WARNINGs

Verapamil should be avoided in patients with severe LV dysfunction (eg, ejection fraction <30%) or moderate-to-severe symptoms of cardiac failure and in patients with any degree of ventricular dysfunction if they are receiving a beta blocker. Control mild heart failure with optimum digitalization and diuretics before VERELAN is used. Verapamil may occasionally produce hypotension. Elevations of liver enzymes have been reported.

Several cases of hepatocellular injury have been demonstrated to be produced by verapamil. Periodic monitoring of liver function in patients on verapamil is prudent. Some patients with paroxysmal and/or chronic atrial flutter/fibrillation and an accessory AV pathway (eg, WPW syndrome) have developed an increased antegrade conduction across the accessory pathway bypassing the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving LV verapamil. Because of this risk, oral verapamil is contraindicated in such patients. AV block may occur (second- or third-degree, 0.8%). Development of marked first-degree block or progression to second- or third-degree block requires reduction in dosage or, rarely, discontinuation and institution of appropriate therapy. Sinus bradycardia, second- or third-degree AV block, sinus arrest, pulmonary edema or severe hypotension were seen in some critically ill patients with hypertrophic cardiomyopathy who were treated with verapamil.

PRECAUTIONs

Verapamil should be given cautiously to patients with impaired hepatic function (in severe dysfunction use about 30% of the normal dose) or impaired renal function, and patients should be monitored for abnormal prolongation of the PR interval or other signs of overdose. Verapamil may decrease neuromuscular transmission in patients with Duchenne's muscular dystrophy and may prolong recovery from the neuromuscular blocking agent vecuronium. It may be necessary to decrease verapamil dosage in patients with attenuated neuromuscular transmission. Combined therapy with beta-adrenergic blockers and verapamil may result in additive negative effects on heart rate, atrioventricular conduction and/or cardiac contractility; there have been reports of severe AV block, including complete heart block. The risks of such combined therapy may outweigh the benefits. The combination should be used only with caution and close monitoring. Decreased metabolite clearance may occur with combined use. Chronic verapamil treatment can increase serum digoxin levels by 50% to 75% during the first week of therapy, which may result in digitalis toxicity. In patients with hepatic cirrhosis, verapamil may reduce total body clearance and extracellular clearance of digoxin. The digoxin dose should be reduced when verapamil is given and the patient carefully monitored. Verapamil will usually have an additive effect in patients receiving blood pressure-lowering agents. Disopyramide should not be given within 48 hours before or after verapamil administration. Concomitant use of verapamil and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Combined verapamil and quinidine therapy in patients with hypotrophic cardiomyopathy should be avoided, since significant hypotension may result. Verapamil has been given concurrently with short- and long-acting nitrates without any undesirable drug interactions. Interaction between imidazole and chronically administered verapamil has not been studied. In healthy volunteers, cardiac effects of verapamil were reduced or unchanged. Concomitant use of lithium and verapamil may result in a lowering of serum lithium levels or increased sensitivity to lithium. Patients receiving both drugs must be monitored carefully.

VERELAN® verapamil HCl

The following adverse reactions have been reported with VERELAN: Most common: Bradycardia, AV conduction disturbances, and hypotension. Common: Vomiting, diarrhea, constipation, headache, dizziness, flushing, hypotension, rash, phlebitis, varicosity, edema, urticaria, erythema, hair loss, chest pain, myocardial infarction, syncope, claudication, myalgia, and arthralgia.

Adverse Reactions

Arthralgia, hypotension, headache, rash, chest pain, hypotension, flushing, and edema have also been reported in clinical trials with VERELAN. The most common adverse reactions associated with VERELAN therapy were: Bradycardia, AV conduction disturbances, and hypotension.

Adverse Reactions

Verapamil may cause a slight reduction in mean arterial pressure, which may be accompanied by increased systemic vascular resistance. Therefore, patients with severe hypertension, particularly those with significant left ventricular hypertrophy or with preexisting vascular disease, may require special attention and titrantion. In patients receiving verapamil who are being treated concomitantly with other antihypertensive agents, decreases in mean arterial pressure and heart rate of greater than 20% may occur even at lower doses of these agents. These decreases may be greatest in patients with concomitant impairment of hepatic or renal function. In the absence of concomitant therapy, the incidence of hypotension is approximately 5% during the first week of treatment and increases to approximately 10% after six weeks of therapy. Hypotension may rarely occur during initiation of therapy. In a multicenter, double-blind, placebo-controlled study of 276 patients with essential hypertension, the incidence of hypotension was 6% with verapamil and 2% with placebo. The average hypotensive response was 12% at a verapamil dose of 2.4 mg three times a day, with a range of 5% to 20%. Hypotension is more likely to occur in patients with preexisting hypotension, who may also experience orthostatic hypotension, and in patients with severe cardiac failure. The occurrence of hypotension is usually dose related, and the hypotensive response can be reversed by dosage reduction. In patients who develop hypotension, the dosage should be reduced or the drug withdrawn until the blood pressure stabilizes. If this does not occur, verapamil should not be administered.

In the absence of concomitant therapy, the incidence of hypotension is approximately 5% during the first week of treatment and increases to approximately 10% after six weeks of therapy. Hypotension may rarely occur during initiation of therapy. In a multicenter, double-blind, placebo-controlled study of 276 patients with essential hypertension, the incidence of hypotension was 6% with verapamil and 2% with placebo. The average hypotensive response was 12% at a verapamil dose of 2.4 mg three times a day, with a range of 5% to 20%. Hypotension is more likely to occur in patients with preexisting hypotension, who may also experience orthostatic hypotension, and in patients with severe cardiac failure. The occurrence of hypotension is usually dose related, and the hypotensive response can be reversed by dosage reduction. In patients who develop hypotension, the dosage should be reduced or the drug withdrawn until the blood pressure stabilizes. If this does not occur, verapamil should not be administered.

In the absence of concomitant therapy, the incidence of hypotension is approximately 5% during the first week of treatment and increases to approximately 10% after six weeks of therapy. Hypotension may rarely occur during initiation of therapy. In a multicenter, double-blind, placebo-controlled study of 276 patients with essential hypertension, the incidence of hypotension was 6% with verapamil and 2% with placebo. The average hypotensive response was 12% at a verapamil dose of 2.4 mg three times a day, with a range of 5% to 20%. Hypotension is more likely to occur in patients with preexisting hypotension, who may also experience orthostatic hypotension, and in patients with severe cardiac failure. The occurrence of hypotension is usually dose related, and the hypotensive response can be reversed by dosage reduction. In patients who develop hypotension, the dosage should be reduced or the drug withdrawn until the blood pressure stabilizes. If this does not occur, verapamil should not be administered.