ANLODIN® TABLET

Ingredient(s):
Anlodin Tablet 5mg:
Each tablet contains:
Amlodipine Besylate ……..…..…..……..…… 6.93mg (eq. to Amlodipine 5mg)
Anlodin Tablet 10mg:
Each tablet contains:
Amlodipine Besylate ……..…..…..…… 13.86mg (eq. to Amlodipine 10mg)

Pharmacodynamics:
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 antihypertensive effect 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 actions:
1) Reduces total peripheral resistance (afterload) by dilating peripheral arterioles. Thus myocardial energy consumption and oxygen requirements are reduced since the heart rate remains stable.
2) Amlodipine may also dilate the main coronary arteries and coronary arterioles, both in normal and ischemic regions. This will increase myocardial oxygen delivery in patients with coronary artery spasm (Prinzmetal's or variant angina) and blunt smoking induced coronary vasoconstriction.

Once daily dosing of amlodipine in hypertensive patient provides clinically significant blood pressure reductions in both the supine and standing positions throughout the 24 hours interval. Amlodipine does not cause acute hypotension due to its slow onset of action.

Once daily dosing of amlodipine in patients with angina increases total exercise time, time to angina onset, and time to 1mm ST segment depression, and decreases both angina attack frequency and nitroglycerin tablet consumption.

Amlodipine did not adversely affect the metabolism and plasma lipid profile, thus is suitable to be used in patients with asthma, diabetes and gout. Amlodipine also did not alter the pharmacokinetics of cyclosporine significantly.

Studies indicated that amlodipine did not lead to clinical deterioration in NYHA Class II-IV heart failure patients measured by exercise tolerance, left ventricular ejection fraction and clinical symptomatology.

Pharmacokinetics:
Amlodipine is well absorbed after oral administration with peak blood levels between 6 to 12 hours post dose. Bioavailability is about 64 – 80%. Plasma protein binding is around 97.5%. Volume of distribution is around 21L/Kg. Absorption is not affected by food.

The terminal elimination half-life is around 35-50 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 to inactive metabolites with 10% of parent compound and 60% of metabolites excreted in urine.

Indication(s):
Amlodipine is indicated in the treatment of hypertension and, in most cases, can be used as monotherapy. Patients insufficiently controlled with a single antihypertensive e.g. thiazide diuretic, beta-blockers or angiotensin-converting enzyme inhibitors, may benefit from the addition of amlodipine. Amlodipine can also be used as first line treatment of myocardial ischemia, both in cases of fixed obstruction (stable angina), and/or in cases following vasoconstriction or vasospasm (Prinzmetal's angina or variant angina). Amlodipine can therefore be used in cases where the clinical picture suggests a possible vasospastic component even if there is no confirmation of this clinical situation. Amlodipine can be used alone or in combination with other anti-angina drugs, in patients suffering from angina who do not respond to nitrates or adequate doses of beta-blockers.

Dosage and Administration:
For hypertension and angina, the usual initial dose is 5mg once daily, may be increased to a maximum of 10mg once daily based on individual patient's response. No dose adjustments are needed with concomitant administration of thiazide diuretics, beta blockers and angiotensin-converting enzyme inhibitors.
Those with impaired renal or hepatic function, and the elderly: refer to *Warning* and *Precautions*.

Route of Administration:
Oral

Side Effect(s) / Adverse Reaction(s):
Amlodipine is well tolerated.
Commonly observed: headache, edema, fatigue, nausea, flushing and dizziness.
Less commonly observed: pruritus, rash, dyspnea, asthenia, muscle cramps, dyspepsia, and gingival hyperplasia.

Rarely observed: erythema multiforme.
As with other calcium-channel blockers, the following side effects are rarely reported and cannot be distinguished from the natural history of the underlying diseases, e.g. myocardial infarction, arrhythmia (including ventricular tachycardia and atrial fibrillation) and chest pain. No pattern of clinically significant laboratory test abnormalities related to amlodipine has been observed.

Contraindication(s):
Known sensitivity to dihydropyridines.

Precaution(s) / Warning(s):
Use in patients with impaired renal function: Amlodipine is extensively metabolized in inactive form and 10% is excreted unchanged in the urine. The degree of renal impairment is not linked to changes in the amlodipine plasma concentrations. Amlodipine can be used in this condition at normal doses. Amlodipine is not dialyzable.

Use in patients with impaired hepatic function: As with all calcium antagonists, the plasma half-life of amlodipine is prolonged in patients with impaired hepatic function. For these patients specific dosage recommendations have not been established. The drug should therefore be used with caution in these patients.

Effects on the ability to drive and operate machinery: Amlodipine can have minor or moderate influence on the ability to drive and use machines. If patients taking amlodipine suffer from dizziness, headache, fatigue or nausea the ability to react may be impaired. Caution is recommended especially at the start of treatment.

Use in the children: No data available on use of amlodipine in children.

Use in the elderly: The time needed for amlodipine to reach the peak plasma concentration in the elderly and in younger subjects is similar. However, the clearance of amlodipine tends to decrease in elderly, causing increases in the AUC and of the elimination half-life of the drug. At similar doses, amlodipine is equally well tolerated in the elderly and young patient, normal dosage regimens are recommended.

FOR SPECIALIST'S USE ONLY

Interaction with Other Medicaments:
Amlodipine has been safely administered together with thiazide diuretics, beta blockers, angiotensin-converting enzyme inhibitors, long-acting nitrates, sublingual nitroglycerin, NSAIDs, antibiotics and oral hypoglycemic drugs.

In healthy male volunteers, effect of warfarin on prothrombin response time is not significantly altered by co-administration of amlodipine. Co-administration of amlodipine also did not alter serum digoxin level or digoxin clearance in normal volunteers. Co-administration of cimetidine did not alter the pharmacokinetics of amlodipine.

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

Incompatibilies: Not relevant.

Pregnancy and Lactation:
Animal reproduction studies have shown that amlodipine has no toxic effects with the exception of delayed parturition and prolonged labor in rats at doses 50 times greater than the maximum dose recommended in humans. Use in pregnancy is only recommended if there is no safer alternative and when the disease itself carries greater risk for the mother and child.

Symptoms and Treatment for Overdosage, and Antidote(s):
In humans, experience with intentional overdose of amlodipine is limited. Gastric lavage may be worthwhile in some cases. Following overdose with amlodipine, available data suggests that excessive peripheral vasodilation with subsequent marked and probably prolonged systemic hypotension could occur. Clinically significant hypotension due to overdose of amlodipine may need active cardiovascular support including monitoring of cardiac and respiratory function, elevation of extremities and attention to circulating fluid volume and urine output. A vasoconstrictor maybe 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.

Shelf-Life:
3 years from the date of manufacture.

Storage Condition(s):
Store at temperature below 30ºC. Protect from light and moisture.

Product Description and Packing(s):
Anlodin Tablet 5mg:
A white color octagon shape tablet, one side is impressed with a score in the middle, “YSP” on the top and “5” on the bottom “ 

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Anlodin Tablet 10mg:
A white color octagon shape tablet, one side is impressed with a score in the middle, 'YSP' on the top and '10' on the bottom. " 

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Blister packing of 10's x 3, 10's x 10, 10's x 50 and 10's x 100.

Manufacturer and Product Registration Holder:
Y.S.P. INDUSTRIES (M) SDN. BHD. (199001001034)
Lot 3, 5, 7, 12 & 14, Jalan P/7, Section 13,
Kawasan Perindustrian Bandar Baru Bangi,
43000 Kajang, Selangor, Malaysia.
Ordering Line:1 800 88 3027
Product Info: 1 800 88 3679

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