

COMPOSITION

Anril ® 0.5 Tablet: Each sublingual tablet contains Nitroglycerin USP 0.5 mg.

PHARMACOLOGY

Nitroglycerin forms free radical nitric oxide (NO) which activates guanylate cyclase, resulting in an increase of guanosine 3'5' monophosphate in smooth muscle and other tissues. These events lead to dephosphorylation of myosin light chains, which regulate the contractile state in smooth muscle and result in vasodilatation.

Absorption

Nitroglycerin is rapidly absorbed following sublingual administration. Mean peak Nitroglycerin plasma concentrations occur at a mean time of approximately 6 to 7 minutes post dose. Maximum plasma Nitroglycerin concentrations (C max) and area under the plasma concentration-time curves (AUC) increase dose proportionally following 0.3 to 0.6 mg. The absolute bioavailability of Nitroglycerin tablet is approximately 40% but tends to be variable due to factors influencing drug absorption such as sublingual hydration and mucosal metabolism.

Distribution

The volume of distribution (V Area) of Nitroglycerin following intravenous administration is 3.3 L/kg. At plasma concentrations between 50 and 500 ng/mL, the binding of Nitroglycerin to plasma proteins is approximately 60%, while that of 1,2- and 1,3-dinitroglycerin is 60% and 30%, respectively.

Metabolism

A liver reductase enzyme is of primary importance in the metabolism of Nitroglycerin to glycerol di- and mononitrate metabolites and ultimately to glycerol and organic nitrate. Known sites of extrahepatic metabolism include red blood cells and vascular walls. In addition to Nitroglycerin, 2 major metabolites 1,2- and 1,3-dinitroglycerin are found in plasma. Mean peak 1,2- and 1,3-dinitroglycerin plasma concentrations occur at approximately 15 minutes postdose. The elimination half-life of 1,2- and 1,3-dinitroglycerin is 36 and 32 minutes, respectively. The 1,2- and 1,3-dinitroglycerin metabolites have been reported to possess approximately 2% and 10% of the pharmacological activity of Nitroglycerin. Higher plasma concentrations of the dinitro metabolites, along with their nearly 10-fold longer elimination half-lives, may contribute significantly to the duration of pharmacologic effect. Glycerol mononitrate metabolites of Nitroglycerin are biologically inactive.

Elimination

Nitroglycerin plasma concentrations decrease rapidly with a mean elimination half-life of 2 to 3 minutes. Half-life values range from 1.5 to 7.5 minutes. Clearance (13.6 L/min) greatly exceeds hepatic blood flow. Metabolism is the primary route of drug elimination.

INDICATION

Indicated for the acute relief of an attack or acute prophylaxis of angina pectoris due to coronary artery disease.

DOSAGE AND ADMINISTRATION

One tablet should be dissolved under the tongue at the first sign of an acute anginal attack. The dose may be repeated approximately every five minutes, until relief is obtained. If the pain persists after a total of 3 tablets in a 15-minute period, prompt medical attention is recommended.

SIDE EFFECT

Headache which may be severe and persistent may occur immediately after use. Vertigo, dizziness, weakness, palpitation and other manifestations of postural hypotension may develop occasionally.

CONTRAINDICATION

Sublingual Nitroglycerin therapy is contraindicated in patients with early myocardial infarction, severe anemia, increased intracranial pressure and those with a known hypersensitivity to Nitroglycerin. Administration of Nitroglycerin is contraindicated in patients who are using sildenafil citrate since sildenafil citrate has been shown to potentiate the hypotensive effects of organic nitrates.

PRECAUTION

Only the smallest dose required for effective control of the acute anginal attack should be used. Excessive use may lead to the development of tolerance. This drug should be used with caution in patients who may be volume-depleted or are already hypotensive.

DRUG INTERACTION

Patients receiving antihypertensive drugs, beta-adrenergic blockers or phenothiazines and nitrates should be observed for possible additive hypotensive effects. Marked orthostatic hypotension has been reported when calcium channel blockers and organic nitrates were used concomitantly. Concomitant use of nitrates and alcohol may cause hypotension. The vasodilatory and hemodynamic effects of Nitroglycerin may be enhanced by concomitant administration of aspirin. Patients receiving sublingual Nitroglycerin should avoid ergotamine and related drugs or be monitored for symptoms of ergotism if this is not possible.

USE IN PREGNANCY AND LACTATION

Nitroglycerin should be given to a pregnant woman only if clearly needed. It is not known whether Nitroglycerin is excreted in human milk.

STORAGE CONDITION

Store below 25 0C protected from light and moisture.

HOW SUPPLIED

Anril ® 0.5 Tablet: Box containing 10 x 10 sublingual tablets in Alu-Alu blister pack.