WARNINGS:
Increased angina and/or myocardial infarction: Rarely, patients, particularly those with severe obstructive coronary artery disease, have developed documented increased frequency, duration and/or severity of angina or acute myocardial infarction on starting calcium channel blocker therapy or at the time of dosage increase. The mechanisms of this effect has been elucidated.

PRECAUTIONS:
Caution should be exercised when administering amlodipine as with other peripheral vasodilator particularly in patients with severe aortic stenosis and to patients with heart failure.

TREATMENT FOR OVERDOSAGE:
Overdosage might be expected to cause excessive peripheral vasodilation with marked hypotension and possibly a reflex tachycardia.

If massive overdose should occur, active cardiac and respiratory monitoring should be instituted. Frequent blood pressure measurements are essential. Should hypotension occur, cardiovascular support including elevation of the extremities and the judicious administration of fluids should be initiated. If hypotension remains unresponsive to these conservative measures, administration of vasopressors (such as phenylephrine) should be considered with attention to circulating volume and urine output. Intravenous calcium gluconate may help to reverse the effects of calcium entry blockade. As amlodipine is highly protein bound, hemodialysis is not likely to be of benefit.

DOSING INFORMATION:
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 physician supervision is recommended.

DOSAGE AND ADMINISTRATION:
Usual adult dose : 5 to 10 mg once a day

NOTE: An initial antihypertensive dose of 2.5mg is recommended for small, fragile or elderly patients, patients with hepatic function impairment, or when adding amlodipine to other antihypertensive therapy. Because of amlodipine's prolonged elimination half-life, dosage increases should be accomplished slowly at five –to-seven days intervals. Rapid titration without complete assessment of the patient's response at each dosage level may result in hypotension. An initial antianginal dose of 5mg is recommended for the elderly and for patients with hepatic function impairment.

Children (6- 17 years old): 2.5 mg to 5.0mg once daily.
Similar doses are given in the treatment of stable angina and Prinzmental's angina

CAUTION:
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

AVAILABILITY:
5mg tablet - Blister Pack x 10's (Box of 30's and 100's)
Blister Pack x 5's (Box of 15's)
10mg tablet - Blister Pack x 10's (Box of 30's and 100's)
Blister Pack x 5's (Box of 15's)

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph

Registration Number: 5mg tablet (DR-XY33804), 10mg tablet (DR-XY33805)
Date of First Authorization: 5mg tablet (September 2007), 10mg tablet (September 2007)

Revision Date: July 2017

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PATRIOT
Pharmaceuticals Corp.

Amlodipine besilate

Vasalat®

Calcium Channel Blocker

FORMULATION:
Each tablet contains:
Amlodipine besilate.....7 mg
(Equivalent to Amlodipine 5 mg)
Amlodipine besilate.....14 mg
(Equivalent to Amlodipine 10 mg)

INDICATIONS:
In the management of hypertension and prophylaxis of angina.

MECHANISM OF ACTION:
Amlodipine is a dihydropyridine calcium-channel blocker, which is also known as calcium antagonists, calcium-entry blockers, and slow-channel blockers. It inhibits the cellular movements of calcium ions across cell membranes. It acts primarily via inhibition of calcium into vascular smooth muscle and, to lesser extent cardiac muscle. As a result, amlodipine produces peripheral arterial vasolidation and lowers blood pressure, with relatively little negative inotropic effect. Amlodipine interacts with calcium ions channels by an ongoing association/dissociation with the receptor binding site, producing a gradual onset of action.

Amlodipine has a greater selectivity for vascular smooth muscle than for myocardium and therefore their main effect is vasodilation. It has little or no action at the sinoatrial (SA) or atrioventricular (AV) nodes and negative inotropic activity is rarely seen at therapeutic doses. It is used for antihypertensive and antianginal properties.

Amlodipine reduces the work of the heart by dilating peripheral arteries and also act on the coronary circulation preventing spasm.

PHARMACOKINETICS:
Amlodipine is well absorbed following oral administration with peak blood concentrations occurring during 6 to 12 hours. The bioavailability is about 64 to 90%. Absorption is not affected by administration with food. Amlodipine is widely distributed, with a volume of distribution of 16 to 12 L/kg. Amlodipine is reported to be about 97.5% bound to plasma proteins. It has a prolonged terminal elimination half-life of 35 to 50 hours and steady-state plasma concentrations are not achieved until after 7 to 8 days of administration. Amlodipine is extensively metabolized in the liver and oxidation to the pyridine analogue represent a major step. Metabolites are mostly excreted together with less than 10% of a dose as unchanged drug. Total body clearance is approximately 0.4L/hr/kg. Patients with hepatic dysfunction may have a delayed clearance of drug. Doses should be reduced in these patients to account for this delay. No dosage adjustment is necessary for patients with renal dysfunction. Amlodipine is not removed by dialysis.

PHARMACODYNAMICS
Following administration of therapeutic doses to patients with hypertension, amlodipine produces vasodilation resulting in a reduction of supine and standing blood pressures. These decreases in blood pressures are accompanied by a significant change in the heart rate of plasma catecholamine levels with chronic dosing. Although the acute intraveneous administration of amlodipine decreases arterial blood pressure and increases heart rate in hemodynamic studies of patients with chronic stable angina, chronic administration of oral amlodipine in clinical trials did not lead to clinically significant changes in heart rate or blood pressures in normotensive patients with angina.

With chronic once daily oral administration of amlodipine, antihypertensive effectiveness is maintained for at least 24 hours. Plasma concentrations correlate with effect in both young and elderly patients. The magnitude of reduction in blood pressure with amlodipine is also correlated with the height of pretreatment elevation, this individuals with moderate hypertension (diastolic pressure 101-114mmHg) had about a 50% greater response than patients with mild hypertension (diastolic pressure 90-104mmHg). Normotensive subjects experienced no clinically significant change in blood pressure (+1/-2 mmHg).

In hypertensive patients with normal renal function, therapeutic doses of amlodipine resulted in a decrease in renal vascular resistance and an increase in glomerular filtration rate and effective renal plasma flow without change in filtration fraction or proteinuria.

As with other calcium channel blockers, hemodynamic measurements of cardiac function at rest and during exercise (or pacing) in patients with normal ventricular function treated with amlodipine have generally demonstrated a small increase in cardiac index without significant influence on dP/dt or on left ventricular and diastolic pressure or volume. In hemodynamic studies, amlodipine has not been associated with a negative inotropic effect when administered in the therapeutic dose range to intact animals and man, even when co-administered with beta-blockers to man. Similar