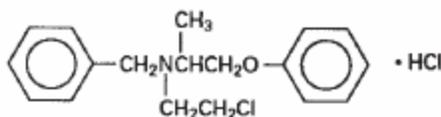


1  
2 **DIBENZYLINE<sup>®</sup>**  
3 **(phenoxybenzamine**  
4 **hydrochloride**  
5 **capsules, USP)**  
6 **10 mg**  
7 **adrenergic, *alpha*-receptor-**  
8 **blocking agent**

9  
10  
11 **DESCRIPTION**

12 Each Dibenzyline capsule, with red cap and body, is imprinted WPC 001 and 10 mg, and contains  
13 10 mg of Phenoxybenzamine Hydrochloride USP. Inactive ingredients consist of D&C Red No.  
14 33, FD&C Red No. 3, FD&C Yellow No. 6, Gelatin NF, Lactose NF, Sodium Lauryl Sulfate NF  
15 and Silicon Dioxide NF.

16  
17 Dibenzyline is *N*-(2-Chloroethyl)-*N*-(1-methyl-2-phenoxyethyl)benzylamine hydrochloride:



19 Phenoxybenzamine hydrochloride is a colorless, crystalline powder with a molecular weight of  
20 340.3, which melts between 136° and 141°C. It is soluble in water, alcohol and chloroform;  
21 insoluble in ether.

22  
23 **CLINICAL PHARMACOLOGY**

24 Dibenzyline (phenoxybenzamine hydrochloride) is a long-acting, adrenergic, *alpha*-receptor-  
25 blocking agent, which can produce and maintain “chemical sympathectomy” by oral  
26 administration. It increases blood flow to the skin, mucosa and abdominal viscera, and lowers  
27 both supine and erect blood pressures. It has no effect on the parasympathetic system.

28  
29 Twenty to 30 percent of orally administered phenoxybenzamine appears to be absorbed in the  
30 active form.<sup>1</sup>

31  
32 The half-life of orally administered phenoxybenzamine hydrochloride is not known; however, the  
33 half-life of intravenously administered drug is approximately 24 hours. Demonstrable effects  
34 with intravenous administration persist for at least 3 to 4 days, and the effects of daily  
35 administration are cumulative for nearly a week.<sup>1</sup>

36

37 **INDICATION AND USAGE**

38 Dibenzyline is indicated in the treatment of pheochromocytoma, to control episodes of  
39 hypertension and sweating. If tachycardia is excessive, it may be necessary to use a *beta*-blocking  
40 agent concomitantly.

41

42 **CONTRAINDICATIONS**

43 Conditions where a fall in blood pressure may be undesirable; hypersensitivity to the drug or any  
44 of its components.

45

46 **WARNING**

47 Dibenzyline-induced *alpha*-adrenergic blockade leaves *beta*-adrenergic receptors unopposed.  
48 Compounds that stimulate both types of receptors may, therefore, produce an exaggerated  
49 hypotensive response and tachycardia.

50

51 **PRECAUTIONS**

52 **General—Administer with caution in patients with marked cerebral or coronary**  
53 **arteriosclerosis or renal damage. Adrenergic blocking effect may aggravate symptoms of**  
54 **respiratory infections.**

55

56 **Drug Interactions<sup>2</sup>**—Dibenzyline (phenoxybenzamine hydrochloride) may interact with  
57 compounds that stimulate both *alpha*- and *beta*-adrenergic receptors (i.e., epinephrine) to produce  
58 an exaggerated hypotensive response and tachycardia. (See WARNING.)

59

60 Dibenzyline blocks hyperthermia production by levarterenol, and blocks hypothermia production  
61 by reserpine.

62

63 **Carcinogenesis and Mutagenesis**

64 Case reports of carcinoma in humans after long-term treatment with phenoxybenzamine have  
65 been reported. Hence long-term use of phenoxybenzamine is not recommended.<sup>3, 4</sup> Carefully  
66 weigh the benefits and risks before prescribing this drug.

67

68 Phenoxybenzamine hydrochloride showed *in vitro* mutagenic activity in the Ames test and mouse  
69 lymphoma assay; it did not show mutagenic activity *in vivo* in the micronucleus test in mice. In  
70 rats and mice, repeated intraperitoneal administration of phenoxybenzamine hydrochloride (three  
71 times per week for up to 52 weeks) resulted in peritoneal sarcomas. Chronic oral dosing in rats  
72 (for up to 2 years) produced malignant tumors of the small intestine and non-glandular stomach,  
73 as well as ulcerative and/or erosive gastritis of the glandular stomach. Whereas squamous cell  
74 carcinomas of the non-glandular stomach were observed at all tested doses of phenoxybenzamine  
75 hydrochloride, there was a no-observed-effect-level of 10 mg/kg for tumors (carcinomas and  
76 sarcomas) of the small intestine. This dose is, on a body surface area basis, about twice the  
77 maximum recommended human dosage of 20 mg b.i.d.

78 **Pregnancy - Teratogenic Effects—Pregnancy Category C**

79 Adequate reproductive studies in animals have not been performed with Dibenzyline  
80 (phenoxybenzamine hydrochloride). It is also not known whether Dibenzyline can cause fetal

81 harm when administered to a pregnant woman. Dibenzyline should be given to a pregnant  
82 woman only if clearly needed.

83

#### 84 **Nursing Mothers**

85 It is not known whether this drug is excreted in human milk. Because many drugs are excreted in  
86 human milk, and because of the potential for serious adverse reactions from phenoxybenzamine  
87 hydrochloride, a decision should be made whether to discontinue nursing or to discontinue the  
88 drug, taking into account the importance of the drug to the mother.

89

#### 90 **Pediatric Use**

91 Safety and effectiveness in pediatric patients have not been established.

92

93

### 94 **ADVERSE REACTIONS**

95 The following adverse reactions have been observed, but there are insufficient data to support an  
96 estimate of their frequency.

97

98 Autonomic Nervous System\*: Postural hypotension, tachycardia, inhibition of ejaculation, nasal  
99 congestion, miosis.

100 \*These so-called "side effects" are actually evidence of adrenergic blockade and vary according  
101 to the degree of blockade.

102

103 Miscellaneous: Gastrointestinal irritation, drowsiness, fatigue.

104

### 105 **OVERDOSAGE**

106 SYMPTOMS - These are largely the result of blocking of the sympathetic nervous system and of  
107 the circulating epinephrine. They may include postural hypotension, resulting in dizziness or  
108 fainting; tachycardia, particularly postural; vomiting; lethargy; shock.

109

### 110 **TREATMENT**

111 When symptoms and signs of overdosage exist, discontinue the drug. Treatment of circulatory  
112 failure, if present, is a prime consideration. In cases of mild overdosage, recumbent position with  
113 legs elevated usually restores cerebral circulation. In the more severe cases, the usual measures to  
114 combat shock should be instituted. Usual pressor agents are *not* effective. Epinephrine is  
115 contraindicated because it stimulates both *alpha*- and *beta*- receptors; since *alpha*- receptors are  
116 blocked, the net effect of epinephrine administration is vasodilation and a further drop in blood  
117 pressure (epinephrine reversal).

118

119 The patient may have to be kept flat for 24 hours or more in the case of overdose, as the effect of  
120 the drug is prolonged. Leg bandages and an abdominal binder may shorten the period of  
121 disability.

122

123 I.V. Infusion of levarterenol bitartrate\*\* may be used to combat severe hypotensive reactions,  
124 because it stimulates *alpha*- receptors primarily. Although Dibenzyline (phenoxybenzamine  
125 hydrochloride) is an *alpha*-adrenergic blocking agent, a sufficient dose of levarterenol bitartrate  
126 will overcome this effect.

127

128 The oral LD<sub>50</sub> for phenoxybenzamine hydrochloride is approximately 2000 mg/kg in rats and  
129 approximately 500 mg/kg in guinea pigs.

130

## 131 **DOSAGE AND ADMINISTRATION**

132 The dosage should be adjusted to fit the needs of each patient. Small initial doses should be  
133 *slowly* increased until the desired effect is obtained or the side effects from blockade become  
134 troublesome. *After each increase, the patient should be observed on that level before instituting*  
135 *another increase.* The dosage should be carried to a point where symptomatic relief and/or  
136 objective improvement are obtained, but not so high that the side effects from blockade become  
137 troublesome.

138

139 Initially, 10 mg of Dibenzyline (phenoxybenzamine hydrochloride) twice a day. Dosage should  
140 be increased every other day, usually to 20 to 40 mg 2 or 3 times a day, until an optimal dosage is  
141 obtained, as judged by blood pressure control.

142

143 Long-term use of phenoxybenzamine is not recommended (see **PRECAUTIONS**  
144 **Carcinogenesis and Mutagenesis**).

145

## 146 **STORAGE**

147 Store at 25°C (77°F); excursions permitted to 15°- 30°C (59°- 86°F) [See USP Controlled Room  
148 Temperature].

149

## 150 **HOW SUPPLIED**

151 Dibenzyline (phenoxybenzamine hydrochloride) capsules, 10 mg, in bottles of 100 (NDC 65197-  
152 001-01).

153

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170

171 \*\* Available as Levophed<sup>®</sup> Bitartrate (brand of norepinephrine bitartrate) from Abbott  
172 Laboratories.

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177

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