SCHEDULING STATUS:
S3

PROPRIETARY NAME AND DOSAGE FORM:
LOSARTAN BIOTECH 50 (film-coated tablets)

COMPOSITION:
Each LOSARTAN BIOTECH 50 tablet contains 50 mg losartan potassium.
The excipients are:
Tablet core: Cellulose microcrystalline, magnesium stearate, povidone, silica colloidal anhydrous, sodium starch glycollate.
Film-coating: Opadry white 0Y-L-28900 consisting of: Hypromellose, macrogol 4000, titanium dioxide (E171).
Contains sugar (lactose monohydrate).

PHARMACOLOGICAL CLASSIFICATION:
A7.1.3 Other hypotensives

PHARMACOLOGICAL ACTION:
Losartan is a nonpeptide angiotensin II receptor antagonist with high affinity and selectivity for the AT_1 receptor, without binding to or blocking other hormone receptors or ion channels important in cardiovascular regulation. Angiotensin II is a potent vasoconstrictor. A primary active hormone of the renin-angiotensin
system, and a major determinant of the pathophysiology of hypertension. Losartan blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II by inhibiting the binding of angiotensin II to the AT_1 receptor.
Pharmacodynamic properties
Losartan is a specific antagonist of the angiotensin II receptor type AT_1, it does not inhibit ACE (kininase II), the enzyme that degrades bradykinin.
Removal of angiotensin II negative feedback on renin secretion leads to increased plasma renin activity, during losartan administration. A 2 to 3 fold increase in angiotensin II in plasma, comes as a result of increases in plasma renin activity. However, antihypertensive activity and suppression of plasma aldosterone concentration were apparent, indicating effective angiotensin II receptor blockade. After discontinuation of losartan, plasma renin activity and angiotensin levels declined.
Pharmacokinetic properties
Absorption:
Following oral administration, with an oral bioavailability of about 33 %. It undergoes first-pass metabolism to form an active carboxylic acid metabolite (which has greater pharmacological activity than losartan) and some inactive metabolites.
About 14 % of intravenously- or orally-administered dose is converted to its active metabolite. The mean peak concentrations of losartan and its active metabolite are reached in 1 hour and 3 to 4 hours respectively.
Both losartan and carboxylic acid metabolite are greater than, or equal to 99 % bound to plasma proteins. The distribution volume of losartan is 34 litres.
The terminal half-life of losartan is 2 hours and its active metabolite is 6 to 9 hours.
Following oral dosing, about 35 % of the dose is excreted in the urine and about 60 % in the faeces. Neither losartan nor the active metabolite can be removed by haemodialysis.
Plasma concentrations of losartan are not altered in patients with impaired renal function and a creatinine clearance above 10 ml/min. Compared to patients with normal renal function, the AUC for losartan is approximately 2-fold greater in patients on haemodialysis.

INDICATIONS:
LOSARTAN BIOTECH 50 is indicated for the treatment of hypertension.

CONTRAINDICATIONS:
Patients who are hypersensitive to LOSARTAN BIOTECH 50 or any of its components.
The use of LOSARTAN BIOTECH 50 during pregnancy and lactation is contraindicated. (see PREGNANCY AND LACTATION).
LOSARTAN BIOTECH 50 should be discontinued as soon as possible, when pregnancy is suspected.
Safety and efficacy has not been established in children.

WARNINGS AND SPECIAL PRECAUTIONS:
Women of childbearing age should ensure adequate contraception.
LOSARTAN BIOTECH 50 is contraindicated in pregnancy and should be used with care if at all during breastfeeding (see CONTRAINDICATIONS).
LOSARTAN BIOTECH 50 should be used with caution in patients with bilateral renal artery stenosis or stenosis of an artery to a single kidney, aortic valve stenosis, hypertrophic obstructive cardiomyopathy.
Since hyperkalaemia may occur, serum-potassium concentrations should be monitored, especially in the elderly and patients with renal impairment and the concomitant use of potassium-sparing diuretics should generally be avoided (see INTERACTIONS).
When impaired renal function is present, changes in renal function as a consequence of inhibiting the renin-angiotensin system including renal failure have been reported in susceptible individuals. These changes in renal function may be reversible upon discontinuation of LOSARTAN BIOTECH 50 therapy, in some patients. In patients whose renal function may depend on the activity of the renin-angiotensin-aldosterone system (e.g. patients with severe congestive heart failure treated with angiotensin converting enzyme inhibitors has been associated with oliguria and/or progressive azotemia and (less frequently) with acute renal failure and/or death. Similar outcomes are likely with LOSARTAN BIOTECH 50 therapy.
Agents affecting the renin-angiotensin system may increase blood urea and serum creatinine in patients with bilateral renal artery stenosis or stenosis of the artery to a solitary kidney. These changes in renal function may be reversible upon discontinuation of LOSARTAN BIOTECH 50 therapy.
Symptomatic hypotension may occur after initiation of LOSARTAN BIOTECH 50.
Patients with volume-depletion (e.g. those treated with high-dose diuretics) may experience hypotension, which may be minimised by initiating treatment with a low dose of LOSARTAN BIOTECH 50.
Halving of the dose should be considered for patients with a history of hepatic impairment (see DOSAGE AND DIRECTIONS FOR USE).

INTERACTIONS:
Combinations containing any of the following medications, depending on the amount present, may also interact with LOSARTAN BIOTECH 50.
Anti-inflammatory medicines, NSAIDs, especially indomethacin, may antagonise the antihypertensive effect of LOSARTAN BIOTECH 50.
Concurrent use with sympathomimetics may reduce the antihypertensive effects of LOSARTAN BIOTECH 50.
Potassium-sparing diuretics, potassium containing medication or potassium supplements used concurrently with LOSARTAN BIOTECH 50 may result in hyperkalaemia since reduction of aldosterone production induced by LOSARTAN BIOTECH 50 may lead to elevation of serum potassium (see WARNINGS AND SPECIAL PRECAUTIONS).

PREGNANCY AND LACTATION:
Pregnancy: See "CONTRAINDICATIONS"
- **LOSARTAN BIOTECH 50 should be discontinued as soon as possible, when pregnancy is suspected.**
- **LOSARTAN BIOTECH 50 should not to be used in pregnancy as teratogenicity has been shown in experimental animals.**

Lactation:
- **Safety has not been established.**

DOSAGE AND DIRECTIONS FOR USE:
The usual starting and maintenance dose is 50 mg once daily for most patients. The maximum antihypertensive effect is achieved 3 to 6 weeks after initiation of therapy. The dose may be increased to 100 mg once daily.
For patients with intravascular volume-depletion (e.g. those treated with high-dose diuretics), a starting dose of 25 mg once daily should be considered (see SPECIAL PRECAUTIONS).
No initial dosage adjustment is necessary for the elderly patients or for patients with renal impairment, including patients on dialysis. A lower dose should be considered for patients with a history of hepatic impairment (see SPECIAL PRECAUTIONS).
LOSARTAN BIOTECH 50 may be administered with other antihypertensive agents of a different class.
LOSARTAN BIOTECH 50 may be administered with or without food.

SIDE EFFECTS:
The following side effects may occur:
Immune system disorders
The following side effects have been reported but frequencies are unknown:
Angioedema (involving swelling of the face, lips, and/or tongue) has been reported rarely in patients treated with LOSARTAN BIOTECH 50.
Gastrointestinal disorders
Less frequent: Diarrhoea, dyspepsia, nausea.
The following side effects have been reported but frequencies are unknown:
Taste disturbances, complete taste loss, acute pancreatitis.
Skin and subcutaneous tissue disorders
Less frequent: Urticaria, rash, atypical cutaneous lymphoid infiltrates.
Cardiac disorders
The following side effects have been reported but frequencies are unknown:
Palpitations, tachycardia.
Vascular disorders
The following side effects have been reported but frequencies are unknown:
Hypotension, orthostatic hypotension.
Musculoskeletal, connective tissue and bone disorders
Less frequent: Back pain, muscle cramps, leg pain, rhabdomyolysis, myalgia.
Nervous system disorders
Frequent: Headache.
Less Frequent: Dizziness, migraine.
Psychiatric disorders
Less Frequent: Insomnia.
Respiratory, thoracic and mediastinal disorders
Less frequent: Cough (dry), nasal congestion, pharyngitis, sinus disorder, upper respiratory infection.
Hepato-biliary disorders
Less frequent: Raised liver enzymes values, severe acute hepatotoxicity, cholestasis, hepatitis.
Blood and the lymphatic system disorders
Frequent: Decreased haemoglobin concentrations.
Less frequent: Symptomatic anaemia.
The following side effect has been reported but frequency is unknown:
neutropenia.
Metabolism and nutrition disorders
Less frequent: Hyperkalaemia, hyponatraemia.
General disorders and administrative site conditions
Less frequent: Abdominal pain, asthenia/fatigue, chest pain, fatigue and oedema/swelling.
Renal and urinary disorders
The following side effect has been reported but the frequency is unknown:
Impaired renal function

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
The symptoms of an overdosage of LOSARTAN BIOTECH 50 would be hypotension and tachycardia. Bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted. Neither LOSARTAN BIOTECH 50 nor the active metabolite can be removed by haemodialysis.

IDENTIFICATION:
LOSARTAN BIOTECH 50 is a white, oval, film-coated tablet with one notch on each side.

PRESENTATION:
LOSARTAN BIOTECH 50 tablets are available in PVC/PVDC aluminium blisters, in pack sizes of 30 tablets.

STORAGE INSTRUCTIONS:
Store at or below 25 °C.
Keep the blisters in the carton until required for use.
KEEP OUT OF REACH OF CHILDREN

REGISTRATION NUMBER:
A40/7.1.3/0069

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE REGISTRATION CERTIFICATES:
Biotech Laboratories (Pty) Ltd
Ground Floor, Block K West, Central Park
400 16th Road, Randjespark, Midrand, 1685
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DATE OF PUBLICATION OF THIS PACKAGE INSERT:
Date of registration: 30 November 2007
Date of notification with regard to amended Reg. 9 and 10: 07 July 2017

PA400069-1

SKEDULERINGSTATUS:
S3

EIENDOMSNAAM EN DOSEERVORM:
LOSARTAN BIOTECH 50 (filmbedekte tablette)

SAMESTELLING:
Elke LOSARTAN BIOTECH 50 tablet bevat 50 mg kaliumlosartan.
Die onaktiewe bestanddele is:
Tablet kern: Mikrokristallyne sellulose, magnesiumstearaat, povidoon, kolloïdale anhidriese silika, natriumstyselglikolaat.
Filmbedekking: Opadry wit OY-L-28900 bestaande uit: Hipromellose, makrogol 4000, titaandioksied (E171).
Bevat suiker (Laktosemonohidraat).

FARMAKOLOGIESE KLASSIFIKASIE:
A7.1.3 Ander hipotensiewe middels

FARMAKOLOGIESE WERKING:
Losartan is 'n non-peptied angiotensien-II-reseptorantagonis met 'n hoë affiniteit en selektiwiteit vir die AT_1-reseptor sonder dat dit aan ander hormoonreseptore of ioonkanale, belangrik vir kardiovaskulêre regulasie, bind of dit blokkeer. Angiotensien II is 'n kragtige vasokonstriktor. Losartan is 'n primêre aktiewe hormoon van die renien-angiotensienstelsel en 'n belangrike bepaler van die patofisiologie van hipertensie. Losartan blokkeer die effek van angiotensien II as vasokonstriktor en afskeier van aldosteroon deur die binding van angiotensien II aan die AT_1-reseptor te inhibeer.
Farmakodinamiese eienskappe
Losartan is 'n spesifieke antagonis van die angiotensien-II-reseptor tipe AT_1, dit inhibeer nie AOE (kininase II) die ensiem wat bradikinien afbreek nie. Blokkering van die negatiewe terugvoer van angiotensien II op renienafskeiding tydens toediening van losartan lei tot hoër aktiwiteit van renien in die plasma. 'n 2- tot 3-voudige toename in die konsentrasie van angiotensien II in die plasma volg na toename in die aktiwiteit van renien in die plasma. Die antihipertensiewe aktiwiteit en onderdrukking van die konsentrasie van aldosteroon in die plasma is 'n aanduiding wat die effektiewe blokkasie van die angiotensien-II-reseptor toon. Na staking van losartan neem die aktiwiteit van renien in die plasma en vlakke van angiotensien af.
Farmakokinetiese eienskappe
Absorpsie:
Na orale toediening, is die biobeskikbaarheid ongeveer 33 %. Dit ondergaan eerstedeurgangmetabolisme om 'n aktiewe karboksielsuurmetaboliet (met sterker farmakologiese aktiwiteit as losartan) en sommige onaktiewe metaboliete te vorm.
Ongeveer 14 % van 'n binneaarse of mondelinge toegediende dosis word na die aktiewe metaboliet omgeskakel. Die gemiddelde piekkonsentrasies van losartan en sy aktiewe metaboliet word onderskeidelik binne 1 en 3 tot 4 uur bereik.
Beide losartan- en die karboksielsuurmetaboliet is groter as, of gelyk aan, 99 % gebind aan plasmaproteïene. Die verdelingsvolume van losartan is ongeveer 34 liter.
Die terminale halfleeftyd van losartan is 2 uur en dié van die aktiewe metaboliet is 6 tot 9 uur.
Na orale dosering word ongeveer 35 % van die dosis uitgeskei in die urine en ongeveer 60 % in die ontlasting. Nie losartan of sy aktiewe metaboliet kan verwyder word deur hemodialise nie.
Die plasmakonsentrasie van losartan in pasiënte met verswakte nierfunksie en 'n kreatinienopruiming van meer as 10 ml/min word nie aangetas nie. In vergelyking met pasiënte met normale nierfunksie, is die AOK vir losartan ongeveer twee maal groter by pasiënte wat hemodialise ontvang.

INDIKASIES:
LOSARTAN BIOTECH 50 is aangedui vir die behandeling van hipertensie.

KONTRAINDIKASIES:
Pasiënte wat hipersensitief is vir LOSARTAN BIOTECH 50 of enige van sy komponente.
Die gebruik van LOSARTAN BIOTECH 50 tydens swangerskap en borsvoeding is 'n kontraïndikasie (sien SWANGERSKAP EN LAKTERING).
LOSARTAN BIOTECH 50 moet so gou as moontlik gestaak word wanneer swangerskap vermoed word.
Die veiligheid en effektiwiteit van LOSARTAN BIOTECH 50 onder kinders is nog nie vasgestel nie.

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS:
Vrouens wat swanger kan raak moet geskikte kontrasepsie verseker.
LOSARTAN BIOTECH 50 is gekontraïndikeer tydens swangerskap en moet met sorg, indien enigsins, tydens borsvoeding gebruik word (sien KONTRAÏNDIKASIES).
LOSARTAN BIOTECH 50 moet met omsigtigheid gebruik word deur pasiënte met bilaterale stenose van nierare of stenose van 'n slagaar van 'n enkele nier, stenose van aortakleppe en hipertrofiese obstruktiewe kardiomiopatie. Aangesien hiperkalemie kan voorkom, moet die konsentrasie van kalium in die serum gemonitor word, veral by bejaarde pasiënte en diegene met verswakte nierfunksie en die gelyktydige gebruik van kaliumsparende diuretika moet oor die algemeen vermy word (sien INTERAKSIES).
Wanneer verswakte nierfunksie teenwoordig is, is veranderinge in nierfunksie as gevolg van die inhibering van die renien-angiotensienstelsel insluitende nierversaking aangemeld by vatbare individue. Hierdie veranderings in nierfunksie kan, in sommige pasiënte, omkeerbaar wees met die staking van LOSARTAN BIOTECH 50-behandeling.
By pasiënte wie se nierfunksie van die aktiwiteit van die renien-angiotensien-aldosteroonstelsel afhang (bv. pasiënte met ernstige kongestiewe hartversaking), het behandeling met angiotensienomskakelingsensiemremmers met oligurie en/ of progressiewe asotemie en (minder dikwels) met akute nierversaking en/ of dood gepaard gegaan. Soortgelyke gevolge is waarskynlik met LOSARTAN BIOTECH 50 behandeling.
Middels wat die renien-angiotensienstelsel beïnvloed kan die konsentrasie van urea in die bloed en kreatien in die serum van die pasiënte met bilaterale nierarstenose of stenose van die aar van 'n enkele nier verhoog. Hierdie veranderings in nierfunksie kan, in sommige pasiënte, omkeerbaar wees met die staking van LOSARTAN BIOTECH 50-behandeling.
Simptomatiese hipotensie kan voorkom na die aanvang van LOSARTAN BIOTECH 50.
Pasiënte met volume-uitputting (bv. diegene wat met hoë dosisse diuretika behandel word) kan hipotensie ervaar wat verminder kan word deur behandeling met 'n lae dosis LOSARTAN BIOTECH 50 te begin.
Halvering van die dosis moet oorweeg word vir pasiënte met 'n geskiedenis van swak lewerfunksie (sien DOSIS EN GEBRUIKSAANWYSINGS).

INTERAKSIES:
Kombinasies van enige van die volgende middels, afhangende van die hoeveelheid, kan ook met LOSARTAN BIOTECH 50 reageer.
Anti-inflammatoriese middels (NSAIMs), veral indometasien, kan die antihipertensiewe effek van LOSARTAN BIOTECH 50 antagoniseer.
Gelyktydige gebruik van simpatomimetika kan die antihipertensiewe effek van LOSARTAN BIOTECH 50 verminder.
Kaliumsparende diuretika, kaliumbevattende medikasie of kaliumaanvullings wat saam met LOSARTAN BIOTECH 50 gebruik word, kan tot hiperkalemie lei, aangesien die vermindering van aldosteroonproduksie, geïnduseer deur LOSARTAN BIOTECH 50, tot verhoogde vlakke van kalium in die serum kan lei (sien WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS).

SWANGERSKAP EN LAKTASIE:
Swangerskap: (Sien KONTRAÏNDIKASIES)
LOSARTAN BIOTECH 50 moet so gou as moontlik gestaak word wanneer swangerskap vermoed word.
LOSARTAN BIOTECH 50 moet nie tydens swangerskap gebruik word nie aangesien teratogenisiteit in laboratoriumdiere getoon is.
Laktasie:
Die veiligheid van gebruik is nie vasgestel nie.

DOSIS EN GEBRUIKSAANWYSINGS:
Die normale aanvangs- en onderhoudsdosis is 50 mg een maal per dag vir die meeste pasiënte. Die maksimum antihipertensiewe effek word 3 tot 6 weke na aanvang van behandeling bereik. Die dosis kan een maal per dag na 100 mg verhoog word.
Vir pasiënte met intravaskulêre volume-uitputting (bv. diegene wat met hoë dosisse diuretika behandel word), moet 'n aanvangsdosis van 25 mg een maal per dag oorweeg word (sien WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS).
Geen aanvanklike aanpassing in die dosis is nodig vir bejaarde pasiënte of vir pasiënte met verswakte nierfunksie, insluitend pasiënte op dialise, nie. 'n Laer dosis moet oorweeg word vir pasiënte met 'n geskiedenis van verswakte lewerfunksie (sien WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS).
LOSARTAN BIOTECH 50 kan saam met ander antihipertensiewe middels van 'n ander klas toegedien word.
LOSARTAN BIOTECH 50 kan met of sonder voedsel toegedien word.

NEWE-EFFEKTE:
Die volgende newe-effekte kan voorkom:
Immuunstelsel afwykings
Die volgende newe-effekte is aangemeld, maar frekwensies is onbekend:
Angio-edeem (met betrekking tot swelling van die gesig, lippe en/ of tong) is selde aangemeld in pasiënte wat met LOSARTAN BIOTECH 50 behandel is.
Gastroïntestinale afwykings
Minder algemeen: Diarree, slegte spysvertering, naarheid.
Die volgende newe-effekte is aangemeld, maar frekwensies is onbekend:
Smaakversteurings, algehele smaakverlies, akute pankreatitis.
Vel- en subkutane weefsel afwykings
Minder algemeen: Urtikarie, veluitslag, atipiese kutane limf infiltrate.
Kardiale afwykings
Die volgende newe-effekte is aangemeld, maar frekwensies is onbekend:
Palpitasies, tagikardie.
Vaskulêre afwykings
Die volgende newe-effekte is aangemeld, maar frekwensies is onbekend:
Hipotensie, ortostatiese hipotensie.
Muskuloskeletale, bindweefsel- en beenafwykings
Minder algemeen: Rugpyn, spierkrampe, beenpyn, rabdomiolise, mialgie.
Senuweestelsel afwykings
Algemeen: Hoofpyn.
Minder algemeen: Duiseligheid, migraine.
Psigiatriese afwykings
Minder algemeen: Slaaploosheid.
Respiratoriese, torakale en mediastinale afwykings
Minder algemeen: Hoes (droog), toe neus, faringitis, sinusversteuring, infeksie van die boonste lugweg.
Hepatobiliêre afwykings
Minder algemeen: Hoër waardes van lewerensieme, ernstige akute lewertoksisiteit, cholestase, hepatitis.
Bloed- en limfstelsel afwykings
Algemeen: Laer konsentrasies hemoglobien.
Minder algemeen: Simptomatiese anemie.
Die volgende newe-effekte is aangemeld, maar frekwensies is onbekend:
Neutropenie.
Metabolisme en voedings afwykings
Minder algemeen: Hiperkalemie, hiponatremie.
Algemene afwykings en toedieningsarea toestande
Minder algemeen: Buikpyn, astenie/ moegheid, borspyn, moegheid en edeem/ swelling.
Nier- en urinêre afwykings
Die volgende newe-effekte is aangemeld, maar frekwensies is onbekend:
Verswakte nierfunksie.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDELING DAARVAN:
Die simptome van oordosering van LOSARTAN BIOTECH 50 is hipotensie en tagikardie. Bradikardie kan as gevolg van parasimpatiese (vagale) stimulasie voorkom. Indien simptomatiese hipotensie voorkom, moet ondersteunende behandeling gegee word. Nie LOSARTAN BIOTECH 50 of sy aktiewe metaboliete kan verwyder word deur hemodialise nie.

IDENTIFIKASIE:
LOSARTAN BIOTECH 50 is 'n wit, ovaalvormige, film bedekte tablet, wat ingekeep is aan beide kante.

AANBIEDING:
LOSARTAN BIOTECH 50 tablette is beskikbaar in PVC/ PVDC/ aluminium stulpverpakkings, in verpakkingsgroottes van 30 tablette.

BERGINGSAANWYSINGS:
Bewaar teen of benede 25 °C.
Bewaar stulpverpakkings in die karton tot benodig vir gebruik.
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMER:
A40/7.1.3/0069

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT:
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Suid Afrika

DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET:
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