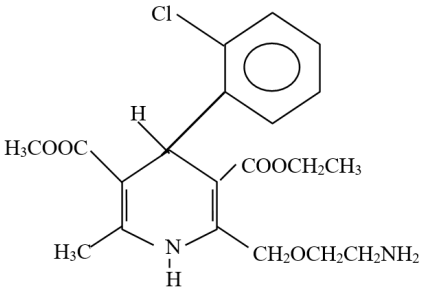
LOCAL PRODUCT DOCUMENT
PT PFIZER INDONESIA

Generic Name	: Amlodipine Besylate
Trade Name	: Norvask
CDS Effective Date	: March 10, 2017
Supersedes	: July 10, 2014

DESCRIPTION

Amlodipine besylate is a dihydropyridine derivative, and has the following chemical name: 3-ethyl-5-methyl-2-(2-aminoethoxymethyl)-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridinedicarboxylate benzene sulphonate.

Amlodipine has the following structural formula:



Amlodipine besylate is slightly soluble in water and sparingly soluble in ethanol and has a molecular weight of 567.1 (free base 408.9).

Amlodipine besylate is available as white, 5 mg and 10 mg octagonal-shaped tablets containing 6.98 mg amlodipine besylate equivalent to 5 mg amlodipine and 13.965 mg amlodipine besylate equivalent to 10 mg amlodipine, respectively. Inert ingredients: sodium starch glycolate, mycrocrystalline cellulose, magnesium stearate, and dibasic calcium phosphate anhydrous.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Amlodipine is a calcium ion influx inhibitor (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle.

The mechanism of the antihypertensive action of amlodipine is due to a direct relaxant effect on vascular smooth muscle. The precise mechanism by which amlodipine relieves angina has not been fully determined, but amlodipine reduces total ischemic burden by the following two actions:

1) Amlodipine dilates peripheral arterioles and thus reduces the total peripheral resistance (afterload) against which the heart works. Since the heart rate remains stable, this unloading of the heart reduces myocardial energy consumption and oxygen requirements.
2) The mechanism of action of amlodipine also probably involves dilatation of the main coronary arteries and coronary arterioles, both in normal and ischemic regions. This dilatation increases myocardial oxygen delivery in patients with coronary artery spasm (Prinzmetal's or variant angina) and blunts smoking-induced coronary vasoconstriction.

In patients with hypertension, once-daily dosing provides clinically significant reductions in blood pressure in both the supine and standing positions throughout the 24-hour interval. Due to the slow onset of action, acute hypotension is not a feature of amlodipine administration.

In patients with angina, once-daily administration of amlodipine increases total exercise time, time to angina onset, and time to 1 mm ST segment depression, and decreases both angina attack frequency and nitroglycerine tablet consumption.

Amlodipine has not been associated with any adverse metabolic effects or changes in plasma lipids and is suitable for use in patients with asthma, diabetes, and gout.

Use in Patients with Heart Failure

Hemodynamic studies and exercise-based controlled clinical trials in NYHA Class II-IV heart failure patients have shown that amlodipine did not lead to clinical deterioration, as measured by exercise tolerance, left ventricular ejection fraction, and clinical symptomatology.

A placebo-controlled study (PRAISE) designed to evaluate patients in NYHA Class III-IV heart failure receiving digoxin, diuretics, and ACE inhibitors has shown that amlodipine did not lead to an increase in risk of mortality or combined mortality and morbidity in patients with heart failure.

In a follow-up, long-term, placebo-controlled study (PRAISE-2) of amlodipine in patients with NYHA class III and IV heart failure without clinical symptoms or objective findings suggestive of underlying ischemic disease, on stable doses of ACE inhibitors, digitalis, and diuretics, amlodipine had no effect on total or cardiovascular mortality. In this same population, amlodipine was associated with increased reports of pulmonary edema despite no significant difference in the incidence of worsening heart failure compared to placebo.

Use in Pediatric Patients (Aged 6 to 17 years)

The efficacy of amlodipine in hypertensive pediatric patients aged 6 to 17 years of age was demonstrated in one 8-week, double-blind, placebo-controlled, randomized withdrawal trial in 268 patients with hypertension. All patients were randomized to the 2.5 mg or 5 mg treatment arms and followed up for 4 weeks after which they were randomized to continue

2.5 mg or 5 mg amlodipine or placebo for an additional 4 weeks. Compared to baseline, once-daily treatment with amlodipine 5 mg resulted in statistically significant reductions in systolic and diastolic blood pressures. Placebo-adjusted mean reduction in seated systolic blood pressure was estimated to be 5.0 mmHg for the 5 mg dose of amlodipine and 3.3 mmHg for the 2.5 mg dose of amlodipine. Subgroup analyses indicated that younger pediatric patients aged 6 to 13 years had efficacy results comparable to those of the older pediatric patients aged 14 to 17 years.

Pharmacokinetic Properties

Absorption

After oral administration of therapeutic doses, amlodipine is well absorbed with peak blood levels between 6 and 12 hours post-dose. Absolute bioavailability has been estimated to be between 64% and 80%. The volume of distribution is approximately 21 L/kg. *In vitro* studies have shown that approximately 97.5% of circulating amlodipines is bound to plasma proteins.

Absorption of amlodipine is unaffected by consumption of food.

Biotransformation/Elimination

The terminal plasma elimination half-life is about 35 to 50 hours and is consistent with once-daily dosing. Steady-state plasma levels are reached after 7 to 8 days of consecutive dosing. Amlodipine is extensively metabolized by the liver to inactive metabolites, with 10% of the parent compound and 60% of metabolites excreted in the urine.

Use in the Elderly

The time to reach peak plasma concentrations of amlodipine is similar in elderly and younger subjects. Amlodipine clearance tends to be decreased with resulting increases in AUC and elimination half-life in elderly patients. Increases in AUC and elimination half-life in patients with CHF were as expected for the patient age group studied.

Use in Pediatrics

In one clinical chronic exposure study, 73 hypertensive pediatric patients aged 12 months to less than or equal to 17 years received amlodipine at an average daily dose of 0.17 mg/kg. Clearance for subjects with median weight of 45 kg was 23.7 L/h and 17.6 L/h for males and females, respectively. This is in a similar range to the published estimates of 24.8 L/h in a 70 kg adult. The average estimate for volume of distribution for a 45 kg patient was 1130 L (25.11 L/kg). Maintenance of the blood pressure effect over the 24-hour dosing interval was observed with little difference in peak and trough variation effect. When compared to historical adult pharmacokinetics the parameters observed in this study indicate that once-daily dosing is appropriate.

Preclinical Safety Data

Carcinogenesis, Mutagenesis, Impairment of Fertility

Rats and mice treated with amlodipine in the diet for 2 years, at concentrations calculated to provide daily dosage levels of 0.5, 1.25, and 2.5 mg/kg/day showed no evidence of carcinogenicity. The highest dose (for mice, similar to, and for rats twice* the maximum recommended clinical dose of 10 mg, on a mg/m^2 basis) was close to the maximum tolerated dose for mice but not for rats.

Mutagenicity studies revealed no drug-related effects at either the gene or chromosome levels.

There was no effect on the fertility of rats treated with amlodipine (males for 64 days and females for 14 days prior to mating) at doses up to 10 mg/kg/day (8 times* the maximum recommended human dose of 10 mg, on a mg/m^2 basis).

*Based on patient weight of 50 kg.

INTERACTION WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION

Amlodipine has been safely administered with thiazide diuretics, alpha-blockers, beta-blockers, ACE inhibitors, long-acting nitrates, sublingual nitroglycerine, non steroidal anti-inflammatory drugs, antibiotics, and oral hypoglycemic drugs.

In vitro data from studies with human-plasma indicate that amlodipine has no effect on protein binding of the drugs tested (digoxin, phenytoin, warfarin, or indomethacin).

Simvastatin

Co-administration of multiple doses of 10 mg amlodipine with 80 mg simvastatin resulted in a 77% increase in exposure to simvastatin compared to simvastatin alone. Limit the dose of simvastatin in patients on amlodipine to 20 mg daily.

Grapefruit Juice

Co-administration of 240 mL grapefruit juice with a single oral dose of 10 mg amlodipine in 20 healthy volunteers had no significant effect on the pharmacokinetics of amlodipine. The study did not allow examination of the effect of genetic polymorphism in CYP3A4, the primary enzyme responsible for metabolism of amlodipine; therefore, administration of amlodipine with grapefruit or grapefruit juice is not recommended as bioavailability may be increased in some patients, resulting in increased blood pressure lowering effects.

CYP3A4 Inhibitors

Co-administration of a 180 mg daily dose of diltiazem with 5 mg amlodipine in elderly hypertensive patients (69 to 87 years of age) resulted in a 57% increase in amlodipine systemic exposure. Co-administration of erythromycin in healthy volunteers (18 to 43 years of age) changed amlodipine systemic exposure (22% increase in area under the concentration versus time curve [AUC]). Although the clinical relevance of these findings is uncertain, pharmacokinetic variations may be more pronounced in the elderly. Strong inhibitors of CYP3A4 (e.g., ketoconazole, itraconazole, ritonavir) may increase the plasma concentrations of amlodipine to a greater extent than diltiazem. Amlodipine should be used with caution when administered with CYP3A4 inhibitors.

Clarithromycin

Clarithromycin is an inhibitor of CYP3A4. There is an increased risk of hypotension in patients receiving clarithromycin with amlodipine. Close observation of patients is recommended when amlodipine is co-administered with clarithromycin.

CYP3A4 Inducers

There is no data available regarding the effect of CYP3A4 inducers on amlodipine. Concomitant use of CYP3A4 inducers (e.g., rifampicin, hypericum perforatum) may decrease the plasma concentrations of amlodipine. Amlodipine should be used with caution when administered with CYP3A4 inducers.

In the following studies, there were no significant changes in the pharmacokinetics of either amlodipine or another drug within the study, when co-administered.

Special Studies: Effect of Other Agents on Amlodipine

Cimetidine

Co-administration of amlodipine with cimetidine did not alter the pharmacokinetics of amlodipine.

Aluminum/Magnesium (Antacid)

Co-administration of aluminum/magnesium (antacid) with a single dose of amlodipine had no significant effect on the pharmacokinetics of amlodipine.

Sildenafil

A single 100 mg dose of sildenafil in subjects with essential hypertension had no effect on the pharmacokinetic parameters of amlodipine. When amlodipine and sildenafil were used in combination, each agent independently exerted its own blood pressure lowering effect.

Special Studies: Effect of Amlodipine on Other Agents

Atorvastatin

Co-administration of multiple 10 mg doses of amlodipine with 80 mg atorvastatin resulted in no significant change in the steady-state pharmacokinetic parameters of atorvastatin.

Digoxin

Co-administration of amlodipine with digoxin did not change serum digoxin levels or digoxin renal clearance in healthy volunteers.

Ethanol (Alcohol)

Single and multiple 10 mg doses of amlodipine had no significant effect on the pharmacokinetics of ethanol.

Warfarin

Co-administration of amlodipine with warfarin did not change the warfarin prothrombin response time.

Cyclosporin

No drug interaction studies have been conducted with cyclosporin and amlodipine in healthy volunteers or other populations, with the exception of renal transplant patients. Various studies in renal transplant patients report that co-administration of amlodipine with cyclosporin affects the trough concentrations of cyclosporin, from no change up to an average increase of 40%. Consideration should be given for monitoring cyclosporin levels in renal transplant patients on amlodipine.

Tacrolimus

There is a risk of increased tacrolimus blood levels when co-administered with amlodipine. In order to avoid toxicity of tacrolimus, administration of amlodipine in a patient treated with tacrolimus requires monitoring of tacrolimus blood levels and dose adjustment of tacrolimus when appropriate.

Mechanistic Target of Rapamycin (mTOR) Inhibitors

mTOR inhibitors such as sirolimus, temsirolimus, and everolimus are CYP3A substrates. Amlodipine is a weak CYP3A inhibitor. With concomitant use of mTOR inhibitors, amlodipine may increase exposure of mTOR inhibitors.

Drug/Laboratory Test Interactions

None known

Pregnancy and Lactation

The safety of amlodipine in human pregnancy or lactation has not been established. Amlodipine does not demonstrate toxicity in animal reproductive studies other than delay in parturition and prolongation of labor in rats at a dose level 50 times the maximum recommended dose in humans. Accordingly, use in pregnancy is only recommended when there is no safer alternative and when the disease itself carries greater risk for the mother and fetus. There was no effect on the fertility of rats treated with amlodipine (see section **Preclinical Safety Data**).

Experience in humans indicates that amlodipine is transferred into human breast milk. The median amlodipine concentration ratio of milk/plasma in 31 lactating women with pregnancy-induced hypertension was 0.85 following amlodipine administration at an initial dose of 5 mg once daily which was adjusted as needed (mean daily dose and body weight adjusted daily dose: 6 mg and 98.7 mcg/kg, respectively). The estimated daily dose of amlodipine in the infant via breast milk was 4.17 mcg/kg.

Effects on Ability to Drive and Use Machines

Clinical experience with amlodipine indicates that it is unlikely to impair a patient's ability to drive or use machinery.

THERAPEUTIC INDICATION

Hypertension

Amlodipine is indicated for the first-line treatment of hypertension and can be used as the sole agent to control blood pressure in the majority of patients. Patients not adequately controlled on a single antihypertensive agent (other than amlodipine) may benefit from the addition of amlodipine, which has been used in combination with a thiazide diuretic, alpha blockers, beta adrenoceptor blocking agent, or an angiotensin-converting enzyme (ACE) inhibitor.

Amlodipine is indicated for the first-line treatment of myocardial ischemia, whether due to fixed obstruction (stable angina) and/or vasospasm/vasoconstriction (Prinzmetal's or variant angina) of coronary vasculature. Amlodipine may be used where the clinical presentation suggests a possible vasospastic/vasoconstrictive component but where vasospasm/vasoconstriction has not been confirmed. Amlodipine may be used alone, as monotherapy, or in combination with other antianginal drugs in patients with angina that is refractory to nitrates and/or adequate doses of beta-blockers.

CONTRAINDICATIONS

Amlodipine is contraindicated in patients with a known hypersensitivity to dihydropyridines* or any of the inert ingredients.

*Amlodipine is a dihydropyridine calcium channel blocker

SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE

Use in Patients with Heart Failure

In a long-term placebo-controlled study (PRAISE-2) of amlodipine in patients with New York Heart Association (NYHA) class III and IV heart failure of nonischemic etiology, amlodipine was associated with increased reports of pulmonary edema despite no significant differences in the incidence of worsening heart failure compared to placebo (see section **Pharmacodynamic Properties**).

Use in Patients with Impaired Hepatic Function

As with all calcium antagonists, amlodipine's half-life is prolonged in patients with impaired liver function and dosage recommendations have not been established in these patients. The drug should therefore, be administered with caution in these patients.

UNDESIRABLE EFFECTS

Amlodipine is well tolerated. In placebo-controlled clinical trials involving patients with hypertension or angina, the most commonly observed side effects were:

MedDRA System Organ Class	**Undesirable Effects**
Nervous System Disorders	headaches, dizziness, somnolence
Cardiac Disorders	palpitations
Vascular Disorders	flushing
Gastrointestinal Disorders	abdominal pain, nausea
General Disorders and Administration Site Conditions	oedema, fatigue

In these clinical trials, no pattern of clinically significant laboratory test abnormalities related to amlodipine has been observed.

Less commonly observed side effects in marketing experience include:

MedDRA System Organ Class	**Undesirable Effects**
Blood and Lymphatic System Disorders	leukopenia, thrombocytopenia
Metabolism and Nutrition Disorders	hyperglycaemia
Psychiatric Disorders	insomnia, mood altered
Nervous System Disorders	hypertonia, hypoaesthesia/paresthesia, neuropathy peripheral, syncope, dysgeusia, tremor, extrapyramidal disorder
Eye Disorders	visual impairment
Ear and Labyrinth Disorders	tinnitus
Vascular Disorders	hypotension, vasculitis
Respiratory, Thoracic, and Mediastinal Disorders	cough, dyspnoea, rhinitis
Gastrointestinal Disorders	change in bowel habits, dry mouth, dyspepsia (including gastritis), gingival hyperplasia, pancreatitis, vomiting
Skin and Subcutaneous Tissue Disorders	alopecia, hiperhidrosis, purpura, skin discoloration, urticaria
Musculoskeletal and Connective Tissue Disorders	Arthralgia, back pain, muscle spasms, myalgia
Renal and Urinary Disorders	pollakiuria, micturition disorder, nocturia
Reproductive System and Breast Disorders	gynaecomastia, erectile dysfunction
General Disorders and Administration Site Conditions	asthenia, malaise, pain
Investigations	weight increased/decreased

Rarely reported events were: allergic reaction including pruritus, rash, angioedema, and erythema multiforme.

Hepatitis, jaundice and hepatic enzyme elevations have also been reported very infrequently (mostly consistent with cholestasis). Some cases severe enough to require hospitalization have been reported in association with use of amlodipine. In many instances, causal association is uncertain.

As with other calcium channel blockers, the following adverse events have been rarely reported and cannot be distinguished from the natural history of the underlying disease: myocardial infarction, arrhythmia (including bradycardia, ventricular tachycardia, and atrial fibrillation) and chest pain.

Pediatric Patients (ages 6-17 years)

Amlodipine is well tolerated in children. Adverse events were similar to those seen in adults. In a study of 268 children, the most frequently reported adverse events were:

MedDRA System Organ Class	**Undesirable Effects**
Nervous System Disorders	headaches, dizziness
Vascular Disorders	vasodilatation
Respiratory, Thoracic, and Mediastinal Disorders	epistaxis
Gastrointestinal Disorders	abdominal pain
General Disorders and Administration Site Conditions	asthenia

The majority of adverse events were mild or moderate. Severe adverse events (predominantly headache) were experienced by 7.2% with amlodipine 2.5 mg, 4.5% with amlodipine 5 mg, and 4.6% with placebo. The most common cause of discontinuation from the study was uncontrolled hypertension. There were no discontinuations due to laboratory abnormalities. There was no significant change in heart rate.

POSOLOGY AND METHOD OF ADMINISTRATION

For both hypertension and angina, the usual initial dose is 5 mg amlodipine once daily, which may be increased to a maximum dose of 10 mg depending on the individual patient's response.

No dose adjustment of amlodipine is required upon concomitant administration of thiazide diuretics, beta blockers, and ACE inhibitors.

Use in the Elderly

Normal dosage regimens are recommended. Amlodipine, used at similar doses in the elderly or younger patients, is equally well tolerated.

Use in Children

The recommended antihypertensive oral dose in pediatric patients aged 6 to 17 years is 2.5 mg to 5 mg once daily. Doses in excess of 5 mg daily have not been studied in pediatric patients (see section **Pharmacodynamic Properties** and section **Pharmacokinetic Properties**).

The effect of amlodipine on blood pressure in patients younger than 6 years of age is not known.

Use in Patients with Impaired Hepatic Function

See section **SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE**.

Use in Patients with Renal Failure

Amlodipine may be used at normal doses in patients with renal failure. Changes in amlodipine plasma concentrations are not correlated with the degree of renal impairment. Amlodipine is not dialyzable.

OVERDOSE

Available data suggest that gross overdose could result in excessive peripheral vasodilatation and possibly reflex tachycardia. Marked and probably prolonged systemic hypotension, up to and including shock with fatal outcome, have been reported.

Administration of activated charcoal to healthy volunteers immediately after or up to 2 hours after amlodipine 10 mg ingestion has been shown to significantly decrease amlodipine absorption. Gastric lavage may be worthwhile in some cases. Clinically significant hypotension due to amlodipine overdose calls for active cardiovascular support, including frequent monitoring of cardiac and respiratory function, elevation of extremities, and attention to circulating fluid volume and urine output. A vasoconstrictor may be helpful in restoring vascular tone and blood pressure, provided there is no contraindication to its use. Intravenous calcium gluconate may be beneficial in reversing the effects of calcium channel blockade. Since amlodipine is highly protein-bound, dialysis is not likely to be of benefit.

SUPPLY

NORVASK® is available as 5 mg tablets, packed in boxes of 3 blisters @ 10 tablets. Reg No. DKL9219803410A1

NORVASK® is available as 5 mg tablets, packed in boxes of 10 blisters @ 10 tablets. Reg No. DKL9219803410A1

NORVASK® is available as 10 mg tablets, packed in boxes of 3 blisters @ 10 tablets. Reg No. DKL9619803410B1

STORE IN DRY PLACE AND STORE BELOW 30ºC

PRESCRIPTION ONLY

HARUS DENGAN RESEP DOKTER

Manufactured by:
PT Pfizer Indonesia.
Jakarta, Indonesia

Leaflet kemasan: Informasi untuk pengguna

Norvask®
Tablet 5 mg, 10 mg
Amlodipine Besilate

Baca semua bagian leaflet ini dengan cermat sebelum mulai menggunakan obat ini karena berisi informasi penting bagi Anda.
- Simpan leaflet ini. Anda mungkin perlu membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter, apoteker, atau perawat Anda.
- Obat ini telah diresepkan hanya untuk Anda. Jangan berikan kepada orang lain. Obat ini dapat membahayakan mereka, sekalipun tanda-tanda penyakit mereka sama dengan Anda.
- Jika Anda mengalami efek samping apa pun, konsultasikan dengan dokter atau perawat Anda. Termasuk setiap kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Lihat bagian 13.

Isi leaflet ini:

1. Nama obat
Norvask®

2. Bentuk sediaan
Tablet

3. Deskripsi obat

Norvask® mengandung bahan aktif amlodipine yang termasuk kelompok obat yang disebut antagonis kalsium. Norvask® tersedia sebagai tablet putih 5 mg dan 10 mg berbentuk segi delapan.

4. Apa kandungan obat ini?

Setiap tablet Norvask® untuk pemberian oral mengandung 5 mg dan 10 mg amlodipine besilate. Bahan inert: natrium pati glikolat, selulosa mikrokristalin, magnesium stearat, dan kalsium fosfat anhidrat dibasik.

5. Kekuatan obat

5 mg, 10 mg.

6. Apa kegunaan obat ini?

NORVASK® digunakan untuk mengobati:

- tekanan darah tinggi (hipertensi).
- iskemia miokard, yaitu kondisi kurangnya aliran darah ke jantung, yang mengakibatkan jantung kekurangan oksigen. Biasanya ditandai dengan adanya nyeri atau rasa tidak nyaman pada dada.

7. Berapa banyak dan seberapa sering Anda seharusnya menggunakan obat ini? Apa yang harus dilakukan jika ada dosis yang terlewat?

Selalu gunakan obat ini dengan tepat sesuai anjuran dokter atau apoteker Anda. Tanyakan kepada dokter atau apoteker jika Anda merasa tidak yakin.

Dosis awal yang dianjurkan adalah 5 mg sekali sehari. Dosis ini dapat ditingkatkan menjadi maksimum 10 mg sekali sehari.

Obat Anda dapat diminum sebelum atau sesudah makan. Anda harus meminum obat Anda pada waktu yang sama setiap hari dengan meminum air. Jangan meminum Norvask® dengan jus grapefruit.

Penggunaan pada anak-anak dan remaja

Untuk anak-anak dan remaja (berusia 6-17 tahun), dosis awal yang disarankan adalah 2,5 mg sehari. Dosis maksimum yang disarankan adalah 5 mg sehari.

Anda harus meminum obat ini secara teratur. Jangan menunggu hingga tablet habis sebelum menemui dokter.

Jika Anda lupa meminum Norvask®

Jika Anda melewatkan satu dosis, minumlah segera setelah Anda ingat. Jangan minum Norvask® jika sudah lebih dari 12 jam sejak Anda melewatkan dosis terakhir Anda. Tunggu dan ambil dosis berikutnya pada waktu yang sesuai. Jangan meminum dosis ganda untuk mengganti dosis yang terlewatkan.

Jika Anda berhenti meminum Norvask®
Dokter Anda akan menentukan berapa lama Anda harus meminum obat. Kondisi sakit Anda dapat kembali jika Anda berhenti meminum obat sebelum waktu yang disarankan.

Jika Anda memiliki pertanyaan lebih lanjut seputar penggunaan obat ini, tanyakan kepada dokter atau apoteker Anda.

8. Kapan seharusnya Anda tidak menggunakan obat ini?

Jangan menggunakan Norvask®

- jika Anda alergi terhadap amlodipine atau terhadap bahan lain yang terkandung dalam obat ini.
- jika anda alergi terhadap obat antagonis kalsium – *dihydropyridines* lainnya.
- konsultasikan kepada dokter atau apoteker bila anda merasa tidak yakin.

9. Apa pertimbangan saat menggunakan obat ini?

Anda harus memberi tahu dokter jika Anda mempunyai atau pernah mengalami kondisi berikut:

- Gagal jantung
- Penyakit hati

10. Apa saja obat lain atau makanan yang harus dihindari selama menggunakan obat ini?

Harap beritahu dokter atau apoteker Anda jika Anda sedang atau belum lama ini meminum obat lain, termasuk obat-obatan yang diperoleh tanpa resep.

Norvask® dapat berpengaruh atau dipengaruhi oleh obat-obatan lain seperti:

- ketokonazol, itrakonazol (obat anti jamur)
- ritonavir (disebut juga inhibitor protease digunakan untuk pengobatan HIV)
- rifampisin, eritromisin, klaritromisin (antibiotik)
- Hypericum perforatum (*St. John's Wort*)
- diltiazem (obat jantung)
- takrolimus, sirolimus, temsirolimus, dan everolimus (obat-obatan yang digunakan untuk mengubah cara kerja sistem imun)
- simvastatin (obat penurun kolesterol))
- siklosporin (suatu imunosupresan)

Norvask® dengan makanan dan minuman
Jus dan buah grapefruit tidak boleh dikonsumsi oleh orang yang meminum Norvask®. Ini karena buah dan jus grapefruit dapat meningkatkan kadar bahan aktif amlodipine di dalam darah, yang dapat menyebabkan peningkatan efek penurun tekanan darah yang tak terduga dari Norvask®.

11. Apakah obat ini aman bagi ibu hamil dan menyusui?

Kehamilan
Keamanan amlodipine pada ibu hamil maupun ibu menyusui belum diketahui. Jika ada dugaan Anda sedang hamil, atau berencana untuk hamil, Anda harus memberitahu dokter Anda sebelum meminum Norvask®.

Menyusui
Amlodipine telah terbukti dapat dialirkan ke dalam ASI dalam jumlah kecil. Jika Anda sedang menyusui atau hendak mulai menyusui, Anda harus memberi tahu dokter Anda sebelum meminum Norvask®.

12. Apakah pasien diizinkan mengemudi dan mengoperasikan mesin saat menggunakan obat ini?
Penggunaan amlodipine kemungkinan tidak akan memengaruhi kemampuan pasien untuk mengemudi atau mengoperasikan mesin.

13. Apa saja potensi efek yang tidak diinginkan dari penggunaan obat ini
Seperti semua obat-obatan yang ada, obat ini bisa menimbulkan efek samping, meskipun tidak semua orang mengalaminya.

Efek samping yang **paling sering** teramati adalah:
- Sakit kepala, pusing, mengantuk
- Palpitasi (jantung berdebar), kulit panas dan memerah
- Sakit perut, merasa ingin muntah (mual)
- Edema (retensi cairan), kelelahan

Efek samping yang **tidak terlalu sering** teramati adalah:
- Penurunan jumlah sel darah putih, penurunan trombosit dalam darah yang dapat mengakibatkan memar yang tidak biasa atau mudah mengalami perdarahan
- Kadar gula dalam darah berlebih (hiperglikemia)
- Perubahan suasana hati, sulit tidur
- Peningkatan ketegangan otot
- Sensasi kebas atau kesemutan pada anggota gerak Anda, hilangnya sensasi nyeri
- Kelainan pada saraf yang dapat menyebabkan otot melemah, kesemutan, atau kebas
- Abnormalitas indra perasa, pingsan
- Gemetar, postur kaku, wajah seperti topeng, gerakan melambat, dan jalan menyeret dan tidak seimbang
- Gangguan penglihatan, penglihatan ganda
- Telinga berdenging
- Tekanan darah rendah
- Peradangan pembuluh darah, sering kali disertai ruam kulit
- Batuk
- Kesulitan bernapas
- Bersin/pilek yang disebabkan oleh peradangan dinding rongga hidung (rinitis)
- Perubahan kebiasaan buang air besar, mulut kering, muntah (rasa ingin muntah)
- Gangguan saluran cerna, perut kembung yang tidak normal (gastritis)
- Pembengkakan gusi
- Peradangan pankreas yang dapat menyebabkan nyeri punggung dan abdominal yang parah disertai dengan perasaan sangat tidak sehat
- Rambut rontok, produksi keringat meningkat, gatal-gatal pada kulit, bercak kemerahan pada kulit, perubahan warna kulit
- Nyeri, merasa tidak enak badan

- Nyeri pada sendi atau otot, sakit punggung
- Kelainan saat buang air kecil, meningkatnya kebutuhan untuk buang air kecil di malam hari, meningkatnya intensitas buang air kecil
- Disfungsi ereksi, rasa tidak nyaman atau terjadi pembesaran payudara pada laki-laki
- Peningkatan atau penurunan berat badan

Kejadian yang **jarang** dilaporkan adalah:
- Reaksi alergi di antaranya gatal-gatal pada kulit, ruam, pembengkakan, dan bercak kemerahan pada kulit
- Fungsi hati yang tidak normal, peradangan hati (hepatitis), kulit menguning (penyakit kuning), peningkatan enzim hati yang dapat memengaruhi hasil beberapa tes kesehatan

Pasien Anak (usia 6–17 tahun)

Menunjukkan kejadian merugikan yang sama seperti pada orang dewasa. Efek samping yang paling sering terlihat adalah:
- Sakit kepala, pusing
- Pelebaran pembuluh darah (vasodilatasi)
- Mimisan
- Sakit perut
- Rasa lemah

Beri tahu dokter atau perawat jika Anda mengamati efek samping mana pun yang disebutkan di atas.

Melaporkan efek samping
Jika Anda mengalami efek samping apa pun, konsultasikan dengan dokter, apoteker, atau perawat Anda. Termasuk setiap kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Dengan melaporkan efek samping, Anda bisa membantu memberikan informasi lebih lanjut mengenai keamanan obat ini.

14. Tanda-tanda dan gejala-gejala overdosis
Meminum tablet terlalu banyak dapat menurunkan tekanan darah Anda hingga menjadi terlalu rendah atau bahkan berbahaya. Jika tekanan darah Anda turun terlalu rendah dapat menyebabkan terjadinya renjatan.

15. Apa yang harus dilakukan jika Anda menggunakan lebih dari dosis yang dianjurkan?
Jika Anda tanpa sengaja meminum terlalu banyak tablet Norvask®, segera hubungi dokter Anda atau datangi unit gawat darurat di rumah sakit terdekat.

Bawa selalu kemasan obat berlabel, baik yang masih ada tablet Norvask® yang tersisa di dalamnya atau tidak.

Jangan meminum tablet lagi hingga dokter Anda memerintahkan Anda.

16. Bagaimana cara menyimpan obat ini?
Jauhkan obat ini dari pandangan dan jangkauan anak-anak.

Jangan gunakan obat ini setelah melewati tanggal kedaluwarsa yang tertera pada wadahnya.

Simpan di tempat kering pada suhu di bawah 30 °C.

17. Nomor otorisasi pemasaran
Norvask® 5 mg tablet, No. Reg.: DKL9219803410A1
Norvask® 10 mg tablet, No. Reg.: DKL9619803410B1

18. Nama dan alamat pendaftar dan/atau pemilik obat sesuai dengan ketentuan yang berlaku
Diproduksi oleh:
PT. Pfizer Indonesia
Jakarta, Indonesia

19. Tanggal revisi
02/2022

20. Peringatan khusus
HARUS DENGAN RESEP DOKTER