CARDOXIN FORTE
COATED TABLETS

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Composition
Each coated tablet contains: dipyridamole 75 mg

Action
Dipyridamole increases coronary blood flow and coronary sinus oxygen saturation. It appears to act predominantly on the small resistance vessels of the coronary vascular bed. The coronary vasodilator effect of dipyridamole is probably due to its ability to inhibit adenosine deaminase in the blood, thus allowing the accumulation of adenosine, a potent vasodilator. It may also cause vasodilation by inhibiting the enzyme phosphodiesterase, thus delaying the hydrolysis of cyclic adenosine monophosphate (cAMP).

In vitro models, induced-thrombotic animal models and several clinical studies have shown that the prophylactic administration of the proper dose of dipyridamole can, in many cases, reduce the number of thromboembolic episodes. This is based on its ability to prevent platelet adhesion and aggregation, thus prolonging platelet survival time.

It is postulated that dipyridamole acts by enhancing prostacyclin effects or inhibiting phosphodiesterase, thus increasing adenyl cyclase formation. It has also been shown to inhibit the formation of thromboxane-A_2, which is known to cause platelet adhesion and aggregation.

Indications
As an adjunct to oral anticoagulants for prophylaxis of thromboembolism associated with prosthetic heart valves.

Reduction of proteinuria in the nephrotic syndrome.

Treatment of membranoproliferative glomerulonephritis.

Prevention of pre-eclampsia in the final trimester of pregnancy (not for use before the sixth month of pregnancy).

Prevention of transplant artery stenosis.

Prevention of post-operative thromboembolic complications of coronary artery surgery.

In combination with acetylsalicylic acid in cases of recurrent deep vein thrombosis resistant to oral anticoagulants.

Prevention of thrombogenic manifestations.

As an alternative to exercise stress in thallium myocardial imaging, particularly in patients unable to exercise or in those for whom exercise may be contraindicated.

Contraindications
Known hypersensitivity to the drug.

Warnings
Use in pregnancy
Reproduction studies have been performed in mice at doses up to 125 mg/kg (15.6 times the maximum recommended daily human dose), rats at doses up to 1000 mg/kg (125 times the maximum recommended daily human dose) and rabbits at doses up to 40 mg/kg (5 times the maximum recommended daily human dose) and have revealed

no evidence of harm to the fetus due to dipyridamole. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. Cardoxin Forte may be used for the prevention of pre-eclampsia in the final trimester of pregnancy. Do not use before the sixth month of pregnancy.

Use in Breastfeeding
As dipyridamole is excreted in human milk, caution should be exercised when dipyridamole tablets are administered to a nursing woman.

Use in Pediatrics:
Safety and efficacy in children younger than 12 years of age have not been established.

Adverse Reactions
Adverse reactions are minimal and transient when dipyridamole is administered at the recommended doses.
Adverse reactions are generally dose-related and reversible. They may include headache, dizziness, gastrointestinal intolerance, nausea, vomiting, diarrhea, peripheral vasodilation, flushing, weakness, syncope and skin rash.
Aggravation of angina pectoris has been reported. However, this is rare and usually occurs at the beginning of therapy.
Headaches and chest pains can usually be reversed by intravenous aminophylline.

Precautions
Cardoxin should be used with caution in patients with rapidly worsening angina, subvalvular aortic stenosis or hemodynamic instability associated with a recently sustained myocardial infarction. It should be used with caution in cardiac glycoside-refractory patients, hypotensive patients and patients with respiratory conditions.
Serious vasodilation may occur during thallium imaging. This can be reversed by the
administration of intravenous aminophylline.

Drug Interactions
Dipyridamole/Heparin/Oral Anticoagulants
Since dipyridamole may inhibit platelet aggregation, patients receiving heparin and dipyridamole concomitantly should be monitored closely to prevent bleeding (the actual incidence of this reaction has not been established). In dosages of 400 mg daily, dipyridamole does not affect prothrombin activity and can be administered with oral anticoagulants. However, some authorities recommend maintenance of prothrombin activity at the upper end of the therapeutic range during concomitant administration of these drugs, in order to avoid possible bleeding.

Dipyridamole/Acetylsalicylic Acid
Acetylsalicylic acid and dipyridamole have additive inhibitory effects on platelet aggregation. Acetylsalicylic acid potentiates the effect of dipyridamole on platelet life-span prolongation.

Dipyridamole/Xanthine Derivatives
Theophylline, aminophylline and other xanthine derivatives (such as those present in coffee, tea and cola beverages) may weaken the effect of dipyridamole and should not be taken at the same time.

Dosage and Administration
Dosage should be determined individually, according to the indication and severity of the clinical picture.
The oral dosage in adult patients is 150-375 mg, divided into 3 or 4 doses daily, taken with half a glass of water 1 hour before meals. The maximum dosage is 600 mg daily.

Patients with Artificial Heart Valves
As an adjunct to oral anticoagulants for prophylaxis of thromboembolism associated with prosthetic heart valves, the recommended dosage is 75-150 mg 4 times daily.

Reduction of Proteinuria in Nephrotic Syndrome
The recommended oral dosage is 75 mg of dipyridamole 3-4 times daily (together with 325 mg acetylsalicylic acid daily).

Treatment of Membranoproliferative Glomerulonephritis
The recommended oral dosage is 75 mg of dipyridamole 3-4 times daily (together with 325 mg acetylsalicylic acid daily).

Prevention of Pre-eclampsia
To prevent pre-eclampsia in the final trimester of pregnancy, the recommended oral dosage is dipyridamole 300 mg daily. Do not use before the sixth month of pregnancy.

Prevention of Transplant Artery Stenosis
The recommended oral dosage is dipyridamole 75-375 mg daily.

Coronary Artery Surgery
The following is the recommended schedule for the prevention of post-operative thromboembolic complications of coronary artery surgery:
For two days prior to surgery, administer dipyridamole 75-150 mg orally 4 times daily.
In the morning of the day scheduled for surgery, administer an oral dose of dipyridamole 75-150 mg.
One hour after surgery, administer dipyridamole 75 mg down a nasogastric tube, and then clamp for 1 1/2 hours.
Seven hours after surgery, administer dipyridamole 75 mg and acetylsalicylic acid 325 mg down a nasogastric tube and then clamp for 1 1/2 hours.
On the day following surgery and thereafter, dipyridamole 75 mg and acetylsalicylic acid 325 mg should be taken orally 3 times daily.

Recurrent Deep Vein Thrombosis

In cases of recurrent deep vein thrombosis resistant to oral anticoagulants, the recommended dosage is 75 mg, 3 times daily, in combination with acetylsalicylic acid.

Prevention of Thrombogenic Manifestations
Dipyridamole 75 mg, 3 times daily.

Dosage in Thallium Imaging
Dipyridamole 300-400 mg orally.

Children
The normal total daily dosage is dipyridamole 5 mg/kg body weight, in divided doses.

Overdosage
Manifestations
Overdosage may lead to headache, gastrointestinal symptoms and hypotension. Coronary vasodilation may cause chest pain in patients with ischemic heart disease.

Treatment
General supportive measures should be employed. Coronary vasodilation can usually be reversed by aminophylline, administered by slow intravenous injection.

Presentation
100 coated tablets

Storage
Store at room temperature.

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