**Drug Profile**

**Milrinone**

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<th>Keywords:</th>
<th>Milrinone, phosphodiesterase inhibitors, medication profiles, pharmacology, anesthesiology, drug, WebPub</th>
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**Dosage**

**Description**

Milrinone is a bipyridine derivative and an analogue of amrinone with 15 to 30 times the potency. It is an inotropic agent used in the treatment of congestive heart failure (CHF) and has a molecular weight of 211.2.

Figure 1. Structure of milrinone.

![Structure of Milrinone](image)

**Mechanisms of Action**

Milrinone increases cardiac output, decreases PCWP, and decreases systemic vascular resistance in patients with CHF. It also has peripheral vasodilator effects and **diastolic relaxant activity**. These actions appear to be related to the dose and plasma concentration of milrinone.

**Pharmacodynamics, Pharmacokinetics and Metabolism**

**Pharmacodynamics**

Milrinone is a **phosphodiesterase inhibitor** that is selective for the peak III 3'5' cyclic adenosine monophosphate (cAMP) phosphodiesterase isoenzyme in cardiac and vascular tissues. It is believed to augment slow calcium influx, increase calcium uptake and release by the sarcoplasmic reticulum, and **increase concentrations of cAMP** which together cause **increased contractility**. Favorable effects on relaxation and distensibility of the left ventricle also occur, which may be due to the ability of cAMP to mediate calcium uptake by the sarcoplasmic reticulum. Although shown to increase cardiac levels of cAMP, ventricular tension develops before significant cAMP concentration has occurred. Additional mechanisms for increased contractility may be the modification of calcium availability to contractile elements or calcium channel facilitation. Milrinone has also been shown to improve conduction in areas of decreased conductivity and in ischemic cells.
Milrinone has peripheral vasodilating effects that result in afterload reduction. It may cause direct coronary dilation as well. There is no apparent increase in myocardial oxygen demand at therapeutic doses. Milrinone has no beta-adrenergic activity and has no affect on Na-K-ATPase. It has been shown to shorten AV node conduction time.

**Pharmacokinetics and Metabolism**

In patients with CHF, milrinone given as an IV bolus showed a volume of distribution of 0.38 L/kg, a mean half-life of 2.3 hours and a plasma clearance of 0.13 liters/kg/hr. Onset of hemodynamic effects is in 5-10 minutes. Milrinone is 70% bound to plasma proteins. The primary route of excretion is in the urine, 83% being unchanged drug. Approximately 90% is recovered in the urine after eight hours. There appears to be no specific effects on hepatic or renal function. The duration of action of IV milrinone is approximately one hour.

**Indications and Usage**

Milrinone is approved for short-term IV use in patients with CHF. It also appears to be useful as a long-term oral phosphodiesterase inhibitor without many of the adverse effects seen with chronic oral use of amrinone. Milrinone’s effect on long term survival is unknown.

**Contraindications, Adverse Reactions, Drug Interactions**

**Contraindications**

Milrinone is contraindicated in patients who are hypersensitive to it.

**Adverse Reactions**

Milrinone IV or orally has been shown to have minimal adverse effects. It may aggravate outflow obstruction in hypertrophic subaortic stenosis. Due to its shortening of AV node conduction time, milrinone may increase the ventricular response to supraventricular dysrhythmias. In some patients, IV and oral milrinone have been shown to increase ventricular ectopy (12.1%), including nonsustained ventricular tachycardia. Life threatening dysrhythmias were infrequent and were associated with other underlying factors. Hypotension (2.9%) and chest pain (1.2%) has also been reported. Safety of use in acute MI is unknown. Headaches were reported in 2.9% of patients and occurred more commonly with hypotension and tachycardia when the oral dose exceeded 15 mg. Use in pregnancy should only be used if potential benefit outweighs potential risk. (Pregnancy category C)

**Drug Interactions**

Milrinone has no known adverse drug interactions, although some sources indicate possible hypotension when administered with disopyramide.

**Dosage and Administration**

Milrinone is supplied in sterile single dose vials of 10 and 20 ml in a 1 mg/ml concentration. It is also supplied in 100 ml pre-mixed flexible containers at 200 μg/ml. Milrinone is administered with a loading dose followed by a maintenance infusion. The recommended loading dose of milrinone is given 50 μg/kg IV bolus over 10 minutes followed by a continuous IV infusion titrated to hemodynamic effect. The usual dosage range for maintenance infusions is 0.25 to 0.75 μg/kg/min. The total IV daily dose should not exceed 1.13 mg/kg/day. Reductions in infusion rates may be necessary in renal impairment

**Table 1. Milrinone Dosing.**

| Loading Dose: | 20 to 50 μg/kg |

Milrinone
Milrinone mixed with furosemide causes an immediate precipitate to form; therefore, these two drugs should not be infused through the same IV line.

Milrinone in oral doses of 7.5 to 15 mg every 6 hours have shown beneficial hemodynamic effects with minimal tachycardia and hypotension.

**References**