NOVAGEN PHARMA

PROFESSIONAL INFORMATION:
SCHEDULING STATUS:

S3

NAME AND DOSAGE FORM:
KEYSAL 5 mg (Tablets)
KEYSAL 10 mg (Tablets)
COMPOSITION:
KEYSAL 5 mg: Each tablet contains amlodipine besilate equivalent to amlodipine 5 mg.
KEYSAL 10 mg: Each tablet contains amlodipine besilate equivalent to amlodipine 10 mg.
Excipients: Cellulose microcrystalline; sodium starch glycolate; calcium hydrogen phosphate anhydrous and magnesium stearate.
Sugar free.

PHARMACOLOGICAL CLASSIFICATION:
A 7.1 Vasodilators, hypotensive medicines.

PHARMACOLOGICAL ACTION:
Pharmacodynamic properties:
Amlodipine is a dihydropyridine calcium channel blocker. It inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle without affecting serum calcium concentrations. Direct relaxation of vascular smooth muscles forms the basis of the antihypertensive action.
In angina pectoris, amlodipine acts a peripheral arteriolar vasodilator resulting in a reduction in total peripheral resistance (afterload). Myocardial energy and oxygen requirements are reduced. Amlodipine exerts its activity by binding to the dihydropyridine binding sites. It exerts minimal action on cardiac conduction, contraction and heart rate.

Pharmacokinetic properties:
Complete absorption of amlodipine is slow following oral administration with peak plasma levels being attained after 6 to 12 hours. Amlodipine has a bioavailability of about 64 % and a plasma elimination half-life of 35 to 50 hours, allowing for once-daily oral dosing. Steady state plasma concentrations are achieved after 7 to 8 days of consecutive dosing. The volume of distribution is about 20 litre/kg. Metabolism is via the liver and is extensive with less than 10 % of amlodipine appearing unchanged in the urine. Metabolites are inactive and primarily (up to 60 %) excreted via the kidney.

INDICATIONS:
KEYSAL is indicated for the:
- Treatment of angina pectoris.
- Treatment of mild-to-moderate hypertension, alone or in combination with other antihypertensives.

CONTRAINDICATIONS:
Hypersensitivity to any of the ingredients.
Hypersensitivity to dihydropyridines.

WARNINGS and SPECIAL PRECAUTIONS:

The substitutability or interchangeability with other amlodipine containing products has not been established.

Use in the Elderly:
Amlodipine clearance is decreased (40 to 60 %) in the elderly, which results in increases of amlodipine concentration in the area under the concentration-time curve (AUC) and elimination half-life. Therefore, elderly patients should start **KEYSAL** therapy at a lower dose.
Use in Renal Failure:
Although **KEYSAL** is excreted primarily via the kidney, mild renal impairment does not appear to have an effect on the plasma concentrations. Severe renal impairment may however require a dosage reduction. **KEYSAL** is not dialysable.
Use in Impaired Hepatic Function
The half-life of **KEYSAL** is significantly prolonged in patients with impaired hepatic function. **KEYSAL** should therefore be administered at lower doses in these patients.
Use in Children
Safety and efficacy has not been established.
Use in Heart Failure
An increased incidence of pulmonary oedema has been reported.
KEYSAL may have a negative inotropic effect. AUC in **KEYSAL** may increase in patients with heart failure.
Porphyria: Safety has not been established.

INTERACTIONS:
Concurrent administration of sublingual nitroglycerin, long acting nitrates, beta-blockers or other antianginal agents with amlodipine may produce additive antihypertensive and antianginal effects. Sublingual nitroglycerin may be used as needed to abort acute angina attacks during amlodipine therapy. Nitrate medication may be used during amlodipine therapy for angina prophylaxis.
Amlodipine will not protect against the consequences of abrupt beta-blocker withdrawal; gradual beta-blocker dose reduction is recommended.
Although no 'rebound effect' has been reported upon discontinuation of amlodipine, a gradual decrease of dosage with medical practitioner supervision is recommended.

HUMAN REPRODUCTION:
Safety in pregnancy and lactation has not been established (see "**CONTRAINDICATIONS**").

DOSAGE AND DIRECTIONS FOR USE:
Hypertension and Angina Pectoris:
Adults:
An initial dosage of 5 mg **KEYSAL** once daily is recommended which may be increased to 10 mg once a day after 10 to 14 days of therapy if there is no improvement.
No dose reduction is required when adding **KEYSAL** to thiazide diuretics, beta-blockers, or angiotensin converting enzyme inhibitors.

SIDE EFFECTS:
Cardiac disorders
Frequent: peripheral oedema, angioedema, palpitations.
Less frequent: syncope, vasculitis.
The following side effects have been reported and frequencies are unknown: hypotension (including orthostatic hypotension), myocardial infarction, arrhythmia (including ventricular tachycardia and atrial fibrillation), chest pain.
Nervous system disorders
Frequent: dizziness, headache, somnolence, flushing.
Less frequent: mood changes, dry mouth, peripheral neuropathy, increased sweating.
The following side effects have been reported and frequencies are unknown: hypertonia, hypoesthesia/paraesthesia, tremor, insomnia, increased sweating, pain.
Gastrointestinal disorders
Frequent: nausea, abdominal pain, vomiting.
Less frequent: altered bowel habits, dyspepsia, gingival hyperplasia, pancreatitis.
The following side effects have been reported and frequencies are unknown: taste perversion.
Musculoskeletal, connective tissue and bone disorders
Frequent: fatigue.
Less frequent: arthralgia, asthenia, back pain, muscle cramps, myalgia.
Hepato-biliary disorders
The following side effects have been reported and frequencies are unknown: hepatitis, jaundice.
Blood and lymphatic system disorders
Less frequent: leucopenia, thrombocytopenia.
The following side effects have been reported and frequencies are unknown: purpura.
Renal and urinary disorders
Less frequent: increased urinary frequency.
Reproductive system and breast disorders
Less frequent: impotence.
Endocrine disorders
Less frequent: gynaecomastia.
The following side effects have been reported and frequencies are unknown: weight increase/decrease.
Investigations
Less frequent: hyperglycaemia.
The following side effects have been reported and frequencies are unknown: raised liver enzymes (mostly consistent with cholestasis).
Skin and subcutaneous tissue disorders
Less frequent: alopecia.
The following side effects have been reported and frequencies are unknown: allergic reactions with pruritus, rash, and erythema multiforme.
Respiratory, thoracic and mediastinal disorders
Less frequent: dyspnoea.
The following side effects have been reported and frequencies are unknown: coughing.
Eye disorders
Less frequent: visual disturbances.
Ear and labyrinth disorders
The following side effects have been reported and frequencies are unknown: tinnitus.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
There is no documented experience with **KEYSAL** overdosage. Gastric lavage may be of benefit. Gross overdosage could result in excessive peripheral vasodilation, resulting in marked and probably prolonged systematic hypotension.
Clinically significant hypotension due to **KEYSAL** overdosage requires active cardiovascular support. Intravenous calcium gluconate may be of benefit in reversing the effects of calcium channel blockade. Since amlodipine is highly protein-bound, dialysis is not likely to be of benefit.
TREATMENT IS SYMPTOMATIC AND SUPPORTIVE.

IDENTIFICATION:
KEYSAL 5 mg
White to off white, flat, bevel edged, barrel shaped uncoated tablets, debossed with 'C' on one side and '58' on the other side.
KEYSAL 10 mg
White to off white, flat, bevel edged, round shaped uncoated tablets, debossed with 'C' on one side and '59' on the other side.
PRESENTATION:
KEYSAL 5 mg:
PVC/PE/Aclar - Alu Blister Pack:
Tablets are packed in 250 micron white opaque PVC film laminated with 25 micron PE coated with 23 micron Aclar and 25 microns printed aluminium foil. Each blister contains 10 tablets.
The blisters will be further packed in a pre-printed carton with a package leaflet.
Pack size: 30's - Each carton contains 3 blisters of 10 tablets each OR;
PVC/PVdC - Alu Blister Pack:
Tablets are packed in 250 micron white opaque PVC film laminated with 90 gsm PVdC and 25 microns printed aluminium foil. Each blister contains 10 tablets.
The blisters will be further packed in a pre-printed carton with a package leaflet.
Pack size: 30's - Each carton contains 3 blisters of 10 tablets each OR;
HDPE container:
Tablets are packed in a white opaque round HDPE container closed with a white opaque polypropylene stock ribbed closure with a wad having an induction sealing liner.
Pack size: 30's - Each HDPE container has 30 tablets each.
The HDPE container will be further packed in a pre-printed carton with a package leaflet.
KEYSAL 10 mg
PVC/PE/Aclar - Alu Blister Pack:
Tablets are packed in 250 micron white opaque PVC film laminated with 25 micron PE coated with 23 micron Aclar and 25 microns printed aluminium foil. Each blister contains 10 tablets.
The blisters will be further packed in a pre-printed carton with a package leaflet.
Pack size: 30's - Each carton contains 3 blisters of 10 tablets each OR;
PVC/PVdC - Alu Blister Pack:
Tablets are packed in 250 micron white opaque PVC film laminated with 90 gsm PVdC and 25 microns printed aluminium foil. Each blister contains 10 tablets.
The blisters will be further packed in a pre-printed carton with a package leaflet.
Pack size: 30's - Each carton contains 3 blisters of 10 tablets each OR;
HDPE container:
Tablets are packed in a white opaque round HDPE container closed with a white opaque polypropylene stock ribbed closure with a wad having an induction sealing liner.
Pack size: 30's - Each HDPE container has 30 tablets each.
The HDPE container will be further packed in a pre-printed carton with a package leaflet.
Not all packs or pack sizes are necessarily marketed.

STORAGE INSTRUCTIONS:
Store at or below 30 °C.

KEEP OUT OF REACH OF CHILDREN.
REGISTRATION NUMBER:
KEYSAL 5 mg: 41/7.1/0749
KEYSAL 10 mg: 41/7.1/0750

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:
Novagen Pharma (Pty) Ltd
Office 2, 100 Sovereign Drive
Route 21 Corporate Park
Nellmapius Drive
Irene – Pretoria
South Africa

DATE OF PUBLICATION OF THE PACKAGE INSERT:
Date of registration: 5 March 2009
Date of latest revision of the text as approved by Council: 5 March 2009
Date of notification with regard to amended Reg. 9 and 10: 16 January 2015

FOR NAMIBIA ONLY:
Schedule: NS2
Registration Numbers:
KEYSAL 5 mg: 14/7.1/0644
KEYSAL 10 mg: 14/7.1/0643

DETACH BEFORE DISPENSING

PATIENT INFORMATION LEAFLET
SCHEDULING STATUS

S3

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM
KEYSAL 5 mg (Tablets)
KEYSAL 10 mg (Tablets)
Amlodipine besilate
Read all of this leaflet carefully before you start taking KEYSAL
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or pharmacist.
- **KEYSAL** 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 KEYSAL CONTAINS
The active substance is amlodipine.
KEYSAL 5 mg: Each tablet contains amlodipine besilate equivalent to amlodipine 5 mg.
KEYSAL 10 mg: Each tablet contains amlodipine besilate equivalent to amlodipine 10 mg.
The other ingredients are cellulose microcrystalline; sodium starch glycolate; calcium hydrogen phosphate anhydrous and magnesium stearate.
Sugar free.

2. WHAT KEYSAL IS USED FOR
KEYSAL is used for the treatment of:
- angina pectoris.
- mild-to moderate hypertension, alone or in combination with other antihypertensives.

3. BEFORE YOU TAKE KEYSAL
Do not take KEYSAL:
- If you are hypersensitive (allergic) to amlodipine besilate or any of the other ingredients of **KEYSAL**.
- If you are hypersensitive (allergic) to dihydropyridines.

Take special care with KEYSAL:
- Elderly patients should start **KEYSAL** therapy at a lower dose.
- Dosage adjustments may be necessary in patients with kidney and liver disease.
- Safety and efficacy in children has not been established.
- Safety in porphyria has not been established.

Pregnancy and Breastfeeding:
Safety of **KEYSAL** in pregnant and lactating women has not been established.
If you are pregnant or breastfeeding your baby please consult your doctor, pharmacist or other healthcare professional for advice before taking **KEYSAL**.

Taking other medicines with KEYSAL:
KEYSAL interacts with nitroglycerin, long acting nitrates, beta-blockers or other antianginal agents.
Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

4. HOW TO TAKE KEYSAL
Always take **KEYSAL** 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 **KEYSAL** is too strong or too weak, talk to your doctor or pharmacist.
Hypertension and Angina Pectoris:
Adults:
An initial dose of 5 mg **KEYSAL** once daily is recommended which may be increased to 10 mg once a day after 10 to 14 days of therapy if there is no improvement.
No dose reduction is required when adding KEYSAL to thiazide diuretics, beta- blockers, or angiotensin-converting enzyme inhibitors.
If you take more KEYSAL than you should:
There is no documented experience with **KEYSAL** overdosage. Gastric lavage may be of benefit. Gross overdosage could result in excessive peripheral vasodilation, resulting in marked and probably prolonged systemic hypotension.
Clinically significant hypotension due to **KEYSAL** overdosage requires active cardiovascular support. Intravenous calcium gluconate may be of benefit in reversing the effects of calcium channel blockade. Since amlodipine is highly protein-bound, dialysis is not likely to be of benefit.
TREATMENT IS SYMPTOMATIC AND SUPPORTIVE.
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.
If you forget to take KEYSAL:
Do not take a double dose to make up for forgotten individual doses.

5. POSSIBLE SIDE EFFECTS
KEYSAL can have side effects.
Cardiac disorders
Frequent: peripheral oedema, angioedema, palpitations.
Less frequent: syncope, vasculitis.
The following side effects have been reported and frequencies are unknown: hypotension (including orthostatic hypotension), myocardial infarction, arrhythmia (including ventricular tachycardia and atrial fibrillation), chest pain.
Nervous system disorders
Frequent: dizziness, headache, somnolence, flushing.
Less frequent: mood changes, dry mouth, peripheral neuropathy, increased sweating.
The following side effects have been reported and frequencies are unknown: hypertonia, hypoesthesia/paraesthesia, tremor, insomnia, increased sweating, pain.
Gastrointestinal disorders
Frequent: nausea, abdominal pain, vomiting.
Less frequent: altered bowel habits, dyspepsia, gingival hyperplasia, pancreatitis.
The following side effects have been reported and frequencies are unknown: taste perversion.
Musculoskeletal, connective tissue and bone disorders
Frequent: fatigue.
Less frequent: arthralgia, asthenia, back pain, muscle cramps, myalgia.
Hepato-biliary disorders
The following side effects have been reported and frequencies are unknown: hepatitis, jaundice.
Blood and the lymphatic system disorders
Less frequent: leucopenia, thrombocytopenia.
The following side effects have been reported and frequencies are unknown: purpura.
Renal and urinary disorders
Less frequent: increased urinary frequency.
Reproductive system and breast disorders
Less frequent: impotence.
Endocrine disorders
Less frequent: gynaecomastia.
The following side effects have been reported and frequencies are unknown: weight increase/decrease.
Investigations
Less frequent: hyperglycaemia.
The following side effects have been reported and frequencies are unknown: raised liver enzymes (mostly consistent with cholestasis).
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Less frequent: alopecia.
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Respiratory, thoracic and mediastinal disorders
Less frequent: dyspnoea.
The following side effects have been reported and frequencies are unknown: coughing.
Eye disorders
Less frequent: visual disturbances.
Ear and labyrinth disorders
The following side effects have been reported and frequencies are unknown: tinnitus.
Not all side effects reported for **KEYSAL** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking this medicine, please consult your doctor, pharmacist or other healthcare professional for advice.
If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

6. STORING AND DISPOSING OF KEYSAL
STORE ALL MEDICINES OUT OF REACH OF CHILDREN.
Store at or below 30 °C.
Return all unused medicine to your pharmacist.
Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

7. PRESENTATION OF KEYSAL
KEYSAL 5 mg:
a) PVC/PE/Aclar - Alu Blister Pack
Tablets are packed in 250 micron white opaque PVC film laminated with 25 micron PE coated with 23 micron Aclar and 25 microns printed aluminium foil. Each blister contains 10 tablets.
The blisters will be further packed in a pre-printed carton with a package leaflet.
Pack size: 30's - Each carton contains 3 blisters of 10 tablets each OR;
b) PVC/PVdC - Alu Blister Pack
Tablets are packed in white opaque 250 micron PVC film laminated with 90 gsm PVdC and 25 microns printed aluminium foil. Each blister contains 10 tablets.
The blisters will be further packed in a pre-printed carton with a package leaflet.
Pack size: 30's - Each carton contains 3 blisters of 10 tablets each OR;
c) HDPE container
Tablets are packed in a white opaque round HDPE container closed with a white opaque polypropylene stock ribbed closure with wad having an induction sealing liner.
The HDPE container will be further packed in a pre-printed carton with a package leaflet.
Pack size: 30's - Each HDPE container contains 30 tablets each.
KEYSAL 10 mg:
a) PVC/PE/Aclar - Alu Blister Pack
Tablets are packed in 250 micron white opaque PVC film laminated with 25 micron PE coated with 23 micron Aclar and 25 microns printed aluminium foil. Each blister contains 10 tablets.
Pack size: 30's - Each carton contains 3 blisters of 10 tablets each.
The blisters will be further packed in a pre-printed carton with a package leaflet.
b) PVC/PVdC - Alu Blister Pack
Tablets are packed in white opaque 250 micron PVC film laminated with 90 gsm PVdC and 25 microns printed aluminium foil. Each blister contains 10 tablets.
Pack size: 30's - Each carton contains 3 blisters of 10 tablets each.
The blisters will be further packed in a pre-printed carton with a package leaflet.
c) HDPE container
Tablets are packed in a white opaque round HDPE container closed with a white opaque polypropylene stock ribbed closure with wad having an induction sealing liner.
The HDPE container will be further packed in a pre-printed carton with a package leaflet.
Pack size: 30's - Each HDPE container contains 30 tablets each.
Not all packs or pack sizes are necessarily marketed.

8. IDENTIFICATION OF KEYSAL
KEYSAL 5 mg:
White to off white, flat, bevel edged, barrel shaped uncoated tablets, debossed with 'C' on one side and '58' on the other side.
KEYSAL 10 mg:
White to off white, flat, bevel edged, round shaped uncoated tablets, debossed with 'C' on one side and '59' on the other side.

9. REGISTRATION NUMBER
KEYSAL 5 mg: 41/7.1/0749
KEYSAL 10 mg: 41/7.1/0750

10. NAME, BUSINESS ADDRESS AND TELEPHONE NUMBER OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION
Novagen Pharma (Pty) Ltd
Office 2, 100 Sovereign Drive
Route 21 Corporate Park
Nellmapius Drive
Irene – Pretoria
South Africa
(t) +27 12 345 3175

11. DATE OF PUBLICATION OF THE PATIENT INFORMATION LEAFLET
Date of registration: 5 March 2009
Date of latest revision of the text as approved by Council: 5 March 2009
Date of notification with regard to amended Reg. 9 and 10: 16 January 2015

FOR NAMIBIA ONLY:
Schedule: NS2
Registration Numbers:
KEYSAL 5 mg: 14/7.1/0644
KEYSAL 10 mg: 14/7.1/0643

NOVAGEN PHARMA

PROFESSIONELE INLIGTING:
SKEDULERINGSTATUS:
S3

EIENDOMSNAAM EN DOSEERVORM:
KEYSAL 5 mg (Tablet)
KEYSAL 10 mg (Tablet)
SAMESTELLING:
KEYSAL 5 mg: Elke tablet bevat amlodipienbesilaat ekwivalent aan 5 mg amlodipien.
KEYSAL 10 mg: Elke tablet bevat amlodipienbesilaat ekwivalent aan 10 mg amlodipien.
Eksipiënte: Mikrokristallyne sellulose, natriumstyselglikolaat, anhidriese kalsiumwaterstoffosfaat en magnesiumstearaat.
Suikervry.

FARMAKOLOGIESE KLASSIFIKASIE:
A 7.1 Vasodilators, hipotensiemiddels.

FARMAKOLOGIESE WERKING:
Farmakodinamiese eienskappe:
Amlodipien is 'n dihidropiridien kalsiumkanaalblokkeerder. Dit inhibeer die transmembraan invloei van kalsiumione na die hart- en kardiovaskulêre gladdespier sonder om serumkalsiumkonsentrasies te affekteer. Direkte ontspanning van vaskulêre gladdespier vorm die basis van die antihipertensiewe werking.
By angina pectoris werk amlodipien as 'n perifere arteriolêre vasodilator wat lei tot 'n afname in totale perifere weerstand (nalading). Miokardiese energie- en suurstofbehoefte word verminder. Amlodipien oefen sy werking uit deur aan die dihidropiridien bindingsplekke te bind. Dit oefen 'n minimale uitwerking op hartgeleiding-, kontraksie en harttempo uit.

Farmakokinetiese eienskappe:
Die volledige absorpsie van amlodipien na mondelikse toediening is stadig en piek plasmavlakke word na 6 tot 12 uur bereik. Amlodipien het 'n biobeskikbaarheid van ongeveer 64 % en 'n plasma-eliminasiehalfleeftyd van 35 tot 50 uur . Laasgenoemde laat toe vir een keer daaglikse dosering. Vastevlak plasmakonsentrasies word na 7 tot 8 dae van opeenvolgende dosering bereik. Die verspreidingsvolume is ongeveer 20 liter/kg. Uitgebreide metabolisme vind in die lewer plaas en minder as 10 % van amlodipien kom onveranderd in die urine voor. Die metabolliete is oraaklief en word hoofsaaklik (tot soveel as 60 %) deur die niere uitgeskei.

INDIKASIES:
KEYSAL word aangedui vir die:
- Behandeling van angina pectoris
- Behandeling van gerinige tot matige hipertensie, alleen of in kombinasie met ander antihipertensiewe middels.

KONTRA-INDIKASIES:
Hipersensitiwiteit teen enige van die bestanddele.
Hipersensitiwiteit teen dihidropiridiene.

WAARSKUWINGS en SPESIALE VOORSORGMAATREËLS:

Die vervangbaarheid of onderlinge uitruilbaarheid met ander amlodipien-bevattende middels is nie vasgestel nie.

Gebruik by bejaardes:
Amlodipienauwering is minder (40 tot 60 %) by bejaardes, wat lei tot toenames in amlodipienkonsentrasies in die area onder die konsentrasie-tydkurwe (AOK), asook eliminasiehalfleeftyd. Daarom behoort **KEYSAL** terapie teen 'n laer dosis by bejaardes begin te word.
Gebruik by nierversaking:
Alhoewel **KEYSAL** hoofsaaklik deur die niere uitgeskei word, wil dit voorkom asof matige nierinkorting geen effek op plasmakonsentrasies het nie. Erge nierinkorting kan egter 'n laer dosering noodsaak. **KEYSAL** is nie dialiseerbaar nie.
Gebruik by ingekorte lewerfunksie:
Die halfleeftyd van **KEYSAL** is aansienlik langer by pasiente met ingekorte lewerfunksie. Daarom behoort **KEYSAL** teen laer dosisse aan hierdie pasiente toegedien te word.
Gebruik by kinders:
Die veiligheid en doeltreffendheid is nie vasgestel nie.
Gebruik by hartversaking:
'n Groter voorkoms van longedeem is aangemeld.
KEYSAL kan 'n negatiewe inotropiese effek uitoefen. Die AOK van **KEYSAL** kan by pasiente met hartversaking toeneem.
Porfirie:
Die veiligheid is nie vasgestel nie.

INTERAKSIES:
Die gelyktydige toediening van ondertonge nitrogliserien, langwerkende nitrate, betablokkeerders of ander anti-anginamiddels saam met amlodipien kan bykomende antihipertensiewe en anti-angina effekte lewer. Ondertonge nitrogliserien kan wanneer nodig, gebruik word om angina-aanvalle gedurende amlodipienterapie te verdryf. Nitraatmedikasie kan vir anginaprofilaktiese gebruik word gedurende terapie met amlodipien. Amlodipien bied geen beskerming teen die gevolge van ontrekking van betablokkeerders nie; 'n geleidelike verlaging in betablokkeerderdosis word aanbeveel.
Alhoewel geen "terugkeereffek" met die staking van amlodipien aangemeld is nie, word 'n geleidelike verlaging van die dosering onder toesig van 'n dokter aanbeveel.

MENSLIKE VOORTPLANTING:
Veiligheid by swangerskap en laktasie is nie vasgestel nie (sien **"KONTRA-INDIKASIES")**

DOSERING EN GEBRUIKSAANWYSINGS:
Hipertensie en angina pectoris:
Volwassenes:
'n Aanvanklike dosis van 5 mg **KEYSAL** een keer per dag word aanbeveel. Dit kan na 10 tot 14 dae van terapie na 10 mg een keer per dag verhoog word indien daar geen verbetering is nie.
Geen dosisverminderinge is nodig wanneer **KEYSAL** by tasieddiuretika, betablokkeerders of angiotensien-omskakelingsensiem-inhibeerders gevoeg word nie.

NEWE-EFFEKTE:
Hartafwykings:
Dikwels: perifere edeem, angioödeem, hartkloppings.
Minder dikwels: sinkopie, vaskulitis.
Die volgende newe-effekte is aangemeld maar die frekwensies is onbekend: hipotensie (insluitend ortostatiese hipotensie), miokardiese infarksie, aritmie (insluitend ventrikulêre tagikardie en atriale fibrillasie), borspyn.
Afwykings van die senuweestelsel:
Dikwels: duiseligheid, hoofpyn, slaapsug, blosing.
Minder dikwels: gemoedsveranderinge, droë mond, perifere neuropatie, toename in sweet.
Die volgende newe-effekte is aangemeld maar die frekwensies is onbekend: hipertonie, hipoëstesie/parestesie, tremor, slaaploosheid, toename in sweet, pyn.
Gastrointestinale afwykings:
Dikwels: naarheid, buikpyn, braking.
Minder dikwels: veranderde stoelganggewoontes, dispepsie, hiperplasie van die tandvleis, pankreatitis.
Die volgende newe-effekte is aangemeld maar die frekwensies is onbekend: smaakafwyking.
Muskuloskeletale-, bindeweefsel en beenafwykings:
Dikwels: moegheid.
Minder dikwels: artralgie, astenie, rugpyn, spierkrampe, mialgie.
Hepato-bilière afwykings:
Die volgende newe-effekte is aangemeld maar die frekwensies is onbekend: hepatitis, geelsug.
Bloed- en limfsisteemafwykings:
Minder dikwels: leukopenie, trombositopenie.
Die volgende newe-effekte is aangemeld maar die frekwensies is onbekend: purpura.
Nier- en urienafwykings
Minder dikwels: toename in urienfrekwensie.
Reproduksiesisteem en borsafwykings:
Minder dikwels: impotensie.
Endokriene afwykings:
Minder dikwels: ginekomastie.
Die volgende newe-effekte is aangemeld maar die frekwensies is onbekend: massatoename/-afname.
Ondersoeke:
Minder dikwels: hiperglukemie.
Die volgende newe-effekte is aangemeld maar die frekwensies is onbekend: toename in lewerensieme (gewoonlik in ooreenstemming met cholestase).
Afwykings van die vel en subkutane weefsel:
Minder dikwels: alopesie.
Die volgende newe-effekte is aangemeld maar die frekwensies is onbekend: allergiese reaksies met pruritus, uitslag, en erythema multiforme.
Respiratoriese-, bors en mediastinale afwykings:
Minder dikwels: dispnee.
Die volgende newe-effekte is aangemeld maar die frekwensies is onbekend: hoes.
Oogafwykings:
Minder dikwels: gesigsafwykings.
Oor- en labirintafwykings:
Die volgende newe-effekte is aangemeld maar die frekwensies is onbekend: tinnitus.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:
Daar is geen gedokumenteerde ondervinding van oordosering met **KEYSAL** nie. Maagspoeling kan voordelig wees. Erge oordosering kan tot oormatige perifere vasodilatasie lei, wat op sy beurt tot merkbare en waarskynlik verlengde sistemiese hipotensie kan lei.
Klinies betekenisvolle hipotensie weens oordosering met **KEYSAL** vereis aktiewe kardiovaskulêre ondersteuning. Intraveneuse kalsiumglukonaat kan voordelig wees in die omkering van die effekte van kalsiumkanaalblokkering. Aangesien amlodipien hoogs proteïengebonde is, is dialise waarskynlik van geen nut nie.
BEHANDELING IS SIMPTOMATIES EN ONDERSTEUNEND.

IDENTIFIKASIE:
KEYSAL 5 mg:
Wit tot naaswit, plat, afgeskuinste rante, ovaalvormige, onbedekte tablette, met 'C' op die een kant en '58' op die ander kant gedruk.
KEYSAL 10 mg:
Wit tot naaswit, plat, afgeskuinste rante, ronde, onbedekte tablette, met 'C' op die een kant en '59' op die ander kant gedruk.

AANBIEDING:
KEYSAL 5 mg:
PVC/PE/Aclar - Alu Stolpverpakking:
Tablette word verpak in 250 mikron wit, ondeursigtige PVC film, gelamineer met 25 mikron PE, bedek met 23 mikron Aclar en 25 mikron gedrukte aluminiumfoelie. Elke stolpverpakking bevat 10 tablette.
Die stolpverpakkings sal verder verpak word in 'n voorafgedrukte karton met 'n verpakkingsbiljet.
Pakgroote: 30's - Elke karton bevat 3 stolpverpakkings van 10 tablette elk OF;
PVC/PVdC - Alu Stolpverpakking:
Tablette word verpak in wit, ondeursigtige 250 mikron PVC film, gelamineer met 90 gvm PVdC en 25 mikron gedrukte aluminiumfoelie. Elke stolpverpakking bevat 10 tablette.
Die stolpverpakkings sal verder verpak word in 'n voorafgedrukte karton met 'n verpakkingsbiljet.
Pakgroote: 30's - Elke karton bevat 3 stolpverpakkings van 10 tablette elk OF;
HDPE houer:
Tablette word verpak in 'n wit ondeursigtige ronde HDPE houer, toegemaak met 'n wit ondeursigtige polipropileen geïnde sluiting met 'n prop met 'n indukseseëlvoering.
Pakgroote: 30's - Elke HDPE houer bevat 30 tablette elk.
Die HDPE houer sal verder verpak word in 'n voorafgedrukte karton met 'n verpakkingsbiljet.
KEYSAL 10 mg:
PVC/PE/Aclar - Alu Stolpverpakking:
Tablette word verpak in 250 mikron wit, ondeursigtige PVC film, gelamineer met 25 mikron PE, bedek met 23 mikron Aclar en 25 mikron gedrukte aluminiumfoelie. Elke stolpverpakking bevat 10 tablette.
Die stolpverpakkings sal verder verpak word in 'n voorafgedrukte karton met 'n verpakkingsbiljet.
Pakgroote: 30's - Elke karton bevat 3 stolpverpakkings van 10 tablette elk OF;
PVC/PVdC - Alu Stolpverpakking:
Tablette word verpak in wit, ondeursigtige 250 mikron PVC film, gelamineer met 90 gvm PVdC en 25 mikron gedrukte aluminiumfoelie. Elke stolpverpakking bevat 10 tablette.
Die stolpverpakkings sal verder verpak word in 'n voorafgedrukte karton met 'n verpakkingsbiljet.
Pakgroote: 30's - Elke karton bevat 3 stolpverpakkings van 10 tablette elk OF;
HDPE houer:
Tablette word verpak in 'n wit ondeursigtige ronde HDPE houer, toegemaak met 'n wit ondeursigtige polipropileen geïnde sluiting met 'n prop met 'n indukseseëlvoering.
Pakgroote: 30's - Elke HDPE houer bevat 30 tablette elk.
Die HDPE houer sal verder verpak word in 'n voorafgedrukte karton met 'n verpakkingsbiljet.
Nie alle verpakkings en pakgrootte word noodwendig bemark nie.

BEWARINGSINSTRUKSIES:
Bewaar by of benede 30 °C.
HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMER:
KEYSAL 5 mg: 41/7.1/0749
KEYSAL 10 mg: 41/7.1/0750

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE:
Novagen Pharma (Pty) Ltd
Kantoor 2, Sovereignrylaan 100
Route 21 Corporate Park
Nellmapuspruiplaan
Irene – Pretoria
Suid-Afrika

DATUM VAN PUBLIKASIE VAN DIE PROFESSIONELE INLIGTING:
Datum van registrasie: 5 Maart 2009
Datum van laaste hersiening van die teks soos goedgekeur deur die Raad: 5 Maart 2009
Datum van kennisgewing met betrekking tot gewysigde Reg. 9 en 10: 16 Januarie 2015

SLEGS VIR NAMIBIË:
Skedule: NS2
Registrasienommers:
KEYSAL 5 mg: 14/7.1/0644
KEYSAL 10 mg: 14/7.1/0643

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PASIËNTINLIGTINGSBILJET
SKEDULERINGSTATUS
S3

EIENDOMSNAAM, STERKTE EN FARMASEUTIESE VORM
KEYSAL 5 mg (Tablette)
KEYSAL 10 mg (Tablette)
Amlodipienbesilaat

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

1. WAT KEYSAL BEVAT

Die aktiewe bestanddeel is amlodipien.
KEYSAL 5 mg: Elke tablet bevat amlodipienbesilaat ekwivalent aan 5 mg amlodipien.
KEYSAL 10 mg: Elke tablet bevat amlodipienbesilaat ekwivalent aan 10 mg amlodipien.
Die ander bestanddele is mikrokristallyne sellulose, natriumstyselglikolaat, anhidriese kalsiumwaterstoffosfaat en magnesiumstearaat.
Suikervry.

2. WAARVOOR KEYSAL GEBRUIK WORD

KEYSAL word gebruik vir die behandeling van:
- angina pectoris.
- geringe tot matige hipertensie, alleen of in kombinasie met ander antihipertensiemiddels

3. VOORDAT U KEYSAL NEEM

Moenie KEYSAL neem:
- As u hipersensitief (allergies) vir amlodipienbesilaat of enige van die ander bestanddele van **KEYSAL** is.
- As u hipersensitief (allergies) vir dihidropiridiene is.

Neem spesiale sorg met KEYSAL:
- Bejaardes behoort terapie met **KEYSAL** teen 'n laer dosis te begin.
- Doseringsaanpassings kan by pasiente met nier- en lewersiekte nodig wees.
- Veiligheid en effektiwiteit by kinders is nie vasgestel nie.
- Veiligheid by porfirie is nie vasgestel nie.

Swangerskap en borsvoeding:
Veiligheid van **KEYSAL** by swanger en lakterende vroue is nie vasgestel nie.
As u swanger is of u baba borsvoed, moet u asseblief u dokter, apteker of ander professionele gesondheidswerker vir advies nader voordat u **KEYSAL** neem.

Die neem van ander mediseyne saam met KEYSAL:
KEYSAL kan interaksies met nitrogliserien, langwerkende nitrate, betablokkeerders en ander anti-anginamiddels.

Stel altyd u dokter in kennis as u enige ander mediseyne neem (dit sluit komplementêre of tradisionele mediseyne in).

4. HOE OM KEYSAL TE NEEM

Neem **KEYSAL** 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 **KEYSAL** te sterk of te swak is, raadpleeg u dokter of apteker.

Hipertensie en Angina pectoris:
Volwassenes:
'n Aanvanklike dosis van 5 mg **KEYSAL** word een keer per dag aanbeveel, wat na 10 tot 14 dae na 10 mg een keer per dag verhoog kan word as daar geen verbetering is nie.
Geen dosisvermindering is nodig wanneer KEYSAL by tasieddiuretika, betablokkeerders of angiotensienomskakelings-ensieminhibeerders gevoeg word nie.

As u te veel KEYSAL geneem het:
Daar bestaan geen gedokumenteerde ondervinding van oordosering met **KEYSAL** nie. Maagspoeling kan tot voordeel wees. Erge oordosering kan tot oormatige perifere vasodilatasie lei, wat tot merkbare en waarskynlik verlengde sistemiese hipotensie lei.
Kliniese bedoende hipotensie weens oordosering met **KEYSAL** vereis aktiewe kardiovaskulêre ondersteuning. Intraveneuse kalsiumglukonaat kan tot voordeel wees in die omkering van die effekte van kalsiumblokkering. Aangesien amlodipien hoogs proteïengebonde is, is dit onwaarskynlik dat dialise van voordeel sal wees.
DIE BEHANDELING IS SIMPTOMATIES EN ONDERSTEUNEND.

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 KEYSAL te neem:
Moenie die dosis verdubbel om vir 'n oorgslane dosis op te maak nie.

5. MOONTLIKE NEWE-EFFEKTE

KEYSAL kan newe-effekte hê.
Hartafwykings
Dikwels: perifere edeem, angioödeem, hartkloppings.
Minder dikwels: sinkopie, vaskulitis.
Die volgende newe-effekte is aangemeld en die frekwensies is onbekend: hipotensie (insluitend ortostatiese hipotensie), miokardiale infarksie, aritmie (insluitend ventrikulêre tagikardie en atriale fibrillasie), borspyn.
Senuweestelselafwykings
Dikwels: duiseligheid, hoofpyn, slaapsug, warmgloede.
Minder dikwels: buitenaardergloed, droë mond, perifere neuropatie, toename in sweet.
Die volgende newe-effekte is aangemeld en die frekwensies is onbekend: hipertonie, hipoëstesie/parestesie, bewerasie, slaaploosheid, toename in sweet, pyn.
Gastrointestinale afwykings
Dikwels: naarheid, buikpyn, braking.
Minder dikwels: veranderde dermgewoontes, dispepsie, hiperplasie van die tandvleis, pankreatitis.
Die volgende newe-effekte is aangemeld en die frekwensies is onbekend: smaakafwyking.
Muskuloskeletale-, bindeweefsel en beenafwykings
Dikwels: moegheid
Minder dikwels: artralgie, astenie, rugpyn, spierkrampe, mialgie.
Hepatobiliêre afwykings
Die volgende newe-effekte is aangemeld en die frekwensies is onbekend: hepatitis, geelsug
Bloed- en limfsisteemafwykings
Minder dikwels: leukopenie, trombositopenie.
Die volgende newe-effekte is aangemeld en die frekwensies is onbekend: purpura.
Nier- en urienafwykings
Minder dikwels: toename in urienfrekwensie.
Reproduksiesisteem en borsafwykings
Minder dikwels: impotensie.
Endokriene afwykings
Minder dikwels: ginekomastie.
Die volgende newe-effekte is aangemeld en die frekwensies is onbekend: massatoename/-verlies.
Ondersoeke
Minder dikwels: hiperglukemie.
Die volgende newe-effekte is aangemeld en die frekwensies is onbekend: verhoogde lewerensieme (hoofsaaklik konsistent met cholestase).
Vel- en subkutane weefselafwykings
Minder dikwels: alopesie.
Die volgende newe-effekte is aangemeld en die frekwensies is onbekend: allergiese reaksies met pruritus, uitslag en erythema multiforme.
Respiratoriese-, bors en mediastinale afwykings
Minder dikwels: dispnee.
Die volgende newe-effekte is aangemeld en die frekwensies is onbekend: hoes.
Oogafwykings
Minder dikwels: gesigsafwykings.
Oor- en labirintafwykings
Die volgende newe-effekte is aangemeld en die frekwensies is onbekend: tinnitus.

Nie al die newe-effekte wat vir **KEYSAL** aangemeld is, word in hierdie biljet ingesluit nie. As u algemene gesondheid agteruitgaan of as u enige ongewone effekte ondervind terwyl u hierdie mediseyne neem, moet u asseblief u dokter, apteker of ander professionele gesondheidswerker om advies raadpleeg.

As u enige newe-effekte waarneem wat nie in hierdie biljet genoem word nie, moet u asseblief u dokter of apteker in kennis stel.

6. BEWARING EN WEGDOENING VAN KEYSAL

BEWAAR ALLE MEDISYNE BUITE DIE BEREIK VAN KINDERS.

Bewaar teen of benede 30 °C.

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

7. AANBIEDING VAN KEYSAL

KEYSAL 5 mg:
a) PVC/PE/Aclar - Alu Stolpverpakking
Tablette word verpak in 250 mikron wit ondeurskynende PVC film, gelamineer met 25 mikron PE, bedek met 23 mikron Aclar en 25 mikron gedrukte aluminiumfoelie. Elke stolpverpakking bevat 10 tablette.
Die stolpverpakkings sal verder verpak word in 'n voorafgedrukte karton met 'n verpakkingsbiljet.
Pakgroote: 30's - Elke karton bevat 3 stolpverpakkings met 10 tablette elk OF;
b) PVC/PVdC - Alu Stolpverpakking
Tablette word verpak in wit ondeurskynende 250 mikron PVC film, gelamineer met 90 gvm PVdC en 25 mikron gedrukte aluminiumfoelie. Elke stolpverpakking bevat 10 tablette.
Die stolpverpakkings sal verder verpak word in 'n voorafgedrukte karton met 'n verpakkingsbiljet.
Pakgroote: 30's - Elke karton bevat 3 stolpverpakkings met 10 tablette elk OF;
c) HDPE houer
Tablette word verpak in 'n wit ondeurskynende ronde HDPE houer, toegemaak met 'n wit ondeurskynende polipropileen geïnde sluiting met 'n prop met 'n indukseseëlvoering.
Die HDPE houer sal verder verpak word in 'n voorafgedrukte karton met 'n verpakkingsbiljet.
Pakgroote: 30's - Elke HDPE houer bevat 30 tablette elk.
KEYSAL 10 mg:
a) PVC/PE/Aclar - Alu Stolpverpakking
Tablette word verpak in 250 mikron wit ondeurskynende PVC film, gelamineer met 25 mikron PE, bedek met 23 mikron Aclar en 25 mikron gedrukte aluminiumfoelie. Elke stolpverpakking bevat 10 tablette.
Die stolpverpakkings sal verder verpak word in 'n voorafgedrukte karton met 'n verpakkingsbiljet.
Pakgroote: 30's - Elke karton bevat 3 stolpverpakkings met 10 tablette elk OF;
b) PVC/PVdC - Alu stolpverpakking
Tablette word verpak in wit ondeurskynende 250 mikron PVC film, gelamineer met 90 gvm PVdC en 25 mikron gedrukte aluminiumfoelie. Elke stolpverpakking bevat 10 tablette.
Die stolpverpakkings sal verder verpak word in 'n voorafgedrukte karton met 'n verpakkingsbiljet.
Pakgroote: 30's - Elke karton bevat 3 stolpverpakkings met 10 tablette elk OF;
c) HDPE houer
Tablette word verpak in 'n wit ondeurskynende ronde HDPE houer, toegemaak met 'n wit ondeurskynende polipropileen geïnde sluiting met 'n prop met 'n indukseseëlvoering.
Die HDPE houer sal verder verpak word in 'n voorafgedrukte karton met 'n verpakkingsbiljet.
Pakgroote: 30's - Elke HDPE houer bevat 30 tablette elk.
Nie alle verpakkings of pakgrootte word noodwendig bemark nie.

8. IDENTIFIKASIE VAN KEYSAL

KEYSAL 5 mg:
Wit tot naaswit, plat, afgeskuinste rante, ovaalvormige, onbedekte tablette, met 'C' op die een kant en '58' op die ander kant gedruk.
KEYSAL 10 mg:
Wit tot naaswit, plat, afgeskuinste rante, ronde, onbedekte tablette, met 'C' op die een kant en '59' op die ander kant gedruk.

9. REGISTRASIENOMMER

KEYSAL 5 mg: 41/7.1/0749
KEYSAL 10 mg: 41/7.1/0750

10. NAAM, BESIGHEIDSADRES EN TELEFOONNOMMER VAN DIE HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE

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11. DATUM VAN PUBLIKASIE VAN DIE PASIËNTINLIGTINGSBILJET

Datum van registrasie: 5 Maart 2009
Datum van die nuutste hersiening van die teks soos deur die Raad goedgekeur: 5 Maart 2009
Datum van kennisgewing met betrekking tot gewysigde Reg. 9 en 10: 16 Januarie 2015

SLEGS VIR NAMIBIË:
Skedule: NS2
Registrasienommers:
Keysal 5 mg: 14/7.1/0644
Keysal 10 mg: 14/7.1/0643