• Drug category : Antihypertensives

Amphine Tab.

(Amlodipine 5mg)

■ **COMPOSITION**

Each tablet contains

Amlodipine..... 5mg (as amlodipine maleate 6.42mg)

■ **INDICATION**

hypertension, myocardial ischemia due to Variant Angina or obstructive Coronary Artery disease (Chronic Stable Angina)

■ **DOSAGE & ADMINISTRATION**

5mg once daily with a maximum dose of 10 mg once daily. Dosage should be adjusted according to the age of patients and symptoms.

■ **PRECAUTIONS**

1. CONTRAINDICATIONS

1) Amlodipine is contraindicated in patients
2) With history of hypersensitivity to Amlodipine or other Dihydropyridine
3) Intent to become pregnant, become pregnant or breast-feeding mother
4) With severe impaired liver function patients
5) With severe aortostenosis patients
6) Shock patients

2. SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE

1) Severe hypotensive patients
2) Renal impairment patients who be needed dialysis
3) Patients

3. ADVERSE REACTIONS

1) Amlodipine is well-tolerated. in most patients. Most common side effects which appeared in clinical trials with hypertension and angina patients are as follows:
   ① Autonomic Nervous System : Flushing
   ② General : fatigue
   ③ Cardiovascular : edema
   ④ Central and Peripheral Nervous System: vertigo, headache
   ⑤ Gastrointestinal : abdominal pain, vomiting
   ⑥ Heat beat : tachycardia
   ⑦ Psychiatric : Dizziness
   ⑧ In care that patients are in hospitel with heavy sympotoms, Amlodipine has been associated as reported, but the relationship is not clear in most of cares.
2) The following postmarketing event has been reported infrequently.
   ① Autonomic Nervous System : dry mouth, sweating increased
   ② General : asthenia, back pain, malaise, pain, weight gain, weight decrease
   ③ Cardiovascular : hypotension, syncope
   ④ Central and Peripheral Nervous System: hypoesthesia, neuropathy peripheral, paresthesia, tremor
   ⑤ Endocrine : gynecomastia
   ⑥ Gastrointestinal : constipation, dyspepsia, diarrhea, pancreatitis, vomiting, gingival hyperplasia
   ⑦ Metabolic and Nutritional : hyperglycemia
   ⑧ Musculoskeletal System: arthralgia, muscle cramps, myalgia
   ⑨ Hemopoietic: purpura, thrombocytopenia.
   ⑩ Psychiatric : sexual dysfunction, insomnia, , depersonalization
   ⑪ Respiratory System: cough, dyspnea, rhinitis
   ⑫ Skin and Appendages: depilation, skin discoloration, urticaria
   ⑬ Special Senses: dysgeusia, tinnitus
   ⑭ Urinary System: micturition frequency, micturition disorder, nocturia
   ⑮ Vascular (exclude heart) : angiitis
   ⑯ Vision : abnormal vision
   ⑰ Leukocyte / R.E.S : leukopenia
   ⑱ Rarely allergic events such as pruritus, rash, angioedema, erythema multiforme hepatitis, jaundice and hepatic enzyme elevations have been reported very rarely in association with mostly cholestasis. Some cases severe enough to require hospitalization have been reported in association with use of amlodipine.
3) The following adverse events have been reported infrequently where a causal relationship is uncertain with Myocardial infarction, arrhythmia, chest pain.
4) The following side effects have been reported.
   ① Cardiovascular : occasionally blood pressure decrease, atrioventricular block and rarely abdominal dysphoria may occur.
   ② Gastrointestinal : Occasionally abdominal pain, diarrhea, loose stools, constipation, etc. may occur.
   ③ Skin : Rarely maculopapular rash, etc. may occur.
   ④ Other : occasionally headache, fever sense, glucose Intolerance decrease, sickness, etc. may occur.

4. GENERAL PRECAUTIONS

1) Use in Patients with Congestive Heart Failure : Amlodipine has been compared to placebo in long term studies of patients with NYHA class III, IV heart failure. In these studies, there was no evidence of worsened heart failure.
2) Use in Patients with Hepatic Failure: The plasma elimination half-life (t 1/2) is extended in patients with impaired hepatic function. caution should be exercised when administering amlodipine to patients with severe hepatic impairment.
3) Mild blood pressure depressant action occur after discontinuation because of long half-life. when other medication is administrated after discontinuation, dosage and interval should be administered cautiously.
4) As the drug effect is only gradually increase daring onset period, it is not recommended to use the drug for unstable angina patients who needed emerent care.

5. DRUG INTERACTIONS

1) Amlodipine has been safely administered with thiazide diuretics, alpha-blockers, beta-blockers, angiotensin-converting enzyme inhibitors, long-acting nitrates, sublingual nitroglycerin, non-steroidal anti-inflammatory drugs, antibiotics, and oral hypoglycemic drugs.
2) Vitro data indicate that amlodipine has no effect on the human plasma protein binding of digoxin, phenytoin, warfarin, and indomethacin.
3) Effect of other agents on amlodipine
   ① Cimetidine : Co-administration of amlodipine with cimetidine, did not alter the pharmacokinetics of amlodipine.
   ② 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.
   ③ Antacid : Co-administration of antacid with a single dose of amlodipine had no significant effect on the pharmacokinetics of amlodipine.
   ④ 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 is independently exerted its own blood pressure lowering effect.
4) Effect of amlodipine on other agents
   ① Atorvastatin: Co-administration of multiple 10 mg doses of amlodipine with 80 mg of atorvastatin resulted in no significant change in the steady state pharmacokinetic parameters of atorvastatin.
   ② Digoxin: Co-administration of amlodipine with digoxin, did not change serum digoxin levels or digoxin renal clearance in normal volunteers.
   ③ Ethanol (alcohol): Single and multiple 10 mg doses of amlodipine, had no significant effect on the pharmacokinetics of ethanol.
   ④ Warfarin: Co-administration of amlodipine with warfarin, did not change the warfarin prothrombin response time.
5) Cyclosporin : in pharmacokinetics study about Cyclosporin, amlodipine had no significant effect on the pharmacokinetics of Cyclosporin .

6. USE IN PREGNANCY AND LACTATION

1) There is no established safety data for pregnant mother. Amlodipine has been shown to prolong both the gestation period and the duration of labor in rats at dose (50 times the maximum recommended human dose) but, except this, No evidence of reproduction toxicity was found. Amlodipine should be used during pregnancy only if the potential benefit higter than the potential risk to the fetus.
2) There is no established safety data for breast-feeding mother. So, it is recommended that breast-feeding should be discontinued while amlodipine is administered.

7. USE IN CHILDREN

There is no established safety data for children.

8. USE IN ELDERLY

The administration of general doses is recommended. Similar tolerance is showed in responses between the elderly and younger patients.

9. EFFECTS ON ABILITY TO DRIVE AND USE MACHINE

Amlodipine doesn't reduce the ability of requiring mental alertness such as operating a motor vehicle or other machine.

10. OVERDOSE

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.

11. PRECLINICAL STUDIES.

1) Carcinogenesis

Rats and mice treated with amlodipine in the diet for up to two years, at concentrations calculated to provide daily dosage levels of 0.5, 1.25, and 2.5 amlodipine mg/kg/day, showed no evidence of carcinogenic effect of the drug. For the mouse, the highest dose was, on a mg/m^2 basis, similar to the maximum recommended human dose of 10 mg amlodipine/day*). For the rat, the highest dose , was on a mg/m^2 basis, about twice the maximum recommended human dose*.

2) Mutagenesis

Mutagenicity studies conducted with amlodipine, revealed no drug related effects at either the gene or chromosome level.

3) Impairment of Fertility

There was no effect on the fertility of rats treated orally with amlodipine maleate (males for 64 days and females for 14 days prior to mating) at doses up to 10 mg amlodipine/kg/day (8 times* the maximum recommended human dose of 10 mg/day on a mg/m2 basis).

*Based on patient weight of 50 kg.

■ **STORAGE** : · Inside an air-tighted container.
· At room temperature and avoid from direct light.

■ **SHELF LIFE** : 2 Years

■ **PACKING** : 100Tabs./Box

※ This drug is manufactured in accordance with Korea Good Manufacturing Practice (KGMP) as recommended by WHO.