Hydralazine Hydrochloride Injection USP

20mg/ml

For slow IV/IM use

Composition:
Each mL contains:
Hydralazine Hydrochloride USP 20 mg
Water for Injection USP q.s.

Description
Hydralazine Hydrochloride Injection, USP is an antihypertensive agent available in 1 mL vials for intravenous and intramuscular administration. Each milliliter of the sterile, colorless, non-pyrogenic solution contains hydralazine hydrochloride USP (20 mg), propylene glycol USP (103.6 mg), and water for injection q.s. The pH of the solution ranges from 3.4 to 4.4. The pH may be adjusted with hydrochloric acid and/or sodium hydroxide.

Clinical Pharmacology
Although the precise mechanism of action of hydralazine is not fully understood, its primary effects are on the cardiovascular system. Hydralazine appears to lower blood pressure by exerting a peripheral vasodilating effect through the direct relaxation of vascular smooth muscle. By altering cellular calcium metabolism, hydralazine interferes with the calcium movements within vascular smooth muscle that are responsible for initiating or maintaining the contractile state.

Indications and Usage
Severe essential hypertension when the drug cannot be administered orally or when there is an urgent need to lower blood pressure.

Contraindications
Hypersensitivity to hydralazine; coronary artery disease; mitral valvular rheumatic heart disease.

Warnings
In some patients, hydralazine may produce a clinical picture resembling systemic lupus erythematosus, including glomerulonephritis. In such patients, hydralazine should be discontinued unless the benefit-risk assessment necessitates continued antihypertensive therapy with this drug. Symptoms and signs usually resolve upon discontinuation of the drug, although residual effects have been detected years later. Long-term steroid treatment may be required. Dosage and Administration
When there is an urgent need, therapy in hospitalized patients may be initiated via the intramuscular route or as a rapid intravenous bolus injection directly into the vein.
Hydralazine hydrochloride injection should be used only when the drug cannot be administered orally. The usual dose is 20 mg to 40 mg, repeated as necessary.
Certain patients (especially those with significant renal impairment) may require a lower dose. Blood pressure should be monitored frequently. It may begin to fall a few minutes after injection, with the mean maximum decrease occurring within 10 to 80 minutes. In cases where intracranial pressure is elevated, lowering blood pressure may increase cerebral ischemia. Most patients can be switched to oral hydralazine hydrochloride within 24 to 48 hours.
The product must be used immediately after opening the vial. It should not be added to infusion solutions. Hydralazine hydrochloride injection may become discolored upon contact with metal; discolored solutions should be discarded.

Precautions
General
The myocardial stimulation produced by hydralazine may precipitate angina attacks and electrocardiographic changes indicative of myocardial ischemia. The drug has been implicated in the occurrence of myocardial infarction. Therefore, it should be used with caution in patients with suspected coronary artery disease.
The "hyperdynamic" circulation caused by hydralazine may exacerbate specific cardiovascular inadequacies. For example, hydralazine may increase blood pressure in patients with mitral valvular disease. The drug may reduce pressor responses to epinephrine. Postural hypotension may result from hydralazine use but is less common than with ganglionic blocking agents. It should be used with caution in patients who have suffered a stroke.
Pregnancy
Animal studies indicate that hydralazine is teratogenic in mice at 20 to 30 times the maximum daily human dose of 200 mg to 300 mg, and possibly in rabbits at 10 to 15 times the maximum daily human dose, but it is not teratogenic in rats. The observed teratogenic effects included cleft palate and malformations of the facial and cranial bones.
Nursing Mothers
Hydralazine has been shown to be excreted in breast milk.
Pediatric Use
Safety and efficacy in pediatric patients have not been established in controlled clinical trials, although there is experience with the use of hydralazine hydrochloride in children. The usually recommended parenteral dosage, administered intramuscularly or intravenously, is 1.7 to 3.5 mg/kg of body weight per day, divided into four to six doses.

Adverse Reactions
Adverse reactions to hydralazine hydrochloride are generally reversible when the dosage is reduced. However, in some cases, it may be necessary to discontinue the drug.
The following adverse reactions have been observed, but there has been insufficient systematic data collection to support an estimate of their frequency.
Frequent: headache, anorexia, nausea, vomiting, diarrhea, palpitations, tachycardia, angina pectoris.
Less frequent: *Digestive:* constipation, paralytic ileus.
Cardiovascular: hypotension, paradoxical pressor response, edema.
Respiratory: dyspnea.
Neurological: peripheral neuritis, evidenced by paresthesia, numbness, and tingling; dizziness; tremors; muscle cramps; psychotic reactions characterized by
depression, disorientation, or anxiety.
Genitourinary: difficulty urinating. Hematologic: blood dyscrasias, consisting of reduced *hemoglobin* and red blood cell count, leukopenia, agranulocytosis, purpura; lymphadenopathy; splenomegaly.
Hypersensitivity reactions: skin rash, urticaria, pruritus, fever, chills, arthralgia, eosinophilia, and, rarely, hepatitis.
Other: nasal congestion, flushing, lacrimation, conjunctivitis.

Overdose
Acute Toxicity
No deaths due to acute intoxication 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, and generalized skin flushing. Complications may include myocardial ischemia and subsequent myocardial infarction, cardiac arrhythmia, and profound shock.
Treatment
There is no specific antidote. Cardiovascular system support is of primary importance. Shock should be treated with plasma expanders. If possible, vasopressors should not be administered; however, if a vasopressor is required, care must be taken not to precipitate or aggravate cardiac arrhythmia. Tachycardia responds to beta-blockers. Digitalization may be necessary, and renal function should be monitored and supported as needed. No experience has been reported with extracorporeal or peritoneal dialysis.

Storage
Store at 20° to 25°C (68° to 77°F).

Keep medicines out of the reach of children.

Presentation: Pack of 10 x 5 mL ampoules.

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