelde basis nagegaan moet word. Moenie enige geskeduleerde doktersbesoeke oorslaan nie.

Stel u dokter in kennis:
- As u 'n vernouing van die hartkleppe (aortiese stenose) het of aan hartspiersiekte (hipertrofiese kardiomiopatie) ly (sien "**Moenie REPREX neem nie**").
- As u aan enige ander hartprobleme ly, soos hartversaking, kongestiewe hartversaking, hartaanval of iskemiese hartsiekte.
- As u aan 'n kollageen vaskulêre siekte (siekte van die bindweefsel) ly, soos sistemiese lupus erythematosus of skleroderma.
- As u aan nierprobleme ly of as u dialise ontvang.
- As u aan lewerprobleme ly of geelsug ontwikkel (geel vel en oë).
- As u aan diabetes ly.
- As u onlangs 'n nieroorplanting ondergaan het.
- As u aan narkose en/of chirurgie blootgestel gaan word.
- As u op 'n soutbeperkte dieet is of soutvervangers gebruik wat kalium bevat.
- As cholesterol met behulp van 'n masjien uit u bloed verwyder gaan word (LDL-aferese).
- As u desensiteringsbehandeling gaan ontvang om die effek van 'n allergie te verminder bv. by- of perdebysteke.
- As u bloeddruk weens etniese affiliasie (veral in pasiënte met 'n swart vel) nie voldoende verlaag word nie.
- As u litium vir manie of depressie gebruik (sien "**Moenie REPREX neem nie**" en "**Die neem van ander medisyne saam met REPREX**").

Die neem van REPREX met voedsel en vloeistof:
REPREX behoort voor 'n maaltyd geneem te word.

Swangerskap en borsvoeding:
Moenie hierdie medikasie gebruik as u swanger, beplan om swanger te raak of as u borsvoed nie.
REPREX kan geboortedefekte in die baba veroorsaak as u dit gedurende swangerskap gebruik. Gebruik 'n effektiewe metode van voorbehoeding. Staak die gebruik van die medisyne en raadpleeg onmiddellik u dokter as u gedurende gebruik swanger raak.

As u swanger is of u baba borsvoed, moenie **REPREX** neem nie, moet u asseblief u dokter, apteker of ander gesondheidsbeampte vir advies nader voordat u **REPREX** neem.

Bestuur en die gebruik van masjinerie:
Moenie bestuur of met masjinerie werk as u duiselig of moeg voel terwyl u **REPREX** neem nie.

Die neem van ander medisyne saam met REPREX:
Voordat u **REPREX** neem moet u u dokter in kennis stel as u enige van die volgende medisyne neem:
- Ander medisyne vir hoë bloeddruk, insluitende diuretika (medisyne wat die hoeveelheid urien wat deur die niere geproduseer word, verhoog).
- Kaliumsparende diuretika (watertablette wat kalium beïnvloed, soos spironolaktoon, triamtereen of amiloried), kaliumsupplemente, kaliumbevattende soutvervangers of medisyne wat die kaliumvlakke in u bloed kan verhoog (bv. siklosporien). **REPREX** moet nie saam met kaliumsparende diuretika geneem word nie (Sien "**Moenie REPREX neem nie**"). Moenie soutvervangers gebruik wat kalium bevat, kaliumsupplemente of ander medisyne wat die kaliumvlakke in u bloed kan verhoog terwyl u **REPREX** neem nie, tensy deur u dokter voorgeskryf.
- Heparien (vir verdunning van die bloed) kan ook die kaliumvlakke in u bloed beïnvloed.
- Litium vir manie of depressie nie (Sien "**Moenie REPREX neem nie**").
- Nie-steroïed anti-inflammatoriese middels (bv. ibuprofen, indometasien) vir die behandeling van pyn en inflammasie of hoë dosisse aspirien.
- Allopurinol (vir jig).
- Medisyne vir diabetes (insulien of tablette).
- Prokaïnamied (vir ongereelde hartklop).
- Medisyne wat die bloedvate verwyd (vasodilatore soos nitrate).
- Medisyne om geestesafwykings soos depressie, angs, skisofrenie of ander psigose te behandel (bv. trisikliese antidepressante, antipsigotika).
- Narkosemiddels (medisyne wat verlies aan sensasie of pyn/bewusteloosheid veroorsaak).
- Medisyne wat gebruik word vir die behandeling van lae bloeddruk, skok of trouma (bv. efedrien, noradrenalien of adrenalien).
- Immuunonderdrukkers (medisyne wat die verdedigingsmeganisme van u liggaam verminder) gebruik vir die behandeling van outo-immuunafwykings of na oorplantingchirurgie (bv. siklosporien)
- As u enige van hierdie medisyne gebruik, mag u moontlik nie **REPREX** kan gebruik nie, of dosisaanpassings kan gemaak word of dit mag nodig wees dat u dokter u noukeurig vir newe effekte moet monitor.

Stel altyd u professionele gesondheidswerker in kennis as u enige ander medisyne gebruik.
(Dit sluit komplementêre of tradisionele medisyne in).

4. HOE OM TE REPREX NEEM
- Neem hierdie medisyne slegs soos deur u dokter voorgeskryf.
- Moenie meer of minder daarvan neem of dit meer dikwels neem as wat u dokter voorgeskryf het nie.
- **REPREX** behoort voor 'n maaltyd geneem te word.

Die normale dosisse is as volg:
- Hoë bloeddruk:
  Die normale dosis is 4 mg soggens voor ontbyt. Na een maand kan u dokter besluit dat die dosis na 8 mg een keer per dag verhoog moet word, indien nodig. As u bejaard is of aan hartversaking ly, sal u dokter 'n laer dosis voorskryf.
- Kongestiewe hartversaking:
  Die normale begindosis is 2 mg een keer per dag soggens. U dokter kan dit na 4 mg een keer per dag verhoog.

As u watertablette gebruik:
- U dokter mag besluit om die gebruik daarvan te staak voordat u met **REPREX** begin.

Neem **REPREX** altyd presies soos deur u dokter voorgeskryf. Bevestig met u dokter of apteker as u onseker is. As u van mening is dat die effek van **REPREX** te sterk of te swak is, moet u u dokter of apteker raadpleeg.

As u te veel REPREX geneem het:

Die volgende effekte kan voorkom: lae bloeddruk, skok, nierprobleme, vinnige asemhaling, vinnige hartklop, ongereelde hartklop, stadige hartklop, duiseligheid, angs en hoes.

In die geval van oordosering, raadpleeg u dokter of apteker. As hulle nie beskikbaar is nie, kontak u naaste hospitaal of gifbeheersentrum.

As u vergeet het om REPREX te neem:
Dit is belangrik dat u u medisyne elke dag neem aangesien gereelde behandeling beter werk.
As u vergeet het om **REPREX** te neem, moet u so gou as moontlik die oorgeslaande dosis neem. As dit egter byna tyd vir u volgende dosis is, slaan die dosis oor en gaan met u normale dosisskedule voort. Moenie 'n dubbel dosis neem om vir 'n oorgeslaande dosis op te maak nie.

5. MOONTLIKE NEWE EFFEKTE

REPREX kan newe effekte hê.

Kry nood mediese hulp as u enige van hierdie tekens van 'n allergiese reaksie toon:
- Moeite met asemhaling.
- Swelling van u gesig, lippe, tong of keel.

Stel u dokter so gou as moontlik in kennis as u enige van hierdie ernstige newe effekte toon:
- Floute, lighoofdigheid, veral in die staande posisie. Dit kan beteken dat u bloeddruk te laag is.
- Geelsug (geel verkleuring van die vel en oë).
- Minder of geen urienvloei.
- Hartkloppings (vinnige ongereelde aksie van die hart) of arritmieë (ongereelde hartklop).
- Angina (borspyn wat voorkom in gevalle van hartsiekte).
- Hartaanval (borspyn, kortademheid, oormatige sweet, swakheid, lighoofdigheid, naarheid, braking hartkloppings, moegheid).
- Beroerte (skielike gevoelloosheid van die gesig, arm of been, veral aan die eenkant van die liggaam, skielike erge hoofpyn, skielike verwardheid, moeite met spraak of om iets te verstaan, skielike moeite met loop, duiseligheid, verlies aan koördinasie).
- Bleek vel, maklike kneusing en bloeding.
- Koors, seer keel, kouekoors en ander tekens van infeksie.
- Erge buik- en rugpyn geassosieer met 'n gevoel van erge ongesteldheid (inflammasie van die pankreas).

Ander newe effekte sluit die volgende in: Slaapprobleme, buiveranderinge, hoofpyn, duiseligheid, vertigo, spelde en naalde, verwardheid, gesigsprobleme, geraas in die ore, hoes, kortademheid, beklemming van die bors, hyging en kortademheid (bronchospasma), borsinfeksie (eosienofiliese pneumonie, verstopte of loopneus (rinitis), diaree, hardlywigheid, naarheid, braking, buikpyn, smaakveranderinge, sooibrand, droë mond, ontsteekte lewer (hepatitis), veluitslag, urtikarie, jeuk, allergiese tipe velreaksie (erythema multiforme), spierkrampe, nierprobleme, impotensie (onvermoë om 'n ereksie te kry), afwykings van die bloed (u dokter kan bloedtoetse uitvoer om dit na te gaan), energietekort, sweet, anemie.

Stel u dokter in kennis as enige van die bogenoemde newe effekte erg is, nie verdwyn nie of as u enige kwellings het terwyl u **REPREX** gebruik.

Nie al die newe effekte wat vir **REPREX** aangemeld is, word in hierdie brosjure ingesluit nie. As u algemene **REPREX** neem, moet u asseblief u dokter, apteker of ander professionele gesondheidweker om advies randpleeg.

6. OPBERGING EN WEGDOEN VAN REPREX

Berg by of benede 25 °C in 'n droë plek. Moenie die stolpstrokies uit die kartonverpakking verwyder tot voor gebruik nie.

Berg alle medisyne buite die bereik and sig van kinders.

Neem alle ongebruikte medisyne na u apteker terug.
Moenie enige ongebruikte medisyne in die drein of riolering (bv. toilette) weggooi nie.

7. AANBIEDING VAN REPREX

REPREX 2 mg, REPREX 4 mg, REPREX 8 mg:

Stolpverpakking:

Tablette is verpak in stolpverpakkings (wat bestaan uit helder PVC film en silwerkleurige aluminium dekkingsfoelie). Elke stolpstrook bevat 10 tablette. Drie stolpstroke is verpak in 'n sak tesame met 'n silika jel sakkie.

<u>Pakgrootte:</u> 30s: Elke karton bevat 3 stolpstroke van 10 tablette elk.

8. IDENTIFIKASIE VAN REPREX

REPREX 2 mg: Wit tot naaswit gekleurde ronde bikonvekse onbedekte tablette, met debossellering "D" aan die een kant en "57" aan die ander kant.
REPREX 4 mg: Wit tot naaswit gekleurde kapsuulvormige onbedekte tablette, met debossellering "D" aan die een kant en "5" and "8" aan beide kante van die breeklyn aan die ander kant.
REPREX 8 mg: Wit tot naaswit gekleurde ronde onbedekte tablette, met debossellering "D" aan die een kant en "5" and "9" aan beide kante van die breeklyn aan die ander kant.

9. REGISTRASIENOMMER / VERWYSINGSNOMMER

SUID-AFRIKA:

REPREX 2 mg: 43/7.1.3 / 1032

REPREX 4 mg: 43/7.1.3 / 1033

REPREX 8 mg: 43/7.1.3 / 1034

NAMIBIË:

REPREX 2 mg: 18/7.1.3/0095

REPREX 4 mg: 18/7.1.3/0096

REPREX 8 mg: 18/7.1.3/0097

10. NAAM EN ADRES VAN DIE REGISTRASIEHOUER

Aurogen South Africa (Edms) Bpk
Woodhill Kantoorpark, Gebou 1, Eerste vloer,
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11. DATUM VAN PUBLIKASIE

Datum van registrasie:
30 September 2011

Datum van hersiening:
18 September 2021

SCHEDULING STATUS
SOUTH AFRICA: S3
NAMIBIA: NS2
PROPRIETARY NAME (and dosage form):

REPREX 2 mg (tablet)
REPREX 4 mg (tablet)
REPREX 8 mg (tablet)

COMPOSITION:

REPREX 2 mg:
Each uncoated tablet contains perindopril tert-butylamine 2 mg. Contains sugar: 29.665 mg lactose.
REPREX 4 mg :
Each uncoated tablet contains perindopril tert-butylamine 4 mg. Contains sugar: 59.33 mg lactose.
REPREX 8 mg:
Each uncoated tablet contains perindopril tert-butylamine 8 mg. Contains sugar: 118.66 mg lactose.

The other ingredients are cellulose microcrystalline, magnesium stearate and silica hydrophobic colloidal anhydrous.

PHARMACOLOGICAL CLASSIFICATION:
A 7.1.3 Vascular medicines- other hypotensives

PHARMACOLOGICAL ACTION:

Pharmacodynamics

Perindopril is a specific, non-sulphydryl competitive angiotensin-I converting enzyme (ACE) inhibitor. It inhibits the conversion of relatively inactive angiotensin I to the active angiotensin II. Angiotensin II is a potent vasoconstrictor and stimulates the release of aldosterone. Decreased angiotensin II levels result in a decrease in vasopressor activity and a reduction in aldosterone secretion, which may result in small increases in serum potassium. It is also thought that ACE – inhibition may inhibit degradation of bradykinin leading to increased bradykinin levels. Perindopril acts through its active metabolite, perindoprilat. The other metabolites are pharmalogically inactive.

Pharmacokinetics:

Following oral administration the absorption of perindopril is rapid (peak concentration within 1 hour), and relatively complete (plasma-availability above 75 %). The peak concentration of the active metabolite, peerindoprilat, is reached within 3 to 4 hours and peak pharmacological activity is obtained within 4 to 6 hours.

In terms of trough versus peak blood pressure effect, the trough effect ranges between 75 –100 % of peak effect. Both perindopril and perindoprilat have a low volume of distribution and plasma protein binding is low. Perindoprilat binds to ACE at both tissue and plasma levels.

Apart from the active perindoprilat, perindopril gives rise to 5 metabolites all of which are inactive. Perindopril is eliminated in the urine and the half-life of its free fraction is approximately one hour. Breakdown of the bond between perindoprilat and the ACE leads to a pharmacodynamic half-life of about 25 hours. In the elderly, as well as in patients with cardiac failure or renal failure, the elimination of perindoprilat is slower. In such patients dosage adjustment should be applied in relation to the degree of reduction in creatinine clearance.
Reduction in blood pressure in patients treated with perindopril was accompanied by a reduction in peripheral resistance with no significant changes in glomerular filtration rate or heart rate. An increase in the compliance of large arteries was also observed, suggesting a direct effect on arterial smooth muscle, consistent with the results of animal studies.

INDICATIONS:

REPREX tablets are indicated in:
- Mild to moderate hypertension.
- Congestive heart failure not adequately controlled by conventional therapy with diuretics and digitalis and in whom vasodilatation is indicated.

CONTRA-INDICATIONS:

REPREX tablets are contra-indicated in:
- Sensitivity to any of the components of **REPREX.**
- 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.
- Porphyria.
- Thiazide diuretics in (fixed dose) combination with **REPREX** should not be given to patients with Addison's disease. This therapy is contra-indicated in patients with severe renal impairment or anuria, and in patients who show hypersensitivity to other sulphonamide-derived medicines.
- Lithium therapy: Concomitant administration with **REPREX** may lead to toxic blood concentrations of lithium.
- Pregnancy and lactation (see **"WARNINGS AND SPECIAL PRECAUTIONS"** and **"PREGNANCY AND LACTATION"**).
- Children: The safety of **REPREX** in children has not been established.

WARNINGS AND SPECIAL PRECAUTIONS:

Should a woman become pregnant while receiving REPREX, the treatment should be stopped promptly and switched to a different class of medicine. Should a woman contemplate pregnancy, the doctor should consider alternate medication. (See "CONTRA-INDICATIONS" and "PREGNANCY AND LACTATION").

Hypotension:
ACE-inhibitors, as in **REPREX** may cause a fall in blood pressure. Symptomatic hypotension is rarely seen in uncomplicated hypertensive patients and is more likely to occur in patients who have been volume-depleted e.g. by diuretic therapy, dietary salt restriction, dialysis, diarrhoea or vomiting, or who have severe renin-dependent hypertension. In patients with symptomatic heart failure, with or without associated renal insufficiency, symptomatic hypotension has been observed. This is most likely to occur in those patients with more severe degrees of heart failure, as reflected by the use of high doses of loop diuretics, hyponatraemia or functional renal impairment. In patients with an increased risk of symptomatic hypotension, initiation of therapy and dose adjustment should be closely monitored. Similar considerations apply to patients with ischaemic heart or cerebrovascular disease in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident.
If hypotension occurs, the patient should be placed in the supine position and, if necessary, should receive an intravenous infusion of normal saline. A transient hypotensive response is not a contra-indication to further doses, which can be given usually without difficulty, once the blood pressure has increased after volume expansion.
In some patients with congestive heart failure, who have normal or low blood pressure, additional lowering of systemic blood pressure may occur with **REPREX.** If hypotension becomes symptomatic, a reduction of the dose or discontinuation of **REPREX** may be necessary.

Aortic and mitral valve stenosis/hypertrophic cardiomyopathy:

REPREX should be given with caution to patients with mitral valve stenosis and obstruction in the outflow of the left ventricle, such as aortic stenosis or hypertrophic cardiomyopathy (see "**CONTRA-INDICATIONS**").

Impaired renal function:

In cases of renal impairment (creatinine clearance < 60 ml/min) the initial **REPREX** dosage should be adjusted according to the patient's creatinine clearance and then as a function of the patient's response to treatment (see "**Renal insufficiency**"). Routine monitoring of potassium and creatinine are part of normal medical practice for these patients. In patients with symptomatic heart failure, hypotension following the initiation of therapy with ACE-inhibitors, as in **REPREX** may lead to some further impairment in renal function. Acute renal failure has been reported in this situation.

In patients with bilateral renal artery stenosis, or stenosis of the artery to a solitary kidney, and who have been treated with ACE-inhibitors, as in **REPREX** increases in blood urea and serum creatinine may occur (see "**CONTRA-INDICATIONS**"). This is usually reversible upon discontinuation of therapy. It is especially likely in patients with renal insufficiency. If renovascular hypertension is also present, there is an increased risk of severe hypotension and renal insufficiency. In these patients, treatment should be started under close medical supervision with low doses and careful dose titration. Since treatment with diuretics may be a contributory factor to the above, they should be discontinued and renal function should be monitored during the first weeks of **REPREX** therapy.

Some hypertensive patients with no apparent pre-existing renal vascular disease have developed increases in blood urea and serum creatinine, especially when **REPREX** was given concomitantly with a diuretic. This is more likely to occur in patients with pre-existing renal impairment. Dosage reduction and/or discontinuation of the diuretic and/or **REPREX** may be required.

In acute myocardial infarction, treatment with **REPREX** should not be initiated in patients with evidence of renal dysfunction (serum creatinine concentrations exceeding 177 micromol/l or proteinuria exceeding 500 mg/24 hours). If renal dysfunction develops during treatment (serum creatinine concentrations exceeding 177 micromol/l or doubling of the pre-treatment value) then **REPREX** may need to be withdrawn (see also "**CONTRA-INDICATIONS**").

In acute myocardial infarction, patients may develop persistent hypotension and/or impaired renal function.

Haemodialysis patients:

Anaphylactic reactions have been reported in patients dialysed with high flux membranes, and treated concomitantly with an ACE-inhibitor, as in **REPREX**. In these patients consideration should be given to using a different type of dialysis membrane or different class of antihypertensive agent.

Kidney transplantation:

There is no experience regarding the administration of **REPREX** in patients with a recent kidney transplant.

Hypersensitivity/angioedema:

Angioedema of the face, lips, mucous membranes, tongue, glottis and/or larynx, and extremities has been reported, in patients treated with **REPREX** (see "**CONTRA-INDICATIONS**"). This may occur at any time during therapy. In such cases, **REPREX** should immediately be discontinued and appropriate monitoring should be initiated and continued until the symptoms have disappeared completely. In those instances where swelling was confined to the face and lips, the condition generally resolved without treatment, although antihistamines have been useful in relieving symptoms.
Angioedema associated with laryngeal oedema may be fatal. Where there is involvement of the tongue, glottis or larynx, and is likely to cause airway obstruction, emergency therapy should immediately be administered. This may include the administration of adrenaline and/or the maintenance of the patient's airway. The patient should be under close medical supervision until the symptoms have disappeared. ACE-inhibitors cause a higher rate of angioedema in black patients than in other ethnic groups.
Patients with a history of angioedema unrelated to ACE-inhibitor therapy as with **REPREX** may be at increased risk of angioedema while receiving an ACE-inhibitor.

Anaphylactic reactions during low-density lipoproteins (LDL) apheresis:
Patients receiving ACE-inhibitors as in **REPREX** during low-density lipoprotein (LDL) apheresis with dextran sulphate have rarely experienced life-threatening anaphylactic reactions. These reactions were avoided by temporarily withholding ACE-inhibitor therapy prior to each apheresis.

Anaphylactic reactions during desensitisation:

Patients receiving ACE-inhibitors as in **REPREX** during desensitisation treatment (e.g. hymenoptera venom) have experienced anaphylactic reactions. These reactions were avoided when the ACE-inhibitors were temporarily withheld, but they reappeared upon rechallenge.

Hepatic failure:

REPREX has been associated with a syndrome that starts with cholestatic jaundice and suddenly progresses to hepatic necrosis and (sometimes) death. The mechanism of this syndrome is not understood. Patients receiving ACE-inhibitors who develop jaundice or marked elevations of hepatic enzymes should discontinue **REPREX** and receive appropriate medical follow-up.

Neutropenia/agranulocytosis/thrombocytopenia/anaemia:

Neutropenia, agranulocytosis, thrombocytopenia and anaemia have been reported in patients receiving ACE-inhibitors as in **REPREX**. In patients with normal renal function and no other complicating factors, neutropenia rarely occurs.
REPREX should be used with extreme caution in patients with collagen vascular disease, immunosuppressant therapy, treatment with allopurinol or procainamide, or a combination of these complicating factors, especially if there is pre-existing impaired renal function. Some of these patients developed serious infections, which in a few instances did not respond to intensive antibiotic therapy. If **REPREX** is used in such patients, periodic monitoring of the white blood cell count is advised and patients should be instructed to report any sign of infection.

Race:

REPREX causes a higher rate of angioedema in black patients than in other ethnic groups. **REPREX** may be less effective in lowering blood pressure in black people than in other ethnic groups, possibly because of a higher prevalence of low-renin levels in the black hypertensive population.

Cough:

Cough has been reported with the use of ACE-inhibitors, as in **REPREX.** Characteristically, the cough is non-productive, persistent and resolves after discontinuation of therapy. **REPREX** induced cough should be considered as part of the differential diagnosis of cough.

Surgery/anaesthesia:

In patients undergoing major surgery or during anaesthesia with agents that produce hypotension, **REPREX** may block angiotensin II formation secondary to compensatory renin release. The treatment should be discontinued one day prior to the surgery. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Hyperkalaemia:

Elevations in serum potassium have been observed in some patients treated with **REPREX**. Patients at risk for the development of hyperkalaemia include those with renal insufficiency, uncontrolled diabetes mellitus, or those using concomitant potassium-sparing diuretics (see **"CONTRA-INDICATIONS"**), potassium supplements or potassium-containing salt substitutes; or those patients taking other medicines associated with increases in serum potassium (e.g. heparin). If concomitant use of the above-mentioned agents is deemed necessary, regular monitoring of serum potassium is recommended.

Diabetic patients:

In diabetic patients treated with oral antidiabetic agents or insulin, glycaemic control should be closely monitored during the first month of treatment with **REPREX** (see "**INTERACTIONS**").

Lithium:

The combination of lithium and **REPREX** is generally not recommended (see "**CONTRA-INDICATIONS**" and "**INTERACTIONS**").

Potassium sparing diuretics, potassium supplements or potassium-containing salt substitutes:

The combination of **REPREX** and potassium sparing diuretics (see **"CONTRA-INDICATIONS"**), potassium supplements or potassium-containing salt substitutes is generally not recommended (see "**INTERACTIONS**").

Clinical laboratory test findings:

At the start of treatment, a fall in haemoglobin may occur. A rise in plasma potassium has been reported.

Special populations:

Dosage should be adjusted in the elderly and in patients with renal insufficiency. (see **"DOSAGE AND DIRECTIONS FOR USE**").

REPREX contains lactose and should not be given to patients with rare hereditary problems, or a history of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption.

Driving and using machinery:

Caution should be exercisedv driving or performing tasks requiring alertness because of possible dizziness.

INTERACTIONS:

Diuretics:

Patients on diuretics, and especially those who are volume and/or salt depleted, may experience excessive reduction in blood pressure after initiation of therapy with **REPREX**. The possibility of hypotensive effects can be reduced by discontinuation of the diuretic, and by increasing volume or salt intake prior to initiating therapy with low and increasing doses of perindopril.

Potassium sparing diuretics, potassium supplements or potassium-containing salt substitutes, other medicines that can cause hyperkalaemia:

Hyperkalaemia may occur in some patients treated with **REPREX.** Potassium sparing diuretics (e.g. spironolactone, triamterene or amiloride) (see "**CONTRA-INDICATIONS**"), potassium supplements or potassium-containing salt substitutes, may lead to significant increases in serum potassium. Therefore, the combination of **REPREX** with the above-mentioned medicines is not recommended. If concomitant use is indicated because of confirmed hypokalaemia, they should be used with caution and serum potassium should frequently be monitored.
An additive hyperkalaemic effect is possible in patients receiving ACE-inhibitors, as in **REPREX** with other medicines that can cause hyperkalaemia (such as ciclosporin), and serum potassium concentrations should be monitored.

Lithium:

Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with **REPREX.** Concomitant use of thiazide diuretics may increase the risk of lithium toxicity and enhance the already increased risk of lithium toxicity with ACE-inhibitors. Combination of **REPREX** with lithium is not recommended (see "**CONTRA-INDICATIONS**"), but if the combination proves necessary, careful monitoring of serum lithium levels should be performed.

Non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin ≥3 g/day:
The administration of non-steroidal anti-inflammatory drugs (NSAIDs) may reduce the antihypertensive effect of **REPREX**. Additionally, NSAIDs and ACE-inhibitors exert an additive effect on the increase in serum potassium and may result in a deterioration of renal function. These effects are usually reversible. Acute renal failure may occur, especially in patients with compromised renal function like the elderly or dehydrated patients.

Antihypertensive agents and vasodilators:

Concomitant use of these agents may increase the hypotensive effects of **REPREX**. Concomitant use with nitroglycerin and other nitrates, or other vasodilators, may further reduce blood pressure.

Antidiabetic agents:

Epidemiological studies have suggested that concomitant administration of ACE-inhibitors, as in **REPREX** and antidiabetic medicines (insulins, oral hypoglycaemic agents) may cause an increased blood-glucose lowering effect with the risk of hypoglycaemia. This phenomenon appeared to be more likely during the first weeks of combined treatment and in patients with renal impairment.

Acetylsalicylic acid, thrombolytics, beta-blockers and nitrates:
REPREX may be used concomitantly with acetylsalicylic acid (when used as a thrombolytic), thrombolytics, beta-blockers and/or nitrates.

Tricyclic antidepressants/antipsychotics/anaesthetics:

Concomitant use of certain anaesthetic medicines, tricyclic antidepressants and antipsychotics with **REPREX** may result in further reduction of blood pressure.

Sympathomimetics:

Sympathomimetics may reduce the antihypertensive effects of **REPREX**.

PREGNANCY AND LACTATION:

Pregnancy:

REPREX is contra-indicated during pregnancy and lactation.

REPREX passes through the placenta and can be presumed to cause disturbance in foetal blood pressure regulatory mechanisms. Oligohydramnios as well as hypotension, oliguria and anuria in newborns have been reported after administration of **REPREX** in the second and third trimester. Cases of defective skull ossification have been observed. Prematurity and low birth mass can occur.
In addition, use of **REPREX** during the first trimester of pregnancy has been associated with an increased risk of birth defects, in particular of the cardiovascular and the central nervous system (see "**CONTRA-INDICATIONS**" and "**WARNINGS AND SPECIAL PRECAUTIONS**").

Lactation:
The safety of **REPREX** during lactation has not been established and therefore mothers on **REPREX** should not breastfeed their babies.

DOSAGE AND DIRECTIONS FOR USE:

Mild to moderate hypertension:

The tablets should be taken before meals.
The recommended dosage is 4 mg orally taken in the morning before breakfast which can be increased to a single dose of 8 mg if necessary after one month of treatment.
In elderly patients and in cardiac failure substantially lower dosage should be used because of impaired clearance.
Insulin and non-insulin dependent diabetics can be treated with the usual doses.

Congestive heart failure:
The treatment should be initiated under close medical supervision. Initial dose of 2 mg orally as a single dose in the morning which may, in most instances, be increased to 4 mg (once blood pressure acceptability has been demonstrated).

Concomitant diuretic therapy in hypertension:
Caution is recommended in patients who are currently being treated with diuretics. As the effects of ACE-inhibitors may be potentiated in a situation where hypovolemia may occur, the diuretic therapy should be discontinued prior to initiation of therapy with **REPREX.** In the case of combination with a diuretic it is not advisable to prescribe a potassium salt or a potassium sparing agent before assay of blood potassium, and attention should be paid to possible overdosage of the diuretic (see "**Contra-indications and Interactions**").

Renal insufficiency:

In patients with renal insuffiency (creatinine clearance 30 – 60 ml/min), the dosage of perindopril must be adjusted in relation to the severity of the insufficiency. The following dosages may be recommended:

Creatinine clearance	Recommended dosage
30 - 60 ml/min	2 mg per day

REPREX is contra-indicated in patients with a creatinine clearance below 30 ml/min.
Perindopril is dialysable (70 ml/min).

SIDE EFFECTS:

Less frequent: Confusion.

Blood and lymphatic system disorders:

Less frequent: Decreases in haemoglobin, haematocrit, thrombocytopenia, leucopenia/neutropenia, agranulocytosis, pancytopenia. Cases in patients with a congenital deficiency of G-6PDH, of haemolytic anaemia are rarely reported.
Anaemias.

Psychiatric disorders:

Less frequent: Mood and/or sleep disturbances.

Nervous system disorders:

Frequent: Headache, dizziness, vertigo, paraesthesia.
Less frequent :Confusion.

Eye disorders:

Frequent: Visual disturbances.

Ear and labyrinth disorders:

Frequent: Tinnitus.

Cardiovascular disorders:

Frequent: Hypotension and effects related to hypotension.
Less frequent: Dysrhythmia, angina pectoris, myocardial infarction and stroke, possibly secondary to excessive hypotension in high-risk patients e.g. in patients with ischaemic heart disease or cerebrovascular disease.
The following side effects have been reported and frequencies are unknown: Orthostatic effects (including hypotension), palpitations.

Respiratory, thoracic and mediastinal disorders:

Frequent: Cough, dyspnoea.
Less frequent: Bronchospasm, eosinophilic pneumonia and rhinitis.

Gastro-intestinal disorders:

Frequent: Unspecific digestive disorders, nausea, vomiting, abdominal pain, taste disturbance, dyspepsia, diarrhoea, constipation.
Less frequent: Pancreatitis, dry mouth.

Hepato-biliary disorders:
Less frequent: Hepatocellular injury or cholestatic jaundice, hepatitis either cytolytic or cholestatic.

Skin and subcutaneous tissue disorders:

Frequent: Rash, pruritus.
Less frequent: Angioedema of face, lips, mucous membranes, tongue, glottis and/or larynx, extremities and urticaria, erythema multiforme.

Musculoskeletal, connective tissue and bone disorders:
Frequent: Muscular cramps.

Renal and urinary disorders:

Less frequent: Renal insufficiency, acute renal failure.

Reproductive system and breast disorders:
Less frequent: Impotence.

General disorders:

Frequent: Asthenia.
Less frequent: Sweating.

Investigations:

Less frequent: Elevation of liver enzymes and serum bilirubin.
The following side effects have been reported and frequencies are unknown: In the presence of renal insufficiency, severe heart failure and renovascular hypertension, there may be an increase in blood urea, plasma creatinine and hyperkalaemia, but it is reversible on discontinuation of the medication.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
Symptoms associated with overdose of **REPREX** may include hypotension, circulatory shock, electrolyte disturbances, renal failure, hyperventilation, tachycardia, palpitations, bradycardia, dizziness, anxiety and cough.
The recommended treatment of an overdose is an intravenous infusion of normal saline solution. If hypotension occurs, the patient should be placed in the shock position. If available, treatment with angiotensin II infusion and/or intravenous catecholamines may also be considered. **REPREX** may be removed from the general circulation by haemodialysis. Pacemaker therapy is indicated for therapy-resistant bradycardia. Vital signs, serum electrolytes and creatinine concentrations should be monitored continuously. Expected symptoms and signs would be linked to hypotension. Further treatment is symptomatic and supportive.

IDENTIFICATION:

REPREX 2 mg
White to off-white coloured round biconvex uncoated tablets, with debossing "D" on one side and "57" on other side.

REPREX 4 mg
White to off-white coloured capsule shaped uncoated tablets, with debossing "D" on one side and "5" and "8" on either side of the breakline on other side.

REPREX 8 mg
White to off-white coloured round biconvex uncoated tablets, with debossing "D" on one side and "5" and "9" on either side of breakline on other side.

PRESENTATION:

REPREX 2 mg, REPREX 4 mg, and REPREX 8 mg:

Blister Packs:

Tablets are packed in blister packs (composed of clear PVC film and silver coloured aluminium lidding foil). Each blister contains 10 tablets. Three blisters are packed in a bag together with a silica gel sachet.

Pack size: 30 s: Each carton contains 3 blisters of 10 tablets each.

STORAGE INSTRUCTIONS:

Store at or below 25 °C in a dry place.

Do not remove the blisters from the carton until required.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

SOUTH AFRICA:
REPREX 2 mg: 43/7.1.3/1032
REPREX 4 mg: 43/7.1.3/1033
REPREX 8 mg: 43/7.1.3/1034
NAMIBIA:
REPREX 2 mg: 18/7.1.3/0095
REPREX 4 mg: 18/7.1.3/0096
REPREX 8 mg: 18/7.1.3/0097

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Aurogen South Africa (Pty) Ltd
Woodhill Office Park, Building 1, First floor,
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DATE OF PUBLICATION OF THIS PROFESSIONAL INFORMATION:
Date of registration:
30 September 2011
Date of revision:
18 September 2021

P1529149

SOUTH AFRICA: S3
NAMIBIA: NS2

REPREX 2 mg (tablet)
REPREX 4 mg (tablet)
REPREX 8 mg (tablet)
Perindopril tert-butylamine

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

1. WHAT REPREX CONTAINS

The active substance is perindopril.
REPREX 2 mg: Each uncoated tablet contains perindopril tert-butylamine 2 mg. Contains sugar: 29.66 mg lactose.
REPREX 4 mg: Each uncoated tablet contains perindopril tert-butylamine 4 mg. Contains sugar: 59.33 mg lactose.
REPREX 8 mg: Each uncoated tablet contains perindopril tert-butylamine 8 mg. Contains sugar: 118.66 mg lactose.
The other ingredients are cellulose microcrystalline, magnesium stearate and silica hydrophobic colloidal anhydrous.

2. WHAT REPREX IS USED FOR

REPREX belongs to a class of medications called angiotensin-converting enzyme (ACE) inhibitors. It works by decreasing certain chemicals that tighten the blood vessels, so blood flows more smoothly and the heart can pump blood more efficiently.
REPREX is used to treat high blood pressure and is also used to treat congestive heart failure (a condition where the heart is unable to pump enough blood to meet the body's needs).

Do not take REPREX:

3. BEFORE YOU TAKE REPREX
- If you have ever had an allergic reaction to perindopril or any ingredient of the product.
- If you have ever had angioedema (a condition that causes difficulty swallowing or breathing and painful swelling of the face, throat, tongue, lips, eyes, hands, feet, ankles, or lower legs) related to previous treatment with an ACE-inhibitor or angiotensin receptor blocker.
- If you have hereditary (inherited) / idiopathic (unknown cause) angioedema.
- If you have hypertrophic obstructive cardiomyopathy (heart muscle disease).
- If you have severe kidney disease.
- If you have renal artery stenosis (narrowing of the artery supplying the kidney with blood).
- If you have aortic stenosis (a narrowing of the aortic valve in the heart, slowing blood flow from the heart into the main artery leaving the heart).
- If you are taking diuretics (water tablets used to reduce the amount of water in the body), such as spironolactone, triamterene, amiloride. These medicines do not cause your body to lose potassium.
- If you are taking a thiazide diuretic and have Addison's disease, or if you are taking a thiazide diuretic and have severe kidney problems, anuria (failure of kidneys to produce urine) or if you are allergic to other "sulpha" medicines.
- If you have porphyria (an inherited disorder of blood pigment metabolism).
- If you are taking lithium.
- If you are pregnant or breastfeeding (See **"Take special care with REPREX"** and **"Pregnancy and Breastfeeding")**.
- **REPREX** must not be given to children.

REPREX can harm an unborn baby. If you get pregnant, immediately stop taking REPREX. Call your doctor right away. Talk to your doctor about other medicines to take to lower your blood pressure.

Take special care with REPREX:
- You should know that loss of water from your body due to vomiting or diarrhoea; being on dialysis; taking diuretics (medicine to increase excretion of urine); and too little salt in your diet can cause a drop in blood pressure, which may cause lightheadedness and fainting. Low blood pressure is also most likely to happen if you have heart problems. If you are at risk of low blood pressure, your doctor may need to monitor your therapy closely. Lie down if you feel faint or dizzy.
- If you develop swelling of the face around your lips, tongue, or throat or difficulty swallowing, you should immediately contact your doctor and stop taking **REPREX**.
- If you are elderly or have severe kidney disease, your doctor may need to adjust your dose.
- **REPREX** has been associated with a decrease in the number of a certain type of white blood cells. Low white blood cells happen more in people who have kidney problems and collagen vascular diseases (diseases of the connective tissue). Low white blood cells can give you a higher chance for getting infections. Call your doctor if you get a fever, sore throat, or other signs of infection that do not go away.
- Do not use salt substitutes which contain potassium, potassium supplements or other medicines which may increase potassium blood levels while taking **REPREX**, unless you doctor has told you to.
- Your doctor may monitor your kidney function or check your blood potassium level. Do not miss any scheduled visits to your doctor.
- A persistent, dry cough may occur while taking **REPREX**.
- To be sure this medication is helping your condition, your blood pressure will need to be checked on a regular basis. Do not miss any scheduled visits to your doctor.

Tell your doctor:
- if you have narrowing of the heart valves (aortic stenosis) or heart muscle disease (hypertrophic cardiomyopathy) (See **"Do not take REPREX"**).
- if you have any other heart problems, such as heart failure, congestive heart failure, heart attack or ischaemic heart disease.
- if you suffer from a collagen vascular disease (disease of the connective tissue) such as systemic lupus erythematosus or scleroderma.
- if you have blood vessel problems in the brain (including stroke).
- if you have kidney problems, or if you are receiving dialysis.
- if you have liver problems or develop jaundice (yellow skin and eyes).
- if you have diabetes.
- if you have recently had a kidney transplant.
- if you are to undergo anaesthesia and / or surgery.
- if you are on a salt restricted diet or use salt substitutes which contain potassium.
- if you are going to have cholesterol removed from your blood by a machine (LDL apheresis).
- if you are going to have desensitisation treatment to reduce the effects of an allergy e.g. allergy to bee or wasp stings.
- if your blood pressure is not sufficiently lowered due to ethnic affiliation (particularly in patients with black skin colour).
- if you are taking lithium for mania or depression (See **"Do not take REPREX"** and **"Taking other medicines with REPREX"**).

Taking REPREX with food and drink:

REPREX should be taken before a meal.

Pregnancy and Breastfeeding:

Do not use this medication if you are pregnant or planning a pregnancy or if you are breastfeeding.
REPREX can cause birth defects in the baby if you take the medication during pregnancy. Use an effective form of birth control. Stop using this medication and tell your doctor right away if you become pregnant during treatment.

If you are pregnant or breastfeeding your baby do not take **REPREX**, please consult your doctor, pharmacist or other healthcare professional for advice before **REPREX.**

Driving and using machinery:

Do not drive or use machines if you feel dizzy or tired when taking **REPREX.**

Taking other medicines with REPREX:
Before taking **REPREX**, tell your doctor if you are using any of the following medicines:
- Other medicines for high blood pressure, including diuretics (medicines which increase the amount of urine produced by the kidneys).
- Potassium-sparing diuretics (water tablets which affect potassium, such as spironolactone, triamterene or amiloride), potassium supplements, potassium containing-salt substitutes, or medicines which may increase potassium levels in your blood (e.g. ciclosporin). **REPREX** must not be taken with potassium-sparing diuretics (See **"Do not take REPREX"**). Do not use salt substitutes which contain potassium, potassium supplements or other medicines which may increase potassium levels in your blood while taking **REPREX**, unless you doctor has told you to.
- Heparin (for thinning the blood) can also affect potassium levels in your blood.
- Lithium for mania or depression (See **"Do not take REPREX"**).
- Non-steroidal anti-inflammatory medications (e.g. ibuprofen, indomethacin) for treating pain and inflammation or high dose aspirin.
- Allopurinol (for gout).
- Medicines for diabetes (insulin or tablets).
- Procainamide (for irregular heartbeat).
- Medicines that make the blood vessels wider (vasodilators, such as nitrates).
- Medicines to treat mental disorders such as depression, anxiety, schizophrenia or other psychosis (e.g. tricyclic antidepressants, antipsychotics).
- Anaesthetics (medicines causing loss of sensation or pain/consciousness).
- Medicines used for the treatment of low blood pressure, shock or asthma (e.g. ephedrine, noradrenaline or adrenaline).
- Immunosuppressants (medicines which reduce the defence mechanism of the body) used for the treatment of auto-immune disorders or following transplant surgery (e.g. ciclosporin).

  If you are using any of these medicines, you may not be able to take **REPREX,** or you may need dosage adjustments or your doctor may need to monitor you carefully for side effects.

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

4. HOW TO TAKE REPREX
- Take this medicine only as directed by your doctor.
- Do not take more or less of it or take it more often than prescribed by your doctor.
- **REPREX** should be taken before a meal.

The usual dosages are as follows:
- High blood pressure:
  The usual dosage is 4 mg taken in the morning before breakfast. After one month your doctor may decide this dosage can be increased to 8 mg once a day, if required.
  If you are elderly or have heart failure, your doctor will prescribe a lower dosage.
- Congestive heart failure:
  The usual starting dose is 2 mg once daily in the morning. Your doctor can increase this dose to 4 mg once a day.

If you are taking water tablets (diuretics):
- Your doctor may decide to stop them before you start taking **REPREX**.

Always take **REPREX** 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 of **REPREX** is too strong or too weak, talk to your doctor or pharmacist.

If you take more REPREX than you should:
The following effects may occur: low blood pressure, shock, kidney problems, fast breathing, fast heartbeat, uneven heartbeat (palpitations), slow heartbeat, feeling dizzy or anxious and cough.

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

If you forget to take REPREX:
It is important to take your medicine every day as regular treatment works better.

If you forget to take **REPREX**, take the missed dose as soon as you remember it. However, if it is almost time for the next dose, skip the missed dose and continue your regular dosing schedule. Do not take a double dose to make up for a missed one.

5. POSSIBLE SIDE EFFECTS
REPREX can have side effects.
Get emergency medical help if you have any of these signs of an allergic reaction:
- Difficulty breathing.
- Swelling of your face, lips, tongue, or throat

Call your doctor at once if you have any of these serious side effects:
- Fainting, feeling light-headed or feeling faint, particularly when standing. This may mean your blood pressure is too low.
- Jaundice (yellowing of the skin and eyes).
- Urinating less than usual, or not at all.
- Palpitations (rapid irregular action of heart) or arrhythmias (irregular heart beat).
- Angina (chest pain that happens in heart disease).
- Heart attack (chest pain, shortness of breath, excess sweating, weakness, light-headedness, nausea, vomiting, palpitations, fatigue).
- Stroke (sudden numbness or weakness of the face, arm or leg, especially on one side of the body; sudden severe headache; sudden confusion, trouble speaking or understanding; sudden trouble walking, dizziness, loss of co-ordination).
- Pale skin, easy bruising or bleeding.
- Fever, sore throat, chills, and other signs of infection.
- Severe abdominal and back pain accompanied with feeling very unwell (inflammation of the pancreas).

Other side effects include: Sleep problems; mood swings; headache; dizziness; feeling of spinning or rotation of surroundings (vertigo); pins and needles; feeling confused; problems with vision; sensation of noises in the ears; cough; shortness of breath; tight feeling in the chest, wheezing and short of breath (bronchospasm); chest infection (eosinophilic pneumonia); blocked up or runny nose (rhinitis); diarrhoea; constipation; nausea (feeling sick); vomiting (being sick); abdominal pain; changes in your sense of taste; heartburn; dry mouth; inflamed liver (hepatitis); skin rash; hives; itching; skin reaction like an allergy (erythema multiforme); muscle cramps; kidney problems; impotence (unable to get an erection); disorders of the blood (your doctor may carry out blood tests to check for this); lack of energy; sweating; anaemia.

Tell your doctor if any of the above side effects are severe, bothersome, do not go away or about any concerns you have while taking **REPREX.**

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

6. STORING AND DISPOSING OF REPREX
Store at or below 25 °C in a dry place. Do not remove the blisters from the carton until required

Store all medicines out of the reach and sight of children.

Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

7. PRESENTATION OF REPREX

REPREX 2 mg, REPREX 4 mg and REPREX 8 mg:

Blister Packs:

Tablets are packed in blister packs (composed of clear PVC film and silver coloured aluminium lidding foil). Each blister contains 10 tablets. Three blisters are packed in a bag together with a silica gel sachet.

Pack size: 30s: Each carton contains 3 blisters of 10 tablets each.

8. IDENTIFICATION OF REPREX

REPREX 2 mg:
White to off-white coloured round biconvex uncoated tablets, with debossing "D" on one side "57" on other side.
REPREX 4 mg:
White to off-white coloured capsule shaped uncoated tablets, with debossing "D" on one side and "5" and "8" on either side of the breakline on other side.
REPREX 8 mg:
White to off-white coloured round biconvex uncoated tablets, with debossing "D" on one side and "5" and "9" on either side of breakline on other side.

9. REGISTRATION NUMBER/REFERENCE NUMBER

SOUTH AFRICA:
REPREX 2 mg: 43/7.1.3/1032
REPREX 4 mg: 43/7.1.3/1033
REPREX 8 mg: 43/7.1.3/1034
NAMIBIA:
REPREX 2 mg: 18/7.1.3/0095
REPREX 4 mg: 18/7.1.3/0096
REPREX 8 mg: 18/7.1.3/0097

10. NAME AND ADDRESS OF REGISTRATION HOLDER

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11. DATE OF PUBLICATION

Date of registration:
30 September 2011

Date of revision:
18 September 2021