SCHEDULING STATUS
S3

PROPRIETY NAME AND DOSAGE FORM
BIO NIFEDIPINE XL 30 (controlled release tablet)
BIO NIFEDIPINE XL 60 (controlled release tablet)

COMPOSITION
BIO NIFEDIPINE XL 30: Each controlled release tablet contains 30 mg nifedipine.
BIO NIFEDIPINE XL 60: Each controlled release tablet contains 60 mg nifedipine.
Inactive ingredients: Polyethylene oxide, hypromellose, potassium chloride, methyl alcohol, isopropyl alcohol, magnesium stearate, colloidal silicon dioxide, sodium chloride, ferric oxide red, cellulose acetate, polyethylene glycol, purified water, opadry brown (consisting of Hypromellose, iron oxide red, iron oxide yellow, polyethylene glycol and titanium dioxide), opacode black.
SUGAR FREE

PHARMACOLOGICAL CLASSIFICATION
A.7.1 Vasodilators, hypotensive medicines.

PHARMACOLOGICAL ACTION
Pharmacodynamic properties
Nifedipine is a calcium channel antagonist and a peripheral arterial vasodilator which acts directly on vascular smooth muscle with a resultant reduction in peripheral resistance.

Pharmacokinetic properties
General characteristics
The mechanism of release of nifedipine from BIO NIFEDIPINE XL is by membrane-controlled, osmotic push-pull process; nifedipine is released at a zero-order rate over 24 hours. The rate of delivery is not influenced by gastrointestinal pH or motility. After swallowing the excipients of the tablet remain intact and are eliminated as an insoluble shell in the faeces.
Absorption
Administration in the presence of food does not influence the availability of nifedipine.
Distribution
Nifedipine is about 95 % bound to plasma protein (albumin).
Biotransformation
Nifedipine is metabolised in the gut wall and liver, primarily by oxidative processes. The metabolites are predominantly eliminated by the kidneys, with approximately 5-15 % being excreted via the bile in the faeces.
Elimination
The terminal half-life of nifedipine osmotic push-pull release process does not represent a meaningful parameter as a plateau-like plasma concentration is maintained during release from the tablets and absorption.
Hepatic impairment
The elimination half-life is distinctly prolonged and the total clearance is reduced in patients with impaired hepatic function. BIO NIFEDIPINE XL should not be administered to these patients.

INDICATIONS
BIO NIFEDIPINE XL is indicated in following conditions:
- Mild to moderate hypertension
- Prophylaxis of chronic stable angina pectoris.

CONTRAINDICATIONS
Hypersensitivity to nifedipine or to any of the ingredients of BIO NIFEDIPINE XL.
Pregnancy and lactation.
Porphyria.
Clinically significant aortic stenosis, cardiovascular shock, unstable angina.
During or within one month of a myocardial infarction.
Hepatic impair.
History of gastrointestinal obstruction, oesophageal obstruction or any degree of decreased lumen diameter of the gastrointestinal tract.
Inflammatory bowel disease.
Concomitant use with rifampicin (see "Interactions").
Safety and efficacy in children has not been established.
The use of BIO NIFEDIPINE XL in men involved with in vitro fertilisation is contraindicated as nifedipine has been associated with reversible biochemical changes in the spermatozoa's head section that may result in impaired sperm function.

WARNINGS and SPECIAL PRECAUTIONS
Concomitant administration of BIO NIFEDIPINE XL with β-receptor blockers and diuretics can enhance the antihypertensive effect (see "Interactions"). The patients should be carefully monitored.
Grapefruit juice inhibits the metabolism of BIO NIFEDIPINE XL (see "Interactions").
As BIO NIFEDIPINE XL can cause an increase in blood glucose, care must be taken in patients with diabetes mellitus.
Dialysis patients with malignant hypertension and irreversible kidney failure with hypovolaemia should be closely monitored as a marked fall in blood pressure may occur.
Symptoms of gastrointestinal obstruction have occurred in patients with a history of gastrointestinal disorders.
BIO NIFEDIPINE XL should be used with caution in patients with poor cardiac reserve and in angina patients with hypotension; as well in patients with heart failure.
BIO NIFEDIPINE XL must not be used in patients with Kock pouch (ileostomy after proctocolectomy)

Effects on ability to drive and use machines
BIO NIFEDIPINE XL can impair the ability to drive or to operate machinery, especially during the start of treatment, changing the dose and in combination with alcohol. The intensity of the reaction to BIO NIFEDIPINE XL varies from patient to patient.

INTERACTIONS
Nifedipine, such as contained in BIO NIFEDIPINE XL is metabolised via the cytochrome P450 3A4 system, located both in the intestinal mucosa and in the liver. Medicines that are known to either inhibit or to induce this enzyme system may therefore alter the first pass (after oral administration) or the clearance of nifedipine.
The extent as well as the duration of interactions should be taken into account when administering BIO NIFEDIPINE XL together with the following medicines:
Rifampicin
The co-administration of rifampicin and BIO NIFEDIPINE XL, distinctly reduces the bioavailability of BIO NIFEDIPINE XL and thus lowering the efficacy. The use of rifampicin with BIO NIFEDIPINE XL is therefore contraindicated (see "Contraindications").
Macrolide antibiotics
Macrolide antibiotics are known to inhibit the cytochrome P450 3A4 mediated metabolism of other medicines. The potential for increase in nifedipine concentrations upon co-administration should be borne in mind.
Amprenavir, indinavir, nelfinavir, ritonavir, saquinavir
This class of medicines is known to inhibit the cytochrome P450 3A4 system. In vitro, indinavir and ritonavir have been shown to inhibit the cytochrome P450 3A4 mediated metabolism of nifedipine. When administered together with BIO NIFEDIPINE XL, a substantial increase in plasma concentrations of nifedipine due to a decreased first pass metabolism and a decreased elimination cannot be excluded. If co-administered, blood pressure should be monitored and if necessary a dose reduction of BIO NIFEDIPINE XL be considered.
Ketoconazole, itraconazole, fluconazole
This class of medicine inhibits the cytochrome P450 3A4 system. When administered orally together with BIO NIFEDIPINE XL a substantial increase in bioavailability of nifedipine due to decreased first pass metabolism cannot be excluded. If co-administered, blood pressure should be monitored and if necessary a dose reduction of BIO NIFEDIPINE XL be considered.
Fluoxetine
Fluoxetine has been shown to inhibit the cytochrome P450 3A4 mediated metabolism of nifedipine. Therefore an increase in plasma concentrations of nifedipine upon co-administration cannot be excluded. If co-administered, blood pressure should be monitored and if necessary a dose reduction of BIO NIFEDIPINE XL be considered.
Nefazodone
Nefazodone is known to inhibit the cytochrome P450 3A4 system. In vitro, nefazodone have been shown to inhibit the cytochrome P450 3A4 mediated metabolism of other medicines. Therefore when both medicines are co-administered an increase in plasma concentrations of nifedipine cannot be excluded. If co-administered, blood pressure should be monitored and if necessary a dose reduction of BIO NIFEDIPINE XL be considered.
Valproic acid
As valproic acid has been shown to increase in plasma concentrations of the structurally similar calcium channel nimodipine due to enzyme inhibition, an increase in plasma concentration of nifedipine and hence an increase in efficacy cannot be excluded.
Cimetidine
As cimetidine inhibits the cytochrome P450 3A4 system, the co-administration of cimetidine with BIO NIFEDIPINE XL can increase the bioavailability of BIO NIFEDIPINE XL.
Cisapride
Concomitant administration of cisapride and BIO NIFEDIPINE XL can lead to increased BIO NIFEDIPINE XL concentrations; a dosage reduction may be required.
Carbamazepine and phenobarbitone
As carbamazepine and phenobarbitone have been shown to reduce the plasma concentrations of the structurally similar calcium channel blocker nimodipine due to enzyme induction, a decrease in plasma concentrations of nifedipine and hence a decrease in efficacy cannot be excluded.

Effects of BIO NIFEDIPINE XL on other medicines
When administered concomitantly, BIO NIFEDIPINE XL may increase the blood pressure lowering effect of anti-hypertensives such as:
Diuretics,
β-Blockers,
ACE-Inhibitors,
Angiotensin receptor blockers,
Other calcium channel antagonists,
α-adrenergic blocking agents,
PDE5 inhibitors,
α-methyldopa.
Severe hypotension has been reported in patients receiving BIO NIFEDIPINE XL and β-receptor blockers simultaneously (see "Warnings and Special Precautions"). Caution is advised as administration of these two agents together can lead to heart failure. The use of any other antihypertensive medication with BIO NIFEDIPINE XL can lead to severe hypotension.
Digoxin

Concomitant administration of BIO NIFEDIPINE XL and digoxin can reduce digoxin clearance and hence an increase in plasma concentrations. The patient should be closely monitored for digoxin overdosage.
Phenytoin
Phenytoin induces the cytochrome P450 3A4 system. Upon co-administration with phenytoin, the bioavailability of BIO NIFEDIPINE XL is reduced and thus its efficacy weakened. When both medicines are concomitantly administered, the clinical response to BIO NIFEDIPINE XL should be monitored and, if necessary, an increase of the BIO NIFEDIPINE XL dose considered. If the dose of BIO NIFEDIPINE XL is increased during co-administration of both medicines, a reduction of the BIO NIFEDIPINE XL dose should be considered when the treatment with phenytoin is discontinued.
Quinidine
BIO NIFEDIPINE XL and quinidine probably have a common metabolic pathway in the liver and might be expected to interact if given concurrently. The blood pressure should be carefully monitored if quinidine is added to existing BIO NIFEDIPINE XL. If necessary, the dose of BIO NIFEDIPINE XL should be reduced.
Tacrolimus
Tacrolimus has been shown to be metabolised via the cytochrome P450 3A4 system. Upon co-administration of BIO NIFEDIPINE XL and tacrolimus the tacrolimus plasma concentrations should be monitored and if necessary a reduction in the dose of tacrolimus considered.
Quinupristin/dalfopristin
Concomitant administration of quinupristin/dalfopristin and BIO NIFEDIPINE XL may lead to increased concentrations of BIO NIFEDIPINE XL. If necessary, the dose of BIO NIFEDIPINE XL should be reduced.
Diltiazem
Diltiazem reduces the hepatic metabolism of BIO NIFEDIPINE XL. The co-administration of these agents should be carefully monitored and a reduction in dosage for both agents may be required.
Grapefruit juice
Grapefruit juice inhibits the cytochrome P450 isoenzyme CYP3A4, particularly in the intestinal wall; this results in increased bioavailability of BIO NIFEDIPINE XL.
Barium
BIO NIFEDIPINE XL can interfere with the results of barium contrast X-ray procedures.

PREGNANCY AND LACTATION
BIO NIFEDIPINE XL is contraindicated during pregnancy and lactation (see "Contraindications").

DOSAGE AND DIRECTIONS FOR USE
The recommended initial dose is BIO NIFEDIPINE XL 30 once daily. If necessary, the dosage can be increased according to individual requirements up to a maximum of 90 mg once daily.
BIO NIFEDIPINE XL should be swallowed whole, and not bitten, chewed or halved. The tablets should be taken at approximately 24 hour intervals; at the same time every day, preferably in the morning. BIO NIFEDIPINE XL can be taken with or without food with a glass of water.
Elderly and patients with renal impairment do not usually require dosage adjustments.

SIDE EFFECTS
Frequently experienced side effects, associated with its vasodilator action are dizziness, flushing, headache, hypotension, peripheral oedema, tachycardia and palpitations.
General disorders and administrative site conditions
Frequent: Asthenia, oedema, headache.
Less frequent: Malaise, pain, dry mouth.

Immune system disorders
Less frequent: Hypersensitivity reaction, chills, fever, allergic reactions, angioedema, anaphylactic reaction.

Cardiac disorders
Frequent: Palpitations.
Less frequent: Chest pain, syncope, tachycardia, chest pain substernal, angina pectoris (excl. unstable).

Vascular disorders
Frequent: Peripheral oedema, vasodilatation.
Less frequent: Hypotension, postural hypotension, cardiovascular disorder.

Gastrointestinal disorders
Frequent: Constipation.
Less frequent: Abdominal pain, diarrhoea, dyspepsia, flatulence and nausea, dry mouth, eructation, gastrointestinal disorder, gingivitis, gum hyperplasia, vomiting, bezoar, dysphagia, oesophagitis, gum disorders, intestinal obstruction, intestinal ulcer, gastro-oesophageal reflux.

Metabolism and nutrition disorders
Less frequent: Anorexia, hyperglycaemia, weight loss.

Nervous system disorders
Frequent: Dizziness.
Less frequent: Insomnia, nervousness, paraesthesia, dysaesthesia, somnolence, vertigo, anxiety, hyposthesia, sleep disorder, tremor.

Muscoskeletal, connective tissue and bone disorders
Less frequent: Leg cramps and pain, arthralgia, joint disorder, myalgia, muscle cramps.

Respiratory, thoracic and mediastinal disorders
Less frequent: Dyspnoea, epistaxis, nasal congestion.

Skin and subcutaneous tissue disorders
Less frequent: Pruritus, rash, macupopular rash, pustular rash, sweating, urticaria, vesiculobullous rash, exfoliative dermatitis, photosensitive dermatitis.

Renal and urinary disorders
Less frequent: Nocturia, polyuria, dysuria, urinary frequency.

Vascular disorders
Less frequent: Face oedema.

Hepato-biliary disorders
Less frequent: Abnormal liver function test, increased GGT (Gamma-glutamyl transpeptidase), jaundice; increased transaminases.

Eye disorders
Less frequent: Abnormal vision, eye disorder, eye pain, blurred vision.

Blood and lymphatic system disorders
Less frequent: Leucopenia, purpura, agranulocytosis.

Reproductive system and breast disorders
Less frequent: Gynaecomastia, erectile dysfunction.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT
If the following symptoms are observed in time, the first therapeutic measure to be considered is gastric lavage with added medical charcoal: flushing, headache, sever hypotension, increase or decrease in heart rate, hyperglycaemia, metabolic acidosis, hypoxia, cardiogenic shock with pulmonary oedema and unconsciousness to the point of coma.
Treatment is symptomatic and supportive. No specific antidote is available
Hypotension (due to cardiogenic shock and arterial vasodilatation): slow IV calcium; 10 – 20 ml of a 10 % calcium gluconate solution. This can be repeated if necessary. If the result is insufficient, vasoconstricting sympatomimetics such as dopamine or noradrenaline can additionally be administered. The dosage of these agents is determined by the effect obtained. Additional volume must be administered with caution because of the danger of overloading the heart.
Bradycardia: β-sympathomimetics and in life-threatening bradycardiac disturbances of heart rhythm, temporary pacemaker therapy is advised.
Haemodialysis serves no purpose, but plasmapheresis is advisable.

IDENTIFICATION
BIO NIFEDIPINE XL 30: Brown coloured, round biconvex film coated tablet free from cracks, plain on one side and laser drilled hole on other side.
BIO NIFEDIPINE XL 60: Brown coloured, round biconvex film coated tablet free from cracks, plain on one side and laser drilled hole on other side.

PRESENTATION
Plain aluminium (no external colour), transparent and colourless PVC blister strips; 10 tablets per strip. 3 Blister strips are packed into an outer cardboard carton.

STORAGE INSTRUCTIONS
Store at or below 25 °C. Protect from light and moisture.
Keep the blister strips in the outer carton and keep the carton closed until required for use.
KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER
BIO NIFEDIPINE XL 30: A43/7.1/0558
BIO NIFEDIPINE XL 60: A43/7.1/0559

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION
Biotech Laboratories (Pty) Ltd.
Ground Floor, Block K West, Central Park, 400 16th Road
Randjespark, Midrand, South Africa

DATE OF PUBLICATION OF THE PACKAGE INSERT
Date of registration: 14 September 2012
Date of latest revision of the text as approved by Council: 14 June 2012
Date of notification with regard to amended Reg. 9 and 10: 02 February 2015

NAMIBIA:
NS2 BIO NIFEDIPINE XL 30 Reg No.13/7.1/0228
NS2 BIO NIFEDIPINE XL 60 Reg No.13/7.1/0229

SKEDULERINGSTATUS:
S3

EIENDOMSNAAM (en dosseervorm):
BIO NIFEDIPINE XL 30 (beheerde vrystellingstablet)
BIO NIFEDIPINE XL 60 (beheerde vrystellingstablet)

SAMESTELLING:
BIO NIFEDIPINE XL 30: Elke beheerde vrystellingstablet bevat 30 mg nifedipien.
BIO NIFEDIPINE XL 60: Elke beheerde vrystellingstablet bevat 60 mg nifedipien.
Onaktiewe bestanddele: Poliëtileen oksied, hypromellose, kaliumchloried, metiel alkohol, isopropiel alkohol, magnesiumstearaat, kolloïdale silisiumdioksied, natriumchloried, ysteroksied rooi, sellulose asetaat, poliëtileen glikol, gesuiwerde water, opadry bruin (bestaande uit hypromellose, ysteroksied rooi, ysteroksied geel, poliëtileen glikol en titanium koolstofdioksied), opacode swart.
Suikervry.

FARMAKOLOGIESE KLASSIFIKASIE:
A.7.1 Vasodilators, hipotensiewe geneesmiddels.

FARMAKOLOGIESE WERKING:
Farmakodinamika
Nifedipien, is `n kalsiumkanaalblokkeerder en `n perifere arteriële vasodilator wat direk inwerk op die vaskulêre gladdespier wat lei tot `n daling in perifere weerstand.

Farmakokinetika:
Algemene kenmerke
Die vrystelling van nifedipien in BIO NIFEDIPINE XL word deur `n membraangekontroleerde, "druk-en-trek" osmotiese proses beheer. Nifedipien word vrygestel deur `n konstante tempo oor `n tydperk van 24 uur. Die tempo van aflewering word nie beïnvloed deur die pH van die maag of die beweeglikheid daarvan nie. Na toediening, bly die onaktiewe komponente van die tablette onveranderd en word as `n onoplosbare omhulsel tydens ontlasting uitgeskei.
Absorpsie
Die beskikbaarheid na die toediening van nifedipien word nie tydends die inname van voedsel beïnvloed nie.
Verspreiding
Omtrent 95 % van nifedipien is plasmaproteïen (albumien) gebonde.
Bio-transformasie
Nifedipien word primêr deur middel van oksidatiewe prosesse gemetaboliseer in die intestinale slymvliese en die lewer. Die metaboliete word hoofsaaklik deur die niere geëlimineer, waarvan omtrent 5-15 % via die gal in die feses uitgeskei word.
Eliminasie
Die terminale halfleeftyd van nifedipien, deur middel van die "druk-en-trek" osmotiese vrystellingsproses, verteenwoordig nie `n betekenisvolle parameter nie, aangesien `n plato plasmakonsentrasie gehandhaaf word tydens die vrystelling en absorpsie van die tablette.
Hepatiese inkorting
Die eliminasie halfleeftyd word aansienlik verleng terwyl die totale opruiming verminder word in pasiënte met belemmerde lewerfunksie. BIO NIFEDIPINE XL moet nie toegedien word aan hierdie pasiënte nie.

INDIKASIES:
BIO NIFEDIPINE XL word aangedui in die volgende toestande:
- Ligte tot matige hipertensie.
- Voorkoming van chroniese stabiele angina pectoris.

KONTRA-INDIKASIES:
Hipersensitiwiteit teenoor nifedipien of enige van die bestanddele in BIO NIFEDIPINE XL.
Swangerskap en gedurende borsvoeding.
Porfirie.
Klinies-betekenisvolle stenose van die aorta, kardiovaskulêre skok en onstabiele angina.
Tydens óf binne een maand na `n miokardiale infarksie.
Lewer inkorting.
Pasiënte met `n geskiedenis van gastroïntestinale obstruksie, esofageale obstruksie of enige aard van verminderde lumendeursnee van die maagdermkanaal.
Inflammatoriese dermsiekte.
Gelyktydige gebruik saam met rifampisien (sien "Interaksies").
Veiligheid en effektiwiteit in kinders is nog nie vasgestel nie.
Die gebruik van BIO NIFEDIPINE XL is gekontra-indikeerd in manlike pasiënte betrokke by in vitro-bevrugting, aangesien nifedipien geassosieer word met omkeerbare biochemiese veranderinge in die kopseksie van die spermatosoa wat kan aanleiding gee tot belemmerde spermfunksie.

WAARSKUWINGS en SPESIALE VOORSORGMAATREELS:
Gelyktydige toediening van BIO NIFEDIPINE XL saam met β-reseptorblokkers kan die antihipertensiewe effek bevorder (sien "Interaksies"). Dié pasiënte moet noukeurig gemonitor word.
Pomelosap inhibeer die metabolisme van BIO NIFEDIPINE XL (sien "Interaksies").
BIO NIFEDIPINE XL kan `n additiewe antihipertensiewe effek veroorsaak wanneer dit saam met ander bloeddrukverlagende geneesmiddels soos beta-reseptor blokkeerders en diuretika (sien "Interaksies") toegedien word.BIO NIFEDIPINE XL kan `n toename in bloedglukose veroorsaak, sorg moet aan die dag gelê word in pasiënte met diabetes mellitus
Dialise pasiënte met kwaadaardige hipertensie en onomkeerbare nierversaking met gepaardgaande hipovolemie, moet noukeurig gemonitor word as `n merkbare afname in bloeddruk voorkom.
Simptome van maagobstruksies het al voorgekom in pasiënte met `n geskiedenis van gastroïntestinale versteurings. BIO NIFEDIPINE XL moet met omsigtigheid gebruik word in pasiënte met swak kardiale reserwes, in angina pasiënte met hipotensie asook in pasiënte met hartversaking. BIO NIFEDIPINE XL moet nie gebruik word in pasiënte met Kock-sakkie (ileostomie na proktokolektomie).

Uitwerking op vermoë om te bestuur en die gebruik van masjinerie
BIO NIFEDIPINE XL kan die vermoë belemmer om te bestuur of masjinerie te bedryf, veral tydens die aanvang van behandeling, die verandering van die dosis en in kombinasie met alkohol. Die intensiteit van die reaksie op BIO NIFEDIPINE XL wissel van pasiënt tot pasiënt.

INTERAKSIES:
Nifedipien, soos vervat in Bio-Nifedipien word gemetaboliseer via die sitochroom P450 3A4-sisteem, aangetref in beide die intestinale mukosa en die lewer. Geneesmiddels wat daarvoor bekend is om hierdie ensiemsisteem óf te inhibeer óf te induseer, mag die eerste deurgangseffek (na orale toediening) of die opruiming van nifedipien verander. Die omvang, sowel as die tydsduur van die interaksies moet in ag geneem word tydens die toediening van BIO NIFEDIPINE XL saam met die volgende medisyne:
Rifampisien
Die gelyktydige toediening van rifampisien en BIO NIFEDIPINE XL, verminder die biobeskikbaarheid van BIO NIFEDIPINE XL beduidend en verlaag dus die doeltreffendheid daarvan. Die gebruik van rifampisien saam met BIO NIFEDIPINE XL word dus teenaangedui in hierdie gevalle (sien "Kontra-indikasies").
Makrolied antibiotika
Makrolied antibiotika is bekend daarvoor om die sitochroom P450 3A4-bemiddelde metabolisme van ander geneesmiddels te inhibeer. Die potensiaal vir `n toename in nifedipien konsentrasies deur gelyke toediening moet in gedagte gehou word.
Amprenavir, indinavir, nelfinavir, ritonavir, sakinavir
Hierdie klas van geneesmiddels is bekend om die sitochroom P450 3A4-sisteem te inhibeer. In vitro, toon indinavir en ritonavir dat die sitochroom P450 3A4-bemiddelde metabolisme van nifedipien geïnhibeer word. As dit saam met BIO NIFEDIPINE XL toegedien word, word `n aansienlike toename in die plasmakonsentrasies van nifedipien waargeneem as gevolg van `n afname in eerste verbygangsmetabolisme asook die afname in eliminasie (wat nie uitgesluit kan word nie). Indien gelyktydig toegedien word, moet die bloeddruk gemonitor word en indien nodig, `n vermindering in die dosis van BIO NIFEDIPINE XL oorweeg word.
Ketokonasool, itrakonasool en flukonasool
Dit is bekend dat geneesmiddels van hierdie klas die sitochroom P450 3A4-sisteem inhibeer. Wanneer hierdie geneesmiddels mondeliks saam met BIO NIFEDIPINE XL toegedien word, kan `n aansienlike toename in die biobeskikbaarheid van BIO NIFEDIPINE XL waargeneem word weens die verminderde eerste deurgangsmetabolisme wat nie uitgesluit kan word nie. Indien gelyktydig toegedien word, moet die bloeddruk gemonitor word en indien nodig, `n vermindering in die dosis van BIO NIFEDIPINE XL oorweeg word.
Fluoksetien
Daar is al aangetoon dat fluoksetien die bemiddeling van sitochroom P450 3A4 metabolisme van nifedipien inhibeer. `n Toename in die plasmakonsentrasies van nifedipien kan daarom nie uitgelsluit word tydens gelyktydige toediening nie. Indien gelyktydig toegedien word, moet die bloeddruk gemonitor word en indien nodig, `n vermindering in die dosis van BIO NIFEDIPINE XL oorweeg word.
Nefasodoon
Dit is bekend dat nefasodoon die sisteem van sitochroom P450 3A4 inhibeer. In vitro, het nefasodoon getoon dat dit die bemiddeling van sitochroom P450 3A4 metabolisme van ander geneesmiddels inhibeer. `n Toename in die plasmakonsentrasies van nifedipien kan daarom nie uitgelsluit word tydens gelyktydige toediening nie. Indien gelyktydig toegedien word, moet die bloeddruk gemonitor word en indien nodig, `n vermindering in die dosis van BIO NIFEDIPINE XL oorweeg word.
Valproësuur
Aangesien aangetoon is dat valproësuur, as gevolg van ensieminhibering, die plasmakonsentrasies van nimodipien (`n kalsiumkanaalblokkeerder met `n soortgelyke struktuur) verhoog, kan `n toename in plasmakonsentrasies en doeltreffendheid van nifedipien nie uitgesluit word nie.
Simetidien
Simetidien inhibeer die werking van die sitochroom P450 3A4-sisteem. Indien simetidien en BIO NIFEDIPINE XL gelyktydig toegedien word, kan dit die biobeskikbaarheid van BIO NIFEDIPINE XL verhoog.
Sisapried
Gelyktydige toediening van sisapried en BIO NIFEDIPINE XL mag lei tot verhoogde BIO NIFEDIPINE XL konsentrasies. ' `n Vermindering in die dosis mag vereis word.
Karbamasepien en fenobarbitoon
Aangesien aangetoon is dat karbamasepien en fenobartitoon, as gevolg van ensieminduserings, die plasmakonsentrasies van nimodipien (`n kalsiumkanaalblokkeerder met `n soortgelyke struktuur) verlaag, kan `n afname in plasmakonsentrasies en doeltreffendheid van nifedipien nie uitgesluit word nie.
Effekte van BIO NIFEDIPINE XL op ander geneesmiddels
Wanneer gelyktydig toegedien word, kan BIO NIFEDIPINE XL die bloeddrukverlagende effek van anti-hipertensiewe geneesmiddels verhoog, soos:
Duiretika
ß-Blokkeerders
ACE-Inhibeerders
Angiotensien reseptor blokkeerders
Ander kalsiumkanaal antagoniste
α-adrenergiese blokkeerders
PDE5 inhibeerders
α-metieldopa

Erge hipotensie is al aangemeld in pasiënte wat BIO NIFEDIPINE XL en β-reseptorblokkeerders gelyktydig gebruik het (sien "Waarskuwings"). Omsigtigheid word aanbeveel met die gelyktydige toediening van hierdie twee agente, aangesien dit kan lei tot hartversaking. Die gelyktydige gebruik van enige ander antihipertensiewe geneesmiddels saam met BIO NIFEDIPINE XL kan lei tot erge hipotensie.
Digoksien
Gelyktydige toediening van BIO NIFEDIPINE XL en digoksien kan lei tot verlaagde digoksienverwydering en gevolglike toename in plasmakonsentrasies van digoksien. Die pasiënt moet noukeurig gemonitor word vir die oordosering van digoksien.
Fenitoïen
Fenitoïen induseer die sitochroom P450 3A4-sisteem. Gelyktydige toediening van BIO NIFEDIPINE XL en fenitoïen veroorsaak `n verlaging in die biobeskikbaarheid en `n afname in die doeltreffendheid daarvan. Met gelyktydige toediening moet die kliniese respons van BIO NIFEDIPINE XL gemonitor word en indien nodig moet `n verhoging in die dosis van BIO NIFEDIPINE XL oorweeg word. Indien die dosis van BIO NIFEDIPINE XL tydens gelyktydige toediening van die twee geneesmiddels verhoog is, moet `n verlaging van BIO NIFEDIPINE XL se dosis oorweeg word wanneer die behandeling met fenitoïen gestaak word.
Kinidien
BIO NIFEDIPINE XL en kinidien het waarskynlik 'n gemeenskaplike metaboliese roete in die lewer en daar mag interaksies plaasvind tydens gelyktydige toediening. Die bloeddruk moet noukeurig gemonitor word indien kinidien by die bestaande BIO NIFEDIPINE XL dosering bygevoeg word. Indien nodig, moet die dosis van BIO NIFEDIPINE XL verminder word.
Takrolimus
Daar is aangetoon dat takrolimus via die sitochroom P450 3A4-sisteem gemetaboliseer word. Wanneer takrolimus en BIO NIFEDIPINE XL saam toegedien word, behoort takrolimus se plasmakonsentrasies gemonitor te word en indien nodig moet `n verlaging van takrolimus se dosis oorweeg word.
Kinupristien/dalfopristien
Die gelyktydige toediening van kinupristien/dalfopristien en BIO NIFEDIPINE XL mag tot verhoogde plasmakonsentrasies van BIO NIFEDIPINE XL lei. Indien nodig, moet die dosis van BIO NIFEDIPINE XL verlaag word.
Diltiasem
Diltiasem verminder die metabolisme van BIO NIFEDIPINE XL in die lewer. Die gelyktydige toediening van hierdie geneesmiddels moet noukeurig gemonitor word en 'n vermindering in die dosis vir beide geneesmiddels mag vereis word.
Pomelosap
Pomelosap inhibeer die sitochroom P450 CYP3A4-isoënsiem, veral in die dermwand. Dit mag lei tot verhoogde biobeskikbaarheid van BIO NIFEDIPINE XL.
Barium
BIO NIFEDIPINE XL kan inmeng met die resultate van bariumteenstelling in X-straal prosedures.

SWANGERSKAP EN LAKTASIE:
BIO NIFEDIPINE XL is gekontra-indikeer tydens swangerskap en laktasie (sien "Kontra-indikasies").

DOSIS EN GEBRUIKSAANWYSINGS:
Die aanbevole aanvangsdosis van BIO NIFEDIPINE XL 30 is een keer per dag. Indien nodig, kan die dosis verhoog word volgens individuele behoeftes tot 'n maksimum van 90 mg een maal per dag.
BIO NIFEDIPINE XL moet heel ingesluk word, en nie gebyt, gekou of gehalveer word nie. Die tablette moet ongeveer 24 uur uitmekaar geneem word op min of meer dieselfde tyd elke dag, verkieslik in die oggend. BIO NIFEDIPINE XL kan met of sonder kos en met 'n glas water geneem word.
Bejaardes en pasiënte met nierinkorting vereis gewoonlik nie dosisaanpassings nie.

NEWE-EFFEKTE:
Gereelde newe-effekte wat ervaar word hou verband met vasodilatoriese effekte soos duiseligheid, gloede, hoofpyn, hipotensie, perifere edeem, tagikardie en hartkloppings.
Algemene versteurings en die plek van toediening
Dikwels: Astenie, edeem, hoofpyn.
Minder dikwels: Moegheid, pyn, droë mond.

Immuunsisteem versteurings
*Minder dikwels:*Hipersensitiwiteitsreaksie, kouekoors, koors, allergiese reaksies, edeem, anafilaktiese reaksie.

Hartsiektes
Dikwels: Hartkloppings.
Minder dikwels: Borspyn, sinkopie, tagikardie, borspyn substernaal, angina pectoris (uitsluitend onstabiel).

Vaskulêre toestande
Dikwels: Perifere edeem, vasodilatasie.
Minder dikwels: Hipotensie, posturale hipotensie, kardiovaskulêre siekte

Gastroïntestinale versteurings
Dikwels: Hardlywigheid.
Minder dikwels: Abdominale pyn, diarree, slegte spysvertering, winderigheid en naarheid, droë mond, eruktasie, gastro-versteuring, tandvleisontsteking, tandvleishiperplasie, braking, bezoar, disfagie, esofagitis, tandvleisversteurings, intestinale obstruksie, dermulkus, gastro-esofageale refluks.

Metabolisme en voeding afwykings
Minder dikwels: anoreksie, hyperglisemie, gewigsverlies.

Senuweestelsel afwykings
Dikwels: Duiseligheid.
Minder dikwels: Slapeloosheid, senuagtigheid, parestesie, disestesie, slaperigheid, duiseligheid, angs, parestesie, slaapversteuring, tremor.

Muskuloskeletale afwykings
Minder dikwels: Beenkrampe en pyn, artralgie, gewrigsversteurings, mialgie, spierkrampe.

Respiratoriese sisteem versteurings
Minder dikwels: Dispnee, epistaxis, nasale kongestie.

Vel en subkutane weefsel versteurings
Minder dikwels: Pruritis, uitslag, maculopapulêre uitslag, pustulêre uitslag, sweet, urtikarie, vesikulobulêre uitslag, eksfoliatiewe dermatitis, fotosensitiewe dermatitis.

Renale en urinêre versteurings
Minder dikwels: Nokturie, poliurie, disurie, urinêre frekwensie.

Vaskulêre toestande
Minder dikwels: Gesigsedeem

Hepatiese afwykings
Minder dikwels: Abnormale lewerfunksietoetsresultate, verhoogde GGT (Gamma-glutamiel transpeptidase), geelsug, verhoogde transaminases.

Oogafwykings
Minder dikwels: Abnormale visie, afwykings van die oë, oë pyn, dowwe visie.

Bloed en limfatiese stelsel afwykings
Minder dikwels: Leukopenie, purpura, agranulositose.

Voortplantingstelsel en bors versteurings
*Minder dikwels:*Ginekomastie, erektiele disfunksie

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDLING DAARVAN:
As die volgende simptome betyds waargeneem word, is die eerste terapeutiese maatreël wat oorweeg word, maagspoeling met mediese houtskool bygevoeg: Gloede, hoofpyn, erge hipotensie, toename of afname in die hartklop, hiperglisemie, metaboliese asidose, hipoksie, kardiogeniese skok met pulmonêre edeem en bewusteloosheid tot die punt van 'n koma. Behandeling is simptomaties en ondersteunend. Geen spesifieke teenmiddel is beskikbaar nie. Hipotensie (as gevolg van kardiogeniese skok en arteriële vasodilatasie): stadige IV kalsium, 10 - 20 ml van 'n 10 % kalsiumglukonaat oplossing. Dit kan herhaal word indien nodig. Indien die resultaat onvoldoende is, kan addisionele vasokonstruktiewe simpatomimetiese middels soos dopamien of noradrenalien toegedien word. Die dosis van hierdie middels word bepaal deur die effek wat verkry word. Addisionele volume moet met omsigtigheid toegedien word as gevolg van die gevaar van oorlaaiïng van die hart.
Bradikardie: behandel met β-simpatomimetiese middels en in die geval van lewensbedreigende bradikardieversteurings van die hartritme word tydelike pasaangeërterapie aanbeveel.
Hemodialise dien geen doel nie, maar plasmaferese is raadsaam.

IDENTIFIKASIE:
BIO NIFEDIPINE XL 30: bruin, ronde bi-konvekse filmbedekte tablet vry van krake, gewoon op die een kant met laser-boor opening aan die keersy.
BIO NIFEDIPINE XL 60: bruin, ronde bi-konvekse filmbedekte tablet vry van krake, gewoon op die een kant met 'n laser-boor opening aan die keersy.

AANBIEDING:
Gewone aluminium (geen eksterne kleur), deursigtig en kleurlose-PVC stulpverpakkingstrokies; 10 tablette per strook. Drie stulppakke word verpak in 'n buitenste karton.

BERGINGSINSTRUKSIES:
Bewaar teen of onder 25 °C. Beskerm teen lig en vog.
Hou die stulppakke in die buitenste karton en hou die karton toe totdat benodig word vir gebruik.
HOU BUITE DIE BEREIK VAN KINDERS.

REGISTRASIENOMMER:
BIO NIFEDIPINE XL 30: A43/7.1/0558
BIO NIFEDIPINE XL 60: A43/7.1/0559

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT:
Biotech Laboratories (Edms) Bpk.
Grond Vloer, Blok K Wes, Central Park,
400 16de Weg, Randjespark, Midrand, Suid Afrika

DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET:
Datum van registrasie: 14 September 2012
Datum van laaste hersiening van die teks soos goedgekeur deur die Raad: 14 Junie 2012
Datum van kennisgewing met betrreking tot gewysig Reg 9 en 10: 02 Februarie 2015

NAMIBIE:
NS2 BIO NIFEDIPINE XL 30 Reg Nr.13/7.1/0228
NS2 BIO NIFEDIPINE XL 60 Reg Nr.13/7.1/0229