

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use amlodipine besylate tablets safely and effectively. See full prescribing information for amlodipine besylate tablets.

Amlodipine Besylate Tablets, USP for oral administration Initial U.S. Approval: 1987

INDICATIONS AND USAGE
Amlodipine besylate tablets are a calcium channel blocker and may be used alone or in combination with other antihypertensive and antianginal agents for the treatment of:

- Hypertension (1.1)
 - Amlodipine besylate tablets are indicated for the treatment of hypertension, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions.
- Coronary Artery Disease (1.2)
 - Chronic Stable Angina
 - Vasospastic Angina (Prinzmetal's or Variant Angina)
 - Angiographically Documented Coronary Artery Disease in patients without heart failure or an ejection fraction <40%.

DOSAGE AND ADMINISTRATION

- Adult recommended starting dose: 5 mg once daily with maximum dose 10 mg once daily. (2.1)
 - Small, fragile, or elderly patients, or patients with hepatic insufficiency may be started on 2.5 mg once daily. (2.1)
- Pediatric starting dose: 2.5 mg to 5 mg once daily. (2.2)

Important Limitation: Doses in excess of 5 mg daily have not been studied in pediatric patients. (2.2)

DOSAGE FORMS AND STRENGTHS

- 2.5 mg, 5 mg, and 10 mg Tablets (3)

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

- Hypertension
- Coronary Artery Disease (CAD)

2 DOSAGE AND ADMINISTRATION

- Adults
- Children

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- Hypotension
- Increased Angina or Myocardial Infarction
- Patients with Hepatic Failure

6 ADVERSE REACTIONS

- Clinical Trials Experience
- Postmarketing Experience

7 DRUG INTERACTIONS

- In Vitro Data
- Cimetidine
- Grapefruit Juice
- Magnesium and Aluminum Hydroxide Antacid
- Sildenafil
- Atorvastatin
- Simvastatin
- Digoxin
- Ethanol (Alcohol)
- Warfarin
- CYP3A4 Inhibitors
- CYP3A4 Inducers

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Hypertension

Amlodipine besylate tablets are indicated for the treatment of hypertension, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. These benefits have been seen in controlled trials of antihypertensive drugs from a wide variety of pharmacologic classes including amlodipine besylate.

Control of high blood pressure should be part of comprehensive cardiovascular risk management, including, as appropriate, lipid control, diabetes management, antithrombotic therapy, smoking cessation, exercise, and limited sodium intake. Many patients will require more than one drug to achieve blood pressure goals. For specific advice on goals and management, see published guidelines, such as those of the National High Blood Pressure Education Program's Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC).

Numerous antihypertensive drugs, from a variety of pharmacologic classes and with different mechanisms of action, have been shown in randomized controlled trials to reduce cardiovascular morbidity and mortality, and it can be concluded that it is blood pressure reduction, and not some other pharmacologic property of the drugs, that is largely responsible for those benefits. The largest and most consistent cardiovascular outcome benefit has been a reduction in the risk of stroke, but reductions in myocardial infarction and cardiovascular mortality also have been seen regularly.

Elevated systolic or diastolic pressure causes increased cardiovascular risk, and the absolute risk increase per mmHg is greater at higher blood pressures, so that even modest reductions of severe hypertension can provide substantial benefit. Relative risk reduction from blood pressure reduction is similar across populations with varying absolute risk, so the absolute benefit is greater in patients who are at higher risk independent of their hypertension (for example, patients with diabetes or hyperlipidemia), and such patients would be expected to benefit from more aggressive treatment to a lower blood pressure goal.

Some antihypertensive drugs have smaller blood pressure effects (as monotherapy) in black patients, and many antihypertensive drugs have additional approved indications and effects (e.g., on angina, heart failure, or diabetic kidney disease). These considerations may guide selection of therapy.

Amlodipine besylate tablets may be used alone or in combination with other antihypertensive agents.

1.2 Coronary Artery Disease (CAD)

Chronic Stable Angina

Amlodipine besylate tablets are indicated for the symptomatic treatment of chronic stable angina. Amlodipine besylate tablets may be used alone or in combination with other antianginal agents.

Vasospastic Angina (Prinzmetal's or Variant Angina)

Amlodipine besylate tablets are indicated for the treatment of confirmed or suspected vasospastic angina. Amlodipine besylate tablets may be used as monotherapy or in combination with other antianginal agents.

Angiographically Documented CAD

In patients with recently documented CAD by angiography and without heart failure or an ejection fraction <40%, amlodipine besylate tablets are indicated to reduce the risk of hospitalization for angina and to reduce the risk of a coronary revascularization procedure.

2 DOSAGE AND ADMINISTRATION

2.1 Adults

The usual initial antihypertensive oral dose of amlodipine besylate tablets is 5 mg once daily, and the maximum dose is 10 mg once daily.

Small, fragile, or elderly patients, or patients with hepatic insufficiency may be started on 2.5 mg once daily and this dose may be used when adding amlodipine besylate tablets to other antihypertensive therapy.

Adjust dosage according to blood pressure goals. In general, wait 7 to 14 days between titration steps. Titrate more rapidly, however, if clinically warranted, provided the patient is assessed frequently.

Angina: The recommended dose for chronic stable or vasospastic angina is 5–10 mg, with the lower dose suggested in the elderly and in patients with hepatic insufficiency. Most patients will require 10 mg for adequate effect.

Coronary artery disease: The recommended dose range for patients with coronary artery disease is 5–10 mg once daily. In clinical studies, the majority of patients required 10 mg [see Clinical Studies (14.4)].

2.2 Children

The effective antihypertensive oral dose in pediatric patients ages 6–17 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 Clinical Pharmacology (12.4), Clinical Studies (14.1)].

3 DOSAGE FORMS AND STRENGTHS

- 2.5, 5, and 10 mg Tablets

4 CONTRAINDICATIONS

Amlodipine besylate tablets are contraindicated in patients with known sensitivity to amlodipine.

5 WARNINGS AND PRECAUTIONS

5.1 Hypotension

Symptomatic hypotension is possible, particularly in patients with severe aortic stenosis. Because of the gradual onset of action, acute hypotension is unlikely.

5.2 Increased Angina or Myocardial Infarction

Worsening angina and acute myocardial infarction can develop after starting or increasing the dose of amlodipine besylate tablets, particularly in patients with severe obstructive coronary artery disease.

5.3 Patients with Hepatic Failure

Because amlodipine besylate tablets are extensively metabolized by the liver and the plasma elimination half-life ($t_{1/2}$) is 56 hours in patients with impaired hepatic function, titrate slowly when administering amlodipine besylate tablets to patients with severe hepatic impairment.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Amlodipine besylate tablets have been evaluated for safety in more than 11,000 patients in U.S. and foreign clinical trials. In general, treatment with amlodipine besylate tablets was well-tolerated at doses up to 10 mg daily. Most adverse reactions reported during therapy with amlodipine besylate tablets were of mild or moderate severity. In controlled clinical trials directly comparing amlodipine besylate tablets (N=1730) at doses up to 10 mg to placebo (N=1250), discontinuation of amlodipine besylate tablets because of adverse reactions was required in only about 1.5% of patients and was not

CONTRAINDICATIONS

- Known sensitivity to amlodipine (4)

WARNINGS AND PRECAUTIONS

- Symptomatic hypotension is possible, particularly in patients with severe aortic stenosis. However, acute hypotension is unlikely. (5.1)
- Worsening angina and acute myocardial infarction can develop after starting or increasing the dose of amlodipine besylate tablets, particularly in patients with severe obstructive coronary artery disease. (5.2)
- Titrate slowly in patients with severe hepatic impairment. (5.3)

ADVERSE REACTIONS

Most common adverse reaction to amlodipine is edema which occurred in a dose related manner. Other adverse experiences not dose related but reported with an incidence >1.0% are fatigue, nausea, abdominal pain, and somnolence. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Epic Pharma at 1-888-374-2791 or www.epic-pharma.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Do not exceed doses greater than 20 mg daily of simvastatin. (7.7)

USE IN SPECIFIC POPULATIONS

- Pregnancy: Use only if the potential benefit justifies the risk. (8.1)
- Nursing: Discontinue when administering amlodipine besylate tablets. (8.3)
- Pediatric: Effect on patients less than 6 years old is not known. (8.4)
- Geriatric: Start dosing at the low end of the dose range. (8.5)

Revised: September 2013

- 7.13 Cyclosporine
- 7.14 Drug/Laboratory Test Interactions

8 USE IN SPECIFIC POPULATIONS

- Pregnancy
- Nursing Mothers
- Pediatric Use
- Geriatric Use

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- Mechanism of Action
- Pharmacodynamics
- Pharmacokinetics and Metabolism
- Pediatric Patients

13 NONCLINICAL TOXICOLOGY

- Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

- Effects in Hypertension
- Effects in Chronic Stable Angina
- Effects in Vasospastic Angina
- Effects in Documented Coronary Artery Disease
- Studies in Patients with Heart Failure

16 HOW SUPPLIED/STORAGE AND HANDLING

- 2.5 mg Tablets
- 2.5 mg Tablets
- 5 mg Tablets
- 10 mg Tablets

*Sections or subsections omitted from the full prescribing information are not listed.

significantly different from placebo (about 1%). The most commonly reported side effects more frequent than placebo are reflected in the table below. The incidence (%) of side effects that occurred in a dose related manner is as follows:

	2.5 mg N=275	5 mg N=296	10 mg N=268	Placebo N=520
Edema	1.8	3.0	10.8	0.6
Dizziness	1.1	3.4	3.4	1.5
Flushing	0.7	1.4	2.6	0.0
Palpitation	0.7	1.4	4.5	0.6

Other adverse reactions that were not clearly dose related but were reported with an incidence greater than 1.0% in placebo-controlled clinical trials include the following:

	Amlodipine Besylate (%) (N=1730)	Placebo (%) (N=1250)
Fatigue	4.5	2.8
Nausea	2.9	1.9
Abdominal Pain	1.6	0.3
Somnolence	1.4	0.6

For several adverse experiences that appear to be drug and dose related, there was a greater incidence in women than men associated with amlodipine treatment as shown in the following table:

	Amlodipine Besylate Male=% (N=1218)	Female=% (N=512)	Placebo Male=% (N=914)	Female=% (N=336)
Edema	5.6	14.6	1.4	5.1
Flushing	1.5	4.5	0.3	0.9
Palpitations	1.4	3.3	0.9	0.9
Somnolence	1.3	1.6	0.8	0.3

The following events occurred in <1% but >0.1% of patients in controlled clinical trials or under conditions of open trials or marketing experience where a causal relationship is uncertain; they are listed to alert the physician to a possible relationship:

Cardiovascular: arrhythmia (including ventricular tachycardia and atrial fibrillation), bradycardia, chest pain, peripheral ischemia, syncope, tachycardia, vasculitis.

Central and Peripheral Nervous System: hypoesthesia, neuropathy peripheral, paresthesia, tremor, vertigo.

Gastrointestinal: anorexia, constipation, dysphagia, diarrhea, flatulence, pancreatitis, vomiting, gingival hyperplasia.

General: allergic reaction, asthenia,¹ back pain, hot flashes, malaise, pain, rigors, weight gain, weight decrease.

Musculoskeletal System: arthralgia, arthrosis, muscle cramps,¹ myalgia.

Psychiatric: sexual dysfunction (male¹ and female), insomnia, nervousness, depression, abnormal dreams, anxiety, depersonalization.

Respiratory System: dyspnea,¹ epistaxis.

Skin and Appendages: angioedema, erythema multiforme, pruritus,¹ rash,¹ rash erythematous, rash maculopapular.

Special Senses: abnormal vision, conjunctivitis, diplopia, eye pain, tinnitus.

Urinary System: micturition frequency, micturition disorder, nocturia.

Autonomic Nervous System: dry mouth, sweating increased.

Metabolic and Nutritional: hyperglycemia, thirst.

Hemopoietic: leukopenia, purpura, thrombocytopenia.

¹These events occurred in less than 1% in placebo-controlled trials, but the incidence of these side effects was between 1% and 2% in all multiple dose studies.

Amlodipine besylate therapy has not been associated with clinically significant changes in routine laboratory tests. No clinically relevant changes were noted in serum potassium, serum glucose, total triglycerides, total cholesterol, HDL cholesterol, uric acid, blood urea nitrogen, or creatinine.

In the CAMELOT and PREVENT studies [see Clinical Studies (14.4)], the adverse event profile was similar to that reported previously (see above), with the most common adverse event being peripheral edema.

6.2 Postmarketing Experience

Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The following postmarketing event has been reported infrequently where a causal relationship is uncertain: gynecomastia. In postmarketing experience, jaundice and hepatic enzyme elevations (mostly consistent with cholestasis or hepatitis), in some cases severe enough to require hospitalization, have been reported in association with use of amlodipine.

Amlodipine besylate tablets have been used safely in patients with chronic obstructive pulmonary disease, well-compensated congestive heart failure, coronary artery disease, peripheral vascular disease, diabetes mellitus, and abnormal lipid profiles.

7 DRUG INTERACTIONS

7.1 In Vitro Data

In vitro data indicate that amlodipine besylate tablets have no effect on the human plasma protein binding of digoxin, phenytoin, warfarin, and indomethacin.

7.2 Cimetidine

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

7.3 Grapefruit Juice

Co-administration of 240 mL of grapefruit juice with a single oral dose of amlodipine 10 mg in 20 healthy volunteers had no significant effect on the pharmacokinetics of amlodipine.

7.4 Magnesium and Aluminum Hydroxide Antacid

Co-administration of a magnesium and aluminum hydroxide antacid with a single dose of amlodipine besylate tablets had no significant effect on the pharmacokinetics of amlodipine besylate tablets.

7.5 Sildenafil

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

7.6 Atorvastatin

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

7.7 Simvastatin

Co-administration of multiple doses of 10 mg of 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.

7.8 Digoxin

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

7.9 Ethanol (Alcohol)

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

7.10 Warfarin

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

7.11 CYP3A4 Inhibitors

Co-administration of a 180 mg daily dose of diltiazem with 5 mg amlodipine in elderly hypertensive patients resulted in a 60% increase in amlodipine systemic exposure. Erythromycin co-administration in healthy volunteers did not significantly change amlodipine systemic exposure. However, strong inhibitors of CYP3A4 (e.g., ketoconazole, itraconazole, ritonavir) may increase the plasma concentrations of amlodipine to a greater extent. Monitor for symptoms of hypotension and edema when amlodipine is co-administered with CYP3A4 inhibitors.

7.12 CYP3A4 Inducers

No information is available on the quantitative effects of CYP3A4 inducers on amlodipine. Blood pressure should be closely monitored when amlodipine is co-administered with CYP3A4 inducers.

7.13 Cyclosporine

A prospective study in renal transplant patients (N=11) showed on an average of 40% increase in trough cyclosporine levels when concomitantly treated with amlodipine.

7.14 Drug/Laboratory Test Interactions

None known.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

There are no adequate and well-controlled studies in pregnant women. Amlodipine should be used during pregnancy only if the potential benefit justifies the risk to the fetus.

No evidence of teratogenicity or other embryo/fetal toxicity was found when pregnant rats and rabbits were treated orally with amlodipine maleate at doses up to 10 mg amlodipine/kg/day (respectively, 8 times² and 23 times² the maximum recommended human dose of 10 mg on a mg/m² basis) during their respective periods of major organogenesis. However, litter size was significantly decreased (by about 50%) and the number of intrauterine deaths was significantly increased (about 5-fold) in rats receiving amlodipine maleate at a dose equivalent to 10 mg amlodipine/kg/day for 14 days before mating and throughout mating and gestation. Amlodipine maleate has been shown to prolong both the gestation period and the duration of labor in rats at this dose.

²Based on patient weight of 50 kg.

8.3 Nursing Mothers

It is not known whether amlodipine is excreted in human milk. In the absence of this information, it is recommended that nursing be discontinued while amlodipine besylate tablets are administered.

8.4 Pediatric Use

Amlodipine besylate tablets 2.5 mg to 5 mg daily is effective in lowering blood pressure in patients 6 to 17 years [see Clinical Studies (14.1)]. Effect of amlodipine besylate tablets on blood pressure in patients less than 6 years of age is not known.

8.5 Geriatric Use

Clinical studies of amlodipine besylate tablets did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. Elderly patients have decreased clearance of amlodipine with a resulting increase in AUC of approximately 40–60%, and a lower initial dose may be required [see Dosage and Administration (2.1)].

10 OVERDOSAGE

Overdosage might be expected to cause excessive peripheral vasodilation with marked hypotension and possibly a reflex tachycardia. In humans, experience with intentional overdosage of amlodipine besylate tablets are limited.

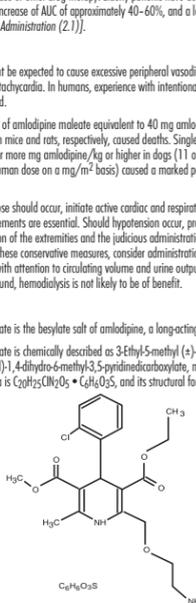
Single oral doses of amlodipine maleate equivalent to 40 mg amlodipine/kg and 100 mg amlodipine/kg in mice and rats, respectively, caused deaths. Single oral amlodipine maleate doses equivalent to 4 or more mg amlodipine/kg or higher in dogs (11 or more times the maximum recommended human dose on a mg/m² basis) caused a marked peripheral vasodilation and hypotensive overdosage.

If massive overdosage should occur, initiate active cardiac and respiratory monitoring. Frequent blood pressure measurements are essential. Should hypotension occur, provide cardiovascular support including elevation of the extremities and the judicious administration of fluids. If hypotension remains unresponsive to these conservative measures, consider administration of vasopressors (such as phenylephrine) with attention to circulating volume and urine output. As amlodipine besylate tablets is highly protein bound, hemodialysis is not likely to be of benefit.

11 DESCRIPTION

Amlodipine besylate is the besylate salt of amlodipine, a long-acting calcium channel blocker.

Amlodipine besylate is chemically described as 3-Ethyl-5-methyl (+)-2-[[2-aminooxy]methyl]-4-(2-chlorophenyl)-1,4-dihydro-6-methyl-3,5-pyridinedicarboxylate, monobenzenesulphonate. Its empirical formula is C₂₇H₂₅ClN₂O₅ · C₆H₅O₃S, and its structural formula is:



Amlodipine besylate is a white crystalline powder with a molecular weight of 567.1. It is slightly soluble in water and sparingly soluble in ethanol. Amlodipine besylate tablets, USP are formulated as white tablets equivalent to 2.5, 5, and 10 mg of amlodipine for oral administration. In addition to the active ingredient, amlodipine besylate, each tablet contains the following inactive ingredients: microcrystalline cellulose, corn starch, sodium starch glycolate and magnesium stearate.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Amlodipine is a dihydropyridine calcium antagonist (calcium ion antagonist or slow-channel blocker) that inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle. Experimental data suggest that amlodipine binds to both dihydropyridine and nondihydropyridine binding sites. The contractile processes of cardiac muscle and vascular smooth muscle are dependent upon the movement of extracellular calcium ions into these cells through specific ion channels.

Amlodipine inhibits calcium ion influx across cell membranes selectively, with a greater effect on vascular smooth muscle cells than on cardiac muscle cells. Negative inotropic effects can be detected in vitro but such effects have not been seen in intact animals at therapeutic doses. Serum calcium concentration is not affected by amlodipine. Within the physiologic pH range, amlodipine is an ionized compound (pKa=8.

Figure 2 - Effects on Primary Endpoint of Amlodipine Besylate versus Placebo across Sub-Groups

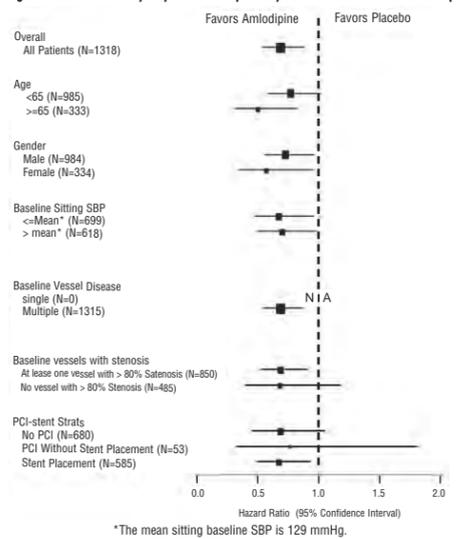


Table 1 below summarizes the significant composite endpoint and clinical outcomes from the composites of the primary endpoint. The other components of the primary endpoint including cardiovascular death, resuscitated cardiac arrest, myocardial infarction, hospitalization for heart failure, stroke/TIA, or peripheral vascular disease did not demonstrate a significant difference between amlodipine besylate and placebo.

Table 1. Incidence of Significant Clinical Outcomes for CAMELOT

Clinical Outcomes N (%)	Amlodipine Besylate (N=663)	Placebo (N=655)	Risk Reduction (p-value)
Composite CV Endpoint	110 (16.6)	151 (23.1)	31% (0.003)
Hospitalization for Angina*	51 (7.7)	84 (12.8)	42% (0.002)
Coronary Revascularization*	78 (11.8)	103 (15.7)	27% (0.033)

*Total patients with these events

14.5 Studies in Patients with Heart Failure

Amlodipine besylate has been compared to placebo in four 8 to 12 week studies of patients with NYHA Class II/III heart failure, involving a total of 697 patients. In these studies, there was no evidence of worsened heart failure based on measures of exercise tolerance, NYHA classification, symptoms, or left ventricular ejection fraction. In a long-term (follow-up of at least 6 months, mean 13.8 months) placebo-controlled mortality/morbidity study of amlodipine besylate 5 to 10 mg in 1153 patients with NYHA Classes III (n=931) or IV (n=222) heart failure on stable doses of diuretics, digoxin, and ACE inhibitors, amlodipine besylate had no effect on the primary endpoint of the study which was the combined endpoint of all-cause mortality and cardiac morbidity (as defined by life-threatening arrhythmia, acute myocardial infarction, or hospitalization for worsened heart failure), or on NYHA classification, or symptoms of heart failure. Total combined all-cause mortality and cardiac morbidity events were 222/571 (39%) for patients on amlodipine besylate and 246/583 (42%) for patients on placebo; the cardiac morbid events represented about 25% of the endpoints in the study.

Another study (PRAISE-2) randomized patients with NYHA Class III (80%) or IV (20%) heart failure without clinical symptoms or objective evidence of underlying ischemic disease, on stable doses of ACE inhibitors (99%), digitalis (99%), and diuretics (99%), to placebo (n=827) or amlodipine besylate (n=827) and followed them for a mean of 33 months. There was no statistically significant difference between amlodipine besylate and placebo in the primary endpoint of all-cause mortality (95% confidence limits from 8% reduction to 29% increase on amlodipine besylate). With amlodipine besylate there were more reports of pulmonary edema.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 2.5 mg Tablets

Amlodipine Besylate Tablets USP, equivalent to 2.5 mg of amlodipine are white to off-white, round, flat-faced, beveled-edge tablets, debossed "C" on one side and "55" on the other side. They are supplied as follows:

NDC 42806-055-09 Bottle of 90
NDC 42806-055-05 Bottle of 500
NDC 42806-055-10 Bottle of 1000

16.2 5 mg Tablets

Amlodipine Besylate Tablets USP, equivalent to 5 mg of amlodipine are white to off-white, round, flat-faced, beveled-edge tablets, de-bossed "C56" on one side and plain on the other side. They are supplied as follows:

NDC 42806-056-09 Bottle of 90
NDC 42806-056-05 Bottle of 500
NDC 42806-056-10 Bottle of 1000

16.3 10 mg Tablets

Amlodipine Besylate Tablets USP, equivalent to 10 mg of amlodipine are white to off-white, round, flat-faced, beveled-edge tablets, de-bossed "C57" on one side and plain on the other side. They are supplied as follows:

NDC 42806-057-09 Bottle of 90
NDC 42806-057-05 Bottle of 500
NDC 42806-057-10 Bottle of 1000

16.4 Storage

Store bottles at 20° - 25°C (68° - 77°F) [See USP Controlled Room Temperature]. Dispense in tight, light-resistant containers (USP). Protect from light.

PATIENT INFORMATION LEAFLET AMLODIPINE BESYLATE TABLETS, USP

Read this information carefully before you start taking **amlodipine besylate tablets** and each time you refill your prescription. There may be new information. This information does not replace talking with your doctor. If you have any questions about **amlodipine besylate tablets**, ask your doctor. Your doctor will know if **amlodipine besylate tablets** are right for you.

What are Amlodipine Besylate Tablets?

Amlodipine besylate tablets are a type of medicine known as a calcium channel blocker (CCB). It is used to treat high blood pressure (hypertension) and a type of chest pain called angina. It can be used by itself or with other medicines to treat these conditions.

High Blood Pressure (hypertension)

High blood pressure comes from blood pushing too hard against your blood vessels. **Amlodipine besylate tablets** relaxes your blood vessels, which lets your blood flow more easily and helps lower your blood pressure. Drugs that lower blood pressure lower your risk of having a stroke or heart attack.

Angina

Angina is a pain or discomfort that keeps coming back when part of your heart does not get enough blood. Angina feels like a pressing or squeezing pain, usually in your chest under the breastbone. Sometimes you can feel it in your shoulders, arms, neck, jaws, or back.

Amlodipine besylate tablets can relieve this pain.

Who should not use amlodipine besylate tablets?

Do not use **amlodipine besylate tablets** if you are allergic to amlodipine (the active ingredient in **amlodipine besylate tablets**), or to the inactive ingredients. Your doctor or pharmacist can give you a list of these ingredients.

What should I tell my doctor before taking amlodipine besylate tablets?

Tell your doctor about any prescription and non-prescription medicines you are taking, including natural or herbal remedies.

Tell your doctor if you:

- ever had heart disease
- ever had liver problems
- are pregnant, or plan to become pregnant. Your doctor will decide if **amlodipine besylate tablets** are the best treatment for you.
- are breast-feeding. Do not breast-feed while taking **amlodipine besylate tablets**. You can stop breast-feeding or take a different medicine.

How should I take amlodipine besylate tablets?

- Take **amlodipine besylate tablets** once a day, with or without food.
- It may be easier to take your dose if you do it at the same time every day, such as with breakfast or dinner, or at bedtime. Do not take more than one dose of **amlodipine besylate tablets** at a time.
- If you miss a dose, take it as soon as you remember. Do not take **amlodipine besylate tablets** if it has been more than 12 hours since you missed your last dose. Wait and take the next dose at your regular time.
- **Other medicines:** You can use nitroglycerin and **amlodipine besylate tablets** together. If you take nitroglycerin for angina, don't stop taking it while you are taking **amlodipine besylate tablets**.
- While you are taking **amlodipine besylate tablets**, do not stop taking your other prescription medicines, including any other blood pressure medicines, without talking to your doctor.
- If you took too much **amlodipine besylate tablets**, call your doctor or Poison Control Center, or go to the nearest hospital emergency room right away.

What should I avoid while taking amlodipine besylate tablets?

- **Do not** breast-feed. It is not known if **amlodipine besylate tablets** will pass through your milk.
- **Do not** start any new prescription or non-prescription medicines or supplements, unless you check with your doctor first.

What are the possible side effects of amlodipine besylate tablets?

Amlodipine besylate tablets may cause the following side effects. Most side effects are mild or moderate:

- swelling of your legs or ankles
- tiredness, extreme sleepiness
- stomach pain, nausea
- dizziness
- flushing (hot or warm feeling in your face)
- arrhythmia (irregular heartbeat)
- heart palpitations (very fast heartbeat)

It is rare, but when you first start taking **amlodipine besylate tablets** or increase your dose, you may have a heart attack or your angina may get worse. If that happens, call your doctor right away or go directly to a hospital emergency room.

Tell your doctor if you are concerned about any side effects you experience. These are not all the possible side effects of **amlodipine besylate tablets**. For a complete list, ask your doctor or pharmacist.

How do I store amlodipine besylate tablets?

Keep **amlodipine besylate tablets** away from children. Store **amlodipine besylate tablets** at room temperature 20° to 25°C (between 68° to 77°F). Keep **amlodipine besylate tablets** out of the light. Do not store in the bathroom. Keep **amlodipine besylate tablets** in a dry place. Protect from light.

General advice about amlodipine besylate tablets

Sometimes, doctors will prescribe a medicine for a condition that is not written in the patient information leaflets. Only use **amlodipine besylate tablets** the way your doctor told you to. Do not give **amlodipine besylate tablets** to other people, even if they have the same symptoms you have. It may harm them.

You can ask your pharmacist or doctor for information about **amlodipine besylate tablets**, or you can visit the Epic Pharma website at www.epic-pharma.com or call 1-888-374-2791.

Manufactured by:
Epic Pharma, LLC
Laurelton, NY 11413
Made in USA

Rev. 09/13
MF055REV09/13
OE1189