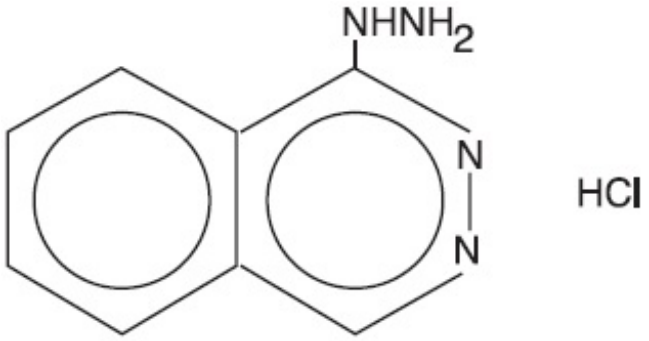
HYDRALAZINE HYDROCHLORIDE- hydralazine hydrochloride tablet
American Health Packaging

Hydralazine Hydrochloride Tablets, USP
Rx Only
8483301/0124

DESCRIPTION

HydrALAZINE hydrochloride, USP, is an antihypertensive, for oral administration. Its chemical name is 1-hydrazinophthalazine monohydrochloride, and its structural formula is:



$C_8H_8N_4 \cdot HCl$ M.W. 196.64

HydrALAZINE hydrochloride, USP is a white to off-white, odorless crystalline powder. It is soluble in water, slightly soluble in alcohol, and very slightly soluble in ether. It melts at about 275°C, with decomposition.

Each tablet for oral administration contains 10 mg, 25 mg, 50 mg or 100 mg hydrALAZINE hydrochloride, USP. Tablets also contain magnesium stearate, microcrystalline cellulose, orange lake blend, silicon dioxide, and sodium starch glycolate. The orange lake blend consists of FD&C yellow #6.

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 renal juxtaglomerular cells 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 cerebral blood flow.

HydrALAZINE is rapidly absorbed after oral administration, and peak plasma levels are reached at 1 to 2 hours. Plasma levels of apparent hydrALAZINE decline with a half-life of 3 to 7 hours. Binding to human plasma protein is 87%. Plasma levels of hydrALAZINE vary widely among individuals. HydrALAZINE is subject to polymorphic acetylation; slow acetylators generally have higher plasma levels of hydrALAZINE and require lower doses to maintain control of blood pressure. HydrALAZINE undergoes extensive hepatic metabolism; it is excreted mainly in the form of metabolites in the urine.

INDICATIONS AND USAGE

Essential hypertension, alone or as an adjunct.

CONTRAINDICATIONS

Hypersensitivity to hydrALAZINE; coronary artery disease; mitral valvular 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 discontinued unless the benefit-to-risk determination requires continued antihypertensive therapy with this drug. Symptoms and signs usually regress when the drug is discontinued but residua have been detected many years later. Long-term treatment with steroids may be necessary. (See **PRECAUTIONS, Laboratory Tests**.)

PRECAUTIONS

General

Myocardial stimulation produced by hydrALAZINE can cause anginal attacks and ECG changes of myocardial ischemia. The drug has been implicated in the production 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 inadequacies. For example, hydrALAZINE may increase pulmonary artery pressure in patients with mitral valvular disease. The drug may reduce the pressor responses to epinephrine. Postural 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 accidents.

In hypertensive patients with normal kidneys who are treated with hydrALAZINE, there

is evidence 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 administration of 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, has been observed. Published evidence suggests an antipyridoxine effect, and that pyridoxine should be added to the regimen if symptoms develop.

Information for Patients

Patients should be informed of possible side effects and advised to take the medication regularly and continuously as directed.

Laboratory Tests

Complete blood counts and antinuclear antibody titer determinations are indicated before and periodically during prolonged therapy with hydrALAZINE even though the patient is asymptomatic. These studies are also indicated if the patient develops arthralgia, fever, chest pain, continued malaise, or other unexplained signs or symptoms.

A positive antinuclear antibody titer requires that the physician carefully weigh the implications of the test results against the benefits to be derived from antihypertensive therapy with hydrALAZINE.

Blood dyscrasias, consisting of reduction in hemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported. If such abnormalities develop, therapy should be discontinued.

Drug/Drug Interactions

MAO inhibitors should be used with caution in patients receiving hydrALAZINE.

When other potent parenteral antihypertensive drugs, such as diazoxide, are used in combination with hydrALAZINE, patients should be continuously observed for several hours for any excessive fall in blood pressure. Profound hypotensive episodes may occur when diazoxide injection and hydrALAZINE are used concomitantly.

Drug/Food Interactions

Administration of hydrALAZINE with food results in higher plasma levels.

Carcinogenesis, Mutagenesis, Impairment of Fertility

In a lifetime study in Swiss albino mice, there was a statistically significant increase in the incidence of lung tumors (adenomas and adenocarcinomas) of both male and female mice given hydrALAZINE continuously in their drinking water at a dosage of about 250 mg/kg per day (about 80 times the maximum recommended human dose). In a 2-year carcinogenicity study of rats given hydrALAZINE by gavage at dose levels of 15, 30, and 60 mg/kg/day (approximately 5 to 20 times the recommended human daily dosage), microscopic examination of the liver revealed a small, but statistically significant, increase in benign neoplastic nodules in male and female rats from the high-dose group and in

female rats from the intermediate-dose group. Benign interstitial cell tumors of the testes were also significantly increased in male rats from the high-dose group. The tumors observed are common in aged rats and a significantly increased incidence was not observed until 18 months of treatment. HydrALAZINE was shown to be mutagenic in bacterial systems (Gene Mutation and DNA Repair) and in one of two rats and one rabbit hepatocyte *in vitro* DNA repair studies. Additional *in vivo* and *in vitro* studies using lymphoma cells, germinal cells, and fibroblasts from mice, bone marrow cells from chinese hamsters and fibroblasts from human cell lines did not demonstrate any mutagenic potential for hydrALAZINE.

The extent to which these findings indicate a risk to man is uncertain. While longterm clinical observation has not suggested that human cancer is associated with hydrALAZINE use, epidemiologic studies have so far been insufficient to arrive at any conclusions.

Pregnancy

Teratogenic Effects
Pregnancy Category C
Animal studies indicate that hydrALAZINE is teratogenic in mice at 20 to 30 times the maximum daily human dose of 200 to 300 mg and possibly in rabbits at 10 to 15 times the maximum daily human dose, but that it is nonteratogenic in rats. Teratogenic effects observed were cleft palate and malformations of facial and cranial bones.

There are no adequate and well-controlled studies in pregnant women. Although clinical experience does not include any positive evidence of adverse effects on the human fetus, hydrALAZINE should be used during pregnancy only if the expected benefit justifies the potential risk to the fetus.

Nursing Mothers

Hydralazine has been shown to be excreted in breast milk.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established in controlled clinical trials, although there is experience with the use of hydrALAZINE in pediatric patients. The usual recommended oral starting dosage is 0.75 mg/kg of body weight daily in four divided doses. Dosage may be increased gradually over the next 3 to 4 weeks to a maximum of 7.5 mg/kg or 200 mg daily.

ADVERSE REACTIONS

Adverse reactions with hydrALAZINE are usually reversible when 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 not been enough systematic collection of data to support an estimate of their frequency.

Common
Headache, anorexia, nausea, vomiting, diarrhea, palpitations, tachycardia, angina pectoris.

Less Frequent:

Digestive: constipation, paralytic ileus.

Cardiovascular: hypotension, paradoxical pressor response, edema.

Respiratory: dyspnea.

Neurologic: peripheral neuritis, evidenced by paresthesia, numbness, and tingling; dizziness; tremors; muscle cramps; psychotic reactions characterized by depression, disorientation, or anxiety.

Genitourinary: difficulty in urination.

Hematologic: 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 LD_{50} in rats: 173 and 187 mg/kg.

Signs and Symptoms

Signs and symptoms of overdosage include hypotension, tachycardia, headache, and generalized skin flushing.

Complications can include myocardial ischemia and subsequent myocardial infarction, cardiac arrhythmia, and profound shock.

Treatment

There is no specific antidote.

The gastric contents should be evacuated, taking adequate precautions against aspiration and for protection of the airway. An activated charcoal slurry may be instilled if conditions permit. These manipulations may have to be omitted or carried out after cardiovascular status has been stabilized, since they might precipitate cardiac arrhythmias or increase the depth of shock.

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 monitored and supported as required.

No experience has been reported with extracorporeal or peritoneal dialysis.

DOSAGE AND ADMINISTRATION

Initiate therapy in gradually increasing dosages; adjust according to individual response.

Start with 10 mg four times daily for the first 2 to 4 days, increase to 25 mg four times daily for the balance of the first week. For the second and subsequent weeks, increase dosage to 50 mg four times daily. For maintenance, adjust dosage to the lowest effective levels.

The incidence of toxic reactions, particularly the L.E. cell syndrome, is high in the group of patients receiving large doses of hydrALAZINE hydrochloride tablets.

In a few resistant patients, up to 300 mg of hydrALAZINE hydrochloride tablets daily may be required for a significant antihypertensive effect. In such cases, a lower dosage of hydrALAZINE hydrochloride tablets combined with a thiazide and/or reserpine or a beta blocker may be considered. However, when combining therapy, individual titration is essential to ensure the lowest possible therapeutic dose of each drug.

HOW SUPPLIED

HydrALAZINE Hydrochloride Tablets, USP are available as:

10 mg – Round, peach core tablet, debossed EP on one side and 101 on the reverse side.
Unit dose packages of 100 (10 x 10) NDC 60687-811-01

25 mg – Round, peach, core tablet, debossed EP over 102 on one side and plain on the reverse side.
Unit dose packages of 100 (10 x 10) NDC 60687-822-01

50 mg – Round, peach, core tablet, debossed EP over 103 on one side and plain on the reverse side.
Unit dose packages of 100 (10 x 10) NDC 60687-833-01

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature].

KEEP THIS AND ALL MEDICATIONS OUT OF THE REACH OF CHILDREN.

FOR YOUR PROTECTION: Do not use if blister is torn or broken.

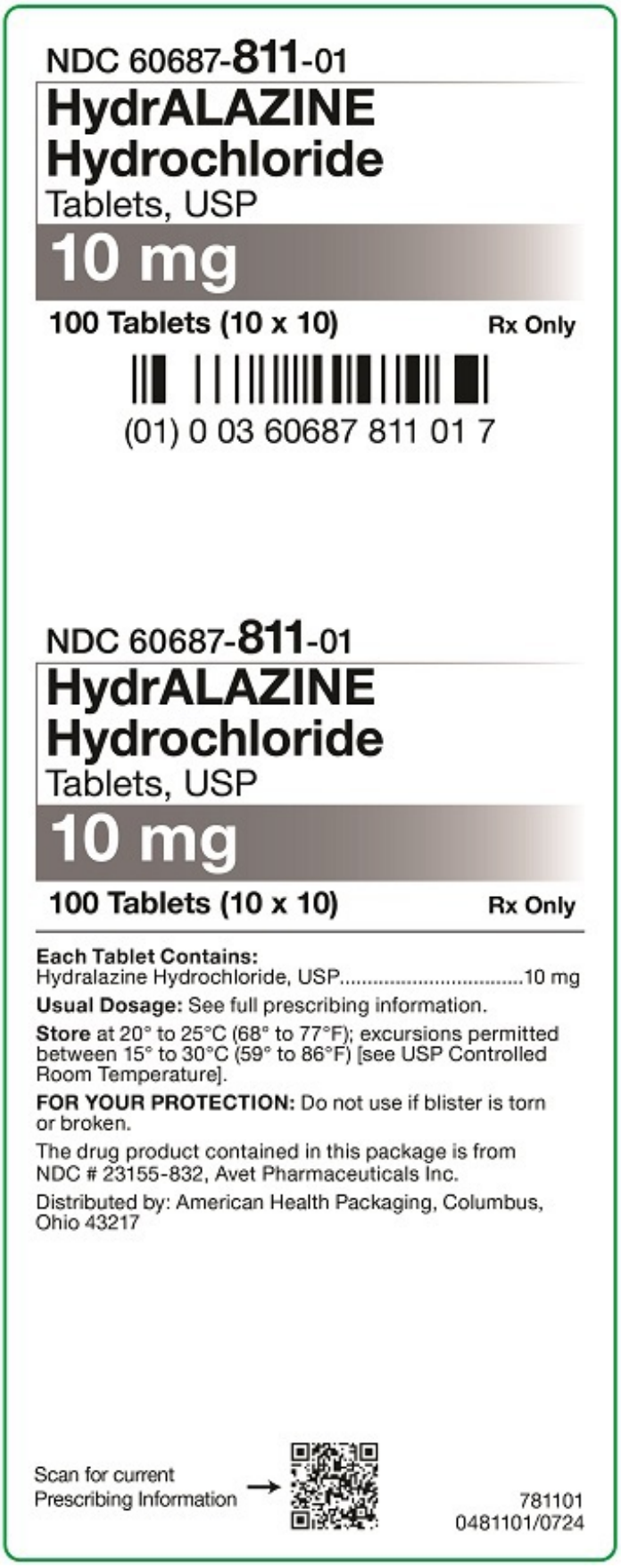
PACKAGING INFORMATION

American Health Packaging unit dose blisters (see How Supplied section) contain drug product from Avet Pharmaceuticals Inc. as follows:
(10 mg / 100 UD) NDC 60687-811-01 packaged from NDC 23155-832
(25 mg / 100 UD) NDC 60687-822-01 packaged from NDC 23155-833
(50 mg / 100 UD) NDC 60687-833-01 packaged from NDC 23155-834

Distributed by:
American Health Packaging
Columbus, OH 43217

8483301/0124

Package/Label Display Panel – Carton – 10 mg



NDC 60687- **811**-01

HydrALAZINE
Hydrochloride
Tablets, USP

10 mg

100 Tablets (10 x 10) **Rx Only**

Each Tablet Contains:
Hydralazine Hydrochloride, USP.....10 mg

Usual Dosage: See full prescribing information.

Store at 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

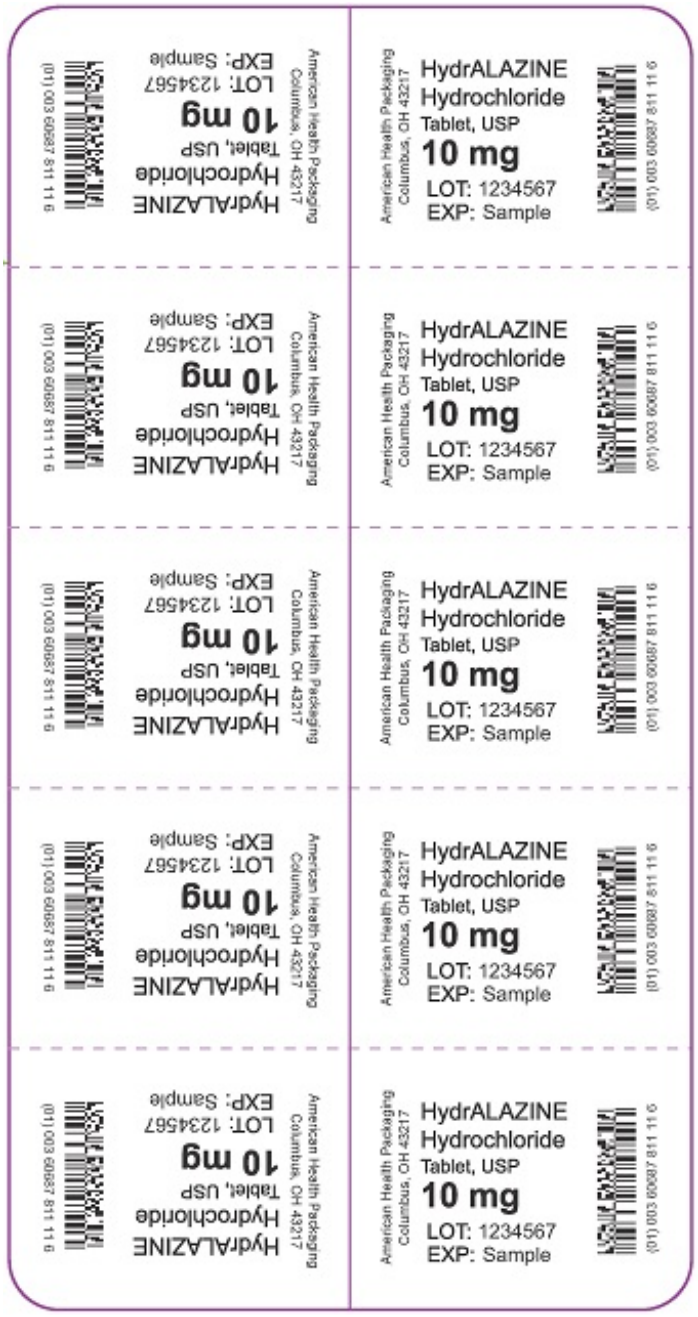
FOR YOUR PROTECTION: Do not use if blister is torn or broken.

The drug product contained in this package is from NDC # 23155-832, Avet Pharmaceuticals Inc.

Distributed by: American Health Packaging, Columbus, Ohio 43217

781101
0481101/0724

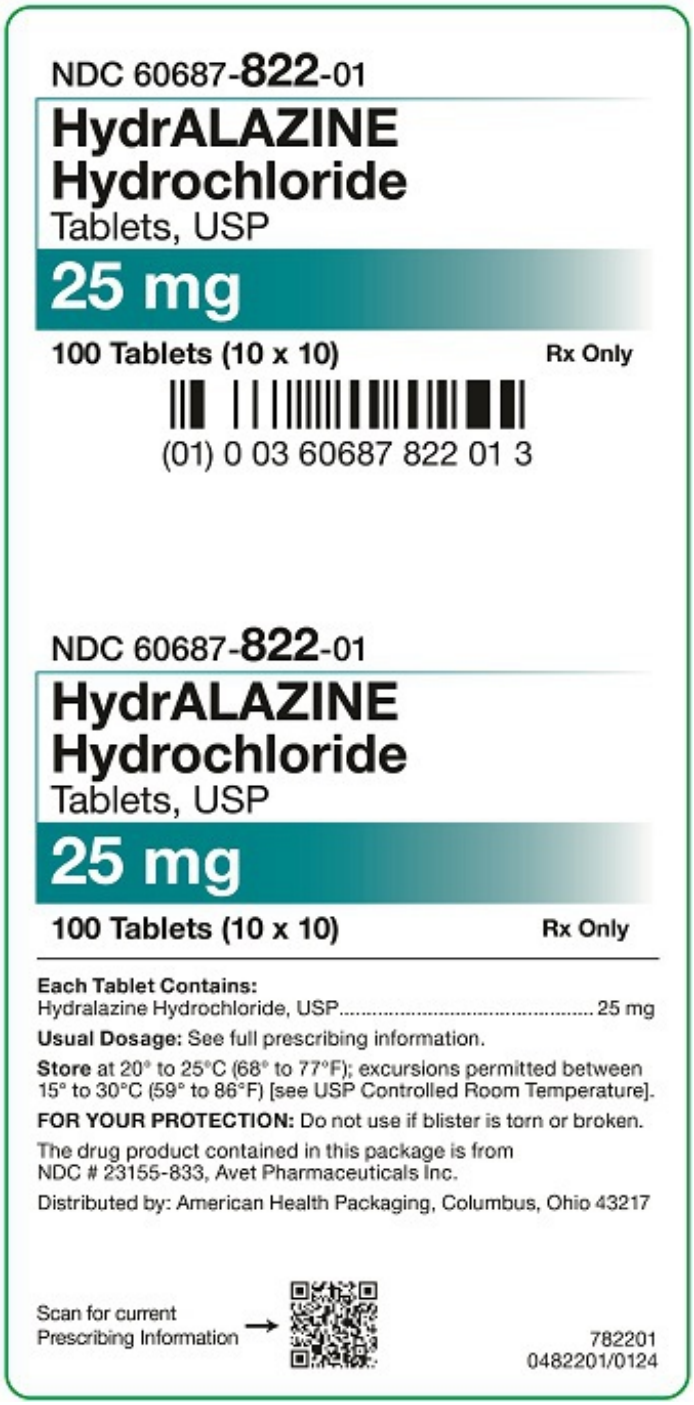
Package/Label Display Panel – Blister – 10 mg



HydrALAZINE
Hydrochloride
Tablet, USP

10 mg

Package/Label Display Panel – Carton – 25 mg



NDC 60687- **822**-01

HydrALAZINE
Hydrochloride
Tablets, USP

25 mg

100 Tablets (10 x 10) **Rx Only**

Each Tablet Contains:
Hydralazine Hydrochloride, USP..... 25 mg

Usual Dosage: See full prescribing information.

Store at 20° to 25°C (68° to 77°F); excursions permitted between

15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

FOR YOUR PROTECTION: Do not use if blister is torn or broken.

The drug product contained in this package is from
NDC # 23155-833, Avet Pharmaceuticals Inc.

Distributed by: American Health Packaging, Columbus, Ohio 43217

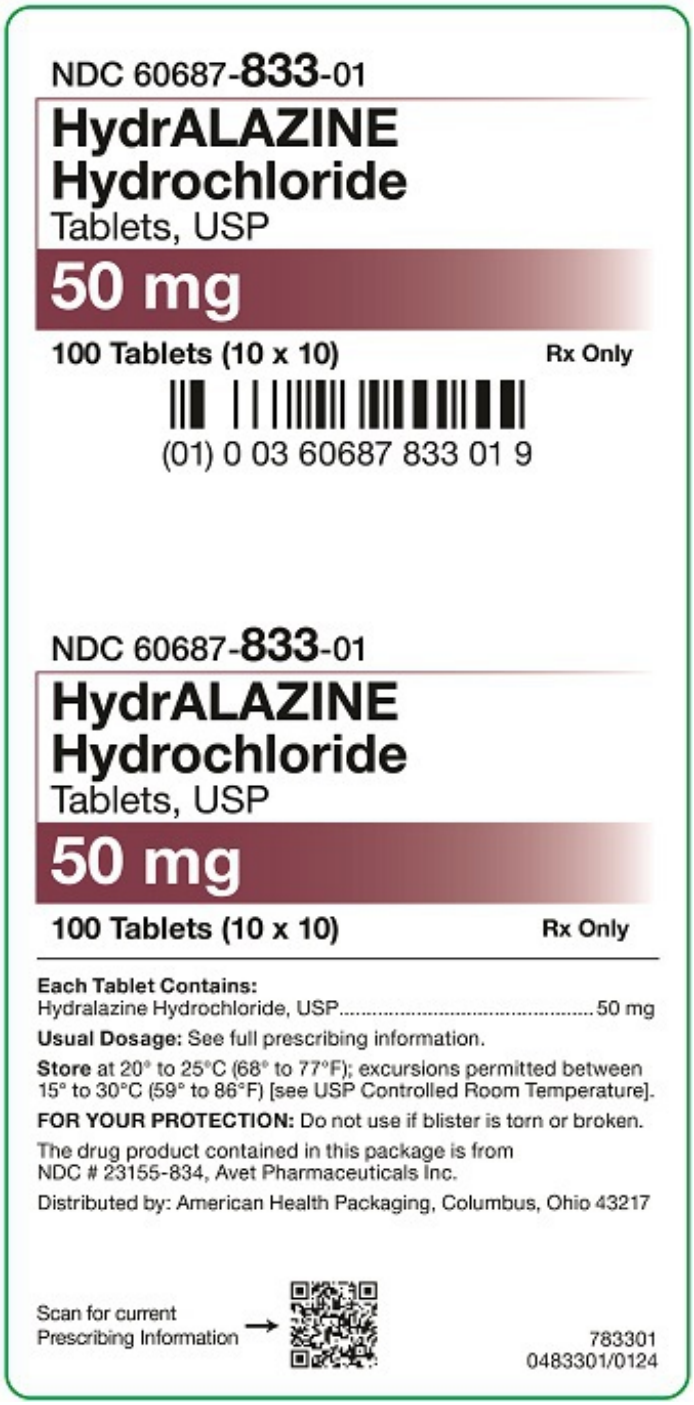
782201
0482201/0124

Package/Label Display Panel – Blister – 25 mg

HydrALAZINE
Hydrochloride
Tablet, USP

25 mg

Package/Label Display Panel – Carton – 50 mg



NDC 60687- **833**-01

HydrALAZINE
Hydrochloride
Tablets, USP

50 mg

100 Tablets (10 x 10) **Rx Only**

Each Tablet Contains:
Hydralazine Hydrochloride, USP..... 50 mg

Usual Dosage: See full prescribing information.

Store at 20° to 25°C (68° to 77°F); excursions permitted between

15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

FOR YOUR PROTECTION: Do not use if blister is torn or broken.

The drug product contained in this package is from
NDC # 23155-834, Avet Pharmaceuticals Inc.

Distributed by: American Health Packaging, Columbus, Ohio 43217

783301
0483301/0124

Package/Label Display Panel – Blister – 50 mg

HydrALAZINE
Hydrochloride
Tablet, USP **50 mg**

HYDRALAZINE HYDROCHLORIDE

hydralazine hydrochloride tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:60687-811(NDC:23155-832)

Route of Administration	ORAL

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HYDRALAZINE HYDROCHLORIDE (UNII: FD171B778Y) (HYDRALAZINE - UNII:26NAK24LS8)	HYDRALAZINE HYDROCHLORIDE	10 mg

Inactive Ingredients

Ingredient Name	Strength
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE 102 (UNII: PNR0YF693Y)	
MICROCRYSTALLINE CELLULOSE 105 (UNII: KO5GYV0DCB)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	

Product Characteristics

Color	pink (Peach)	**Score**	no score
Shape	ROUND	**Size**	6mm
Flavor		**Imprint Code**	EP;101
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60687-811-01	100 in 1 CARTON	09/15/2024	
1	NDC:60687-811-11	1 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA040858	09/15/2024	

HYDRALAZINE HYDROCHLORIDE

hydralazine hydrochloride tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:60687-822(NDC:23155-833)
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
HYDRALAZINE HYDROCHLORIDE (UNII: FD171B778Y) (HYDRALAZINE - UNII:26NAK24LS8)	HYDRALAZINE HYDROCHLORIDE	25 mg

Inactive Ingredients	
Ingredient Name	**Strength**
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE 102 (UNII: PNR0YF693Y)	
MICROCRYSTALLINE CELLULOSE 105 (UNII: KO5GYV0DCB)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	

Product Characteristics			
Color	pink (Peach)	**Score**	no score
Shape	ROUND	**Size**	6mm
Flavor		**Imprint Code**	EP;102
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:60687-822-01	100 in 1 CARTON	04/02/2024	
1	NDC:60687-822-11	1 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA040858	04/02/2024	

HYDRALAZINE HYDROCHLORIDE

hydralazine hydrochloride tablet

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:60687-833(NDC:23155-834)
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
HYDRALAZINE HYDROCHLORIDE (UNII: FD171B778Y) (HYDRALAZINE - UNII:26NAK24LS8)	HYDRALAZINE HYDROCHLORIDE	50 mg

Inactive Ingredients

Ingredient Name	Strength
MAGNESIUM STEARATE (UNII: 70097M6I30)	
MICROCRYSTALLINE CELLULOSE 102 (UNII: PNR0YF693Y)	
MICROCRYSTALLINE CELLULOSE 105 (UNII: KO5GYV0DCB)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	

Product Characteristics

Color	pink (Peach)	**Score**	no score
Shape	ROUND	**Size**	8mm
Flavor		**Imprint Code**	EP;103
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:60687-833-01	100 in 1 CARTON	03/15/2024	
1	NDC:60687-833-11	1 in 1 BLISTER PACK; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA040858	03/15/2024	

Labeler - American Health Packaging (929561009)

Establishment

Name	Address	ID/FEI	Business Operations
American Health Packaging		929561009	repack(60687-811, 60687-822, 60687-833)