HYDRAZINE HYDROCHLORIDE INJECTION, USP
20 mg/mL

DESCRIPTION: Hydralazine hydrochloride injection, USP is an antihypertensive available in a 1 mL vial for intravenous and intramuscular administration. Each milliliter of the sterile, nonpyrogenic colorless solution contains hydralazine hydrochloride USP, 20 mg, propylene glycol USP, 103.6 mg, and water for injection q.s. The pH of the solution is 3.4 to 4.4, pH may be adjusted with hydrochloric acid and/or sodium hydroxide. Hydralazine hydrochloride is 1-Hydrazino-2

Molecular Formula C\textsubscript{6}H\textsubscript{4}N\textsubscript{2}H\textsubscript{2}Cl\textsubscript{2}

Hydralazine hydrochloride, USP is a white to off-white, odorless crystalline powder. It is soluble in water, freely soluble in alcohol, and very slightly soluble in ether. It melts at about 275°C, with decomposition, and has a molecular weight of 196.64.

CLINICAL PHARMACOLOGY: Although the precise mechanism of action of hydralazine is not fully understood, the major effects are on the cardiovascular system. Hydralazine apparently lowers blood pressure by exerting a peripheral vasodilating effect through a direct relaxation of vascular smooth muscle. Hydralazine, by altering cellular calcium metabolism, interferes with the calcium movements within the vascular smooth muscle that are responsible for initiating or maintaining the contractile state.

The peripheral vasodilating effect of hydralazine results in decreased arterial blood pressure (diastolic more than systolic); decreased peripheral vascular resistance; and an increased heart rate, stroke volume, and cardiac output. The preferential dilatation of arterioles, as compared to veins, minimizes postural hypotension and promotes the increase in cardiac output. Hydralazine usually increases renin activity in plasma, presumably as a result of increased secretion of renin by the juxtaglomerular apparatus in response to reflex sympathetic discharge. This increase in renin activity leads to the production of angiotensin II, which then causes stimulation of aldosterone and consequent sodium reabsorption. Hydralazine also maintains or increases renal and beneficial cardiac blood flow.

The average maximal decrease in blood pressure usually occurs 10 to 80 minutes after administration of hydralazine hydrochloride injection. No other pharmacokinetic data on hydralazine hydrochloride injection are available.

INDICATIONS AND USAGE: Severe essential hypertension when the drug cannot be given orally or when there is an urgent need to lower blood pressure.

CONTRAINDICATIONS: Hypersensitivity to hydralazine; coronary artery disease; mitral valvu-
lar rheumatic heart disease.

WARNINGS: In a few patients hydralazine may produce a clinical picture simulating systemic lupus erythematosus including glomerulonephritis. In such patients hydralazine should be discon-
tinued. In less than 1% of patients, hydralazine administration requires discontinuation of the therapy, usually with a return of symptoms. If such abnormalities develop, therapy should be

PRECAUTIONS: General: Myocardial stimulation produced by hydralazine can cause arterial attacks and ECG changes of myocardial ischemia. The drug has been implicated in the produc-
tion of myocardial infarction. It must, therefore, be used with caution in patients with suspected coronary artery disease.

The “hyperdynamic” circulation caused by hydralazine may accentuate specific cardiovascular

INAD Vecuries. For example, hydralazine may increase pulmonary artery pressure in patients with pre-existing pulmonary vascular disease. Such drug may reduce the pressor responses to epinephrine. Pos-
tural hypotension may result from hydralazine but is less common than with ganglionic blocking agents. It should be used with caution in patients with cerebral vascular abnormalities.

It is also necessary that in patients who are treated with hydralazine, there is evi-
dence of increased renal blood flow and a maintenance of glomerular filtration rate. In some

instances where control values were below normal, improved renal function has been noted after discontinue on hydralazine. However, as with any antihypertensive agent, hydralazine should be used with caution in patients with advanced renal damage.

Peripheral neuritis, evidenced by paresthesia, numbness, and tingling; dizziness; dizziness; tinnitus; muscle cramps; psychic reactions characterized by depression, disinhibition, or anxiety.

Generality: difficulty in urination.

Hemotologic: blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, purpura; lymphadenopathy; splenomegaly.

Hypersensitive Reactions: rash, urticaria, pruritus, fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis.

Other: nasal congestion, flushing, lacrimation, conjunctivitis.

OVERDOSAGE: Acute Toxicity: No deaths due to acute poisoning have been reported. Highest known dose survived: adults, 10 g orally.

Oral LD50 in rats: 173 and 187 mg/kg.

Signs and Symptoms: Signs and symptoms of overdose include hypotension, tachycardia, headache, flushing, and generalized skin rash, hepatitis.

Complications can include myocardial ischemia and subsequent myocardial infarction, car-
diac arrhythmia, and profound shock.

Treatment: There is no specific antidote.

Support of the cardiovascular system is of primary importance. Shock should be treated with plasma expanders. If possible, vasopressors should not be given, but if a vasopressor is required, care should be taken not to precipitate or aggravate cardiac arrhythmia. Tachycardia responds to beta blockers. Digitalization may be necessary, and renal function should be moni-
tored and supported as required.

No experience has been reported with extracorporeal or peritoneal dialysis.

DOSE AND ADMINISTRATION: When there is urgent need, therapy in the hospitalized patient may be initiated with rapid intravenous injection of the drug. Intramuscular or intravenous injection of hydralazine hydrochloride injection should be used only when the drug cannot be given orally. The usual dose is 20 mg to 40 mg, repeated as necessary.

Certain patients (especially those with marked renal damage) may require a lower dose. Blood pressure should be checked frequently. If it may begin to fall within a few minutes after injec-
tion, with the average maximal decrease occurring in 10 to 80 minutes. In cases where there has been increased intracranial pressure, lowering the blood pressure may increase cerebral isch-
emia. Many patients can be transferred to oral hydralazine hydrochloride within 24 to 48 hours.

The product should be used immediately after the vial is opened. It should not be added to infusion solutions. Hydralazine hydrochloride injection may discolor upon contact with metal; dis-
colored solutions should be discarded.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.

HOW SUPPLIED:

Manufactured for:
Mylan Institutional LLC
Rockford, IL 61103 U.S.A.

Mylan Institutional
Galway, Ireland

Manufactured by:

Mylan

MARCH 2015
MI:HYDRIJ-R1

0888L100

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