PHENTOLAMINE MESYLATE- phentolamine mesylate injection, powder, for solution
West-Ward Pharmaceuticals Corp

---------

PHENTOLAMINE MESYLATE
FOR INJECTION, USP

Rx ONLY

DESCRIPTION
Phentolamine Mesylate for Injection, USP, is an antihypertensive, available in vials for intravenous and intramuscular administration. Each vial contains phentolamine mesylate USP, 5 mg and mannitol USP, 25 mg in sterile, lyophilized form.

Phentolamine mesylate is \( m-[N-(2-\text{imidazolin-2-ylmethyl})-p-\text{toluidino}]\text{phenol monomethanesulfonate} \) (salt), and its structural formula is:

![Structural formula of phentolamine mesylate]

Molecular Formula \( \text{C}_{17}\text{H}_{19}\text{N}_{3}\text{O} \cdot \text{CH}_{4}\text{O}_{3}\text{S} \)

M.W. 377.47

Phentolamine mesylate USP is a white or off-white, odorless crystalline powder. Its solutions are acid to litmus. It is freely soluble in water and in alcohol, and slightly soluble in chloroform. It melts at about 178°C.

CLINICAL PHARMACOLOGY
Phentolamine mesylate produces an alpha-adrenergic block of relatively short duration. It also has direct, but less marked, positive inotropic and chronotropic effects on cardiac muscle and vasodilator effects on vascular smooth muscle.

Phentolamine has a half-life in the blood of 19 minutes following intravenous administration. Approximately 13% of a single intravenous dose appears in the urine as unchanged drug.

INDICATIONS AND USAGE
Phentolamine Mesylate for Injection is indicated for the prevention or control of hypertensive episodes that may occur in a patient with pheochromocytoma as a result of stress or manipulation during preoperative preparation and surgical excision.

Phentolamine Mesylate for Injection is indicated for the prevention or treatment of dermal necrosis and sloughing following intravenous administration or extravasation of norepinephrine.

Phentolamine Mesylate for Injection is also indicated for the diagnosis of pheochromocytoma by the phentolamine blocking test.
CONTRAINDICATIONS
Myocardial infarction, history of myocardial infarction, coronary insufficiency, angina, or other
evidence suggestive of coronary artery disease; hypersensitivity to phentolamine or related compounds.

WARNINGS
Myocardial infarction, cerebrovascular spasm, and cerebrovascular occlusion have been reported to
occur following the administration of phentolamine, usually in association with marked hypotensive
episodes.

For screening tests in patients with hypertension, the generally available urinary assay of
catecholamines or other biochemical assays have largely replaced the phentolamine and other
pharmacological tests for reasons of accuracy and safety. None of the chemical or pharmacological
tests is infallible in the diagnosis of pheochromocytoma. The phentolamine blocking test is not the
procedure of choice and should be reserved for cases in which additional confirmatory evidence is
necessary and the relative risks involved in conducting the test have been considered.

PRECAUTIONS

General
Tachycardia and cardiac arrhythmias may occur with the use of phentolamine or other alpha-adrenergic
blocking agents. When possible, administration of cardiac glycosides should be deferred until cardiac
rhythm returns to normal.

Drug Interactions
See DOSAGE AND ADMINISTRATION. Diagnosis of pheochromocytoma, Preparation.

Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term carcinogenicity studies, mutagenicity studies, and fertility studies have not been conducted
with phentolamine.

Pregnancy

Teratogenic Effects-Pregnancy Category C
Administration of phentolamine to pregnant rats and mice at oral doses 24 to 30 times the usual daily
human dose (based on a 60 kg human) resulted in slightly decreased growth and slight skeletal
immaturity of the fetuses. Immaturity was manifested by increased incidence of incomplete or unossified
calcanei and phalangeal nuclei of the hind limb and of incompletely ossified sternebrae. At oral doses
60 times the usual daily human dose (based on a 60 kg human), a slightly lower rate of implantation was
found in the rat. Phentolamine did not affect embryonic or fetal development in the rabbit at oral doses
20 times the usual daily human dose (based on a 60 kg human). No teratogenic or embryotoxic effects
were observed in the rat, mouse, or rabbit studies.

There are no adequate and well-controlled studies in pregnant women. Phentolamine should be used
during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human
milk and because of the potential for serious adverse reactions in nursing infants from phentolamine, a
decision should be made whether to discontinue nursing or to discontinue the drug, taking into account
the importance of the drug to the mother.
Pediatric Use
See DOSAGE AND ADMINISTRATION.

ADVERSE REACTIONS
Acute and prolonged hypotensive episodes, tachycardia, and cardiac arrhythmias have been reported. In addition, weakness, dizziness, flushing, orthostatic hypotension, nasal stuffiness, nausea, vomiting, and diarrhea may occur.

OVERDOSAGE
Acute Toxicity
No deaths due to acute poisoning with phentolamine have been reported.
Oral LD50’s (mg/kg): mice, 1000; rats, 1250.

Signs and Symptoms
Overdosage with phentolamine is characterized chiefly by cardiovascular disturbances, such as arrhythmias, tachycardia, hypotension, and possibly shock. In addition, the following might occur: excitation, headache, sweating, pupillary contraction, visual disturbances; nausea, vomiting, diarrhea; hypoglycemia.

Treatment
There is no specific antidote.
A decrease in blood pressure to dangerous levels or other evidence of shocklike conditions should be treated vigorously and promptly. The patient’s legs should be kept raised and a plasma expander should be administered. If necessary, intravenous infusion or norepinephrine, titrated to maintain blood pressure at the normotensive level, and all available supportive measures should be included. Epinephrine should not be used, since it may cause a paradoxical reduction in blood pressure.

DOSAGE AND ADMINISTRATION
The reconstituted solution should be used upon preparation and should not be stored.

1. Prevention or control of hypertensive episodes in the patient with pheochromocytoma. For preoperative reduction of elevated blood pressure, 5 mg of phentolamine mesylate (1 mg for children) is injected intravenously or intramuscularly 1 or 2 hours before surgery, and repeated if necessary.
During surgery, phentolamine mesylate (5 mg for adults, 1 mg for children) is administered intravenously as indicated, to help prevent or control paroxysms of hypertension, tachycardia, respiratory depression, convulsions, or other effects of epinephrine intoxication. (Postoperatively, norepinephrine may be given to control the hypotension that commonly follows complete removal of a pheochromocytoma.)

2. Prevention or treatment of dermal necrosis and sloughing following intravenous administration or extravasation of norepinephrine.
For Prevention: 10 mg of phentolamine mesylate is added to each liter of solution containing norepinephrine. The pressor effect of norepinephrine is not affected.
For Treatment: 5 to 10 mg of phentolamine mesylate in 10 mL of saline is injected into the area of extravasation within 12 hours.

3. Diagnosis of pheochromocytoma - phentolamine blocking test.
The test is most reliable in detecting pheochromocytoma in patients with sustained hypertension and least reliable in those with paroxysmal hypertension. False-positive tests may occur in patients with
hypertension without pheochromocytoma.

a. Intravenous

Preparation

The CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS sections should be reviewed. Sedatives, analgesics, and all other medications except those that might be deemed essential (such as digitalis and insulin) are withheld for at least 24 hours, and preferably 48 to 72 hours, prior to the test. Antihypertensive drugs are withheld until blood pressure returns to the untreated, hypertensive level. This test is not performed on a patient who is normotensive.

Procedure

The patient is kept at rest in a supine position throughout the test, preferably in a quiet, darkened room. Injection of phentolamine is delayed until blood pressure is stabilized, as evidenced by blood pressure readings taken every 10 minutes for at least 30 minutes.

Five milligrams of phentolamine mesylate is dissolved in 1 mL of Sterile Water for Injection. The dose for adults is 5 mg; for children, 1 mg.

The syringe needle is inserted into the vein, and injection is delayed until pressor response to venipuncture has subsided.

Phentolamine is injected rapidly. Blood pressure is recorded immediately after injection, at 30-second intervals for the first 3 minutes, and at 60-second intervals for the next 7 minutes.

Interpretation

A positive response, suggestive of pheochromocytoma, is indicated when the blood pressure is reduced more than 35 mm Hg systolic and 25 mm Hg diastolic. A typical positive response is a reduction in pressure of 60 mm Hg systolic and 25 mm Hg diastolic. Usually, maximal effect is evident within 2 minutes after injection. A return to preinjection pressure commonly occurs within 15 to 30 minutes but may occur more rapidly.

If blood pressure decreases to a dangerous level, the patient should be treated as outlined under OVERDOSAGE.

A positive response should always be confirmed by other diagnostic procedures, preferably by measurement of urinary catecholamines or their metabolites.

A negative response is indicated when the blood pressure is elevated, unchanged, or reduced less than 35 mm Hg systolic and 25 mm Hg diastolic following injection of phentolamine. A negative response to this test does not exclude the diagnosis of pheo-chromocytoma, especially in patients with paroxysmal hypertension in whom the incidence of false-negative responses is high.

b. Intramuscular

If the intramuscular test for pheochromocytoma is preferred, preparation is the same as for the intravenous test. Five milligrams of phentolamine mesylate is then dissolved in 1 mL of Sterile Water for Injection. The dose for adults is 5 mg intramuscularly; for children, 3 mg. Blood pressure is recorded every 5 minutes for 30 to 45 minutes following injection. A positive response is indicated when the blood pressure is reduced 35 mm Hg systolic and 25 mm Hg diastolic, or more, within 20 minutes following injection.

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

HOW SUPPLIED
Phentolamine Mesylate for Injection, USP, 5 mg, for intramuscular or intravenous use, is supplied as follows:

**NDC 0143-9564-01** - 2 mL vials packaged individually.

**NDC 0143-9564-10** - 2 mL vials packaged in cartons of 10 vials.

The reconstituted solution should be used upon preparation and should not be stored.

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

To report SUSPECTED ADVERSE REACTIONS, contact West-Ward Pharmaceuticals Corp. at 1-877-845-0689, or the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

For Product Inquiry call 1-877-845-0689.

**Manufactured by:**

HIKMA FARMACÊUTICA (PORTUGAL), S.A.

Estrada do Rio da Mó, 8, 8A e 8B – Fervença – 2705-906 Terrugem SNT, PORTUGAL

**Distributed by:**

West-Ward Pharmaceuticals

Eatontown, NJ 07724 USA

Revised November 2015

PIN385-WES/4

**PACKAGE LABEL PRINCIPAL DISPLAY PANEL**

NDC 0143-9564-01

Rx only

**Phentolamine Mesylate for Injection, USP**

5 mg/vial

FOR IM OR IV USE

LYOPHILIZED

**USUAL DOSAGE:** See package insert

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

Phentolamine Mesylate for Injection, USP vial label

**PACKAGE LABEL PRINCIPAL DISPLAY PANEL**

NDC 0143-9564-01

Rx only

1 x 2 mL

**Phentolamine Mesylate for Injection, USP**

5 mg/vial

FOR IM OR IV USE

LYOPHILIZED
Each vial contains phentolamine mesylate USP 5 mg and 25 mg mannitol in lyophilized form.

**USUAL DOSAGE:** See package insert

Store at 20º to 25ºC (68º to 77ºF) [See USP Controlled Room Temperature].

The reconstituted solution should be used upon preparation and should not be stored.
Phentolamine Mesylate for Injection, USP
5 mg/vial
FOR IM OR IV USE
LYOPHILIZED

Each vial contains phentolamine mesylate USP 5 mg and 25 mg mannitol in lyophilized form.

USUAL DOSAGE: See package insert
Store at 20º to 25ºC (68º to 77ºF) [See USP Controlled Room Temperature].

The reconstituted solution should be used upon preparation and should not be stored.
PHENTOLAMINE MESYLATE
phentolamine mesylate injection, powder, for solution

**Product Information**

<table>
<thead>
<tr>
<th>Product Type</th>
<th>HUMAN PRESCRIPTION DRUG</th>
<th>Item Code (Source)</th>
<th>NDC:0143-9564</th>
</tr>
</thead>
<tbody>
<tr>
<td>Route of Administration</td>
<td>INTRAMUSCULAR, INTRAVENOUS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Active Ingredient/Active Moiety**

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Basis of Strength</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHENTOLAMINE MESYLATE (UNII: Y7543E5K9T) (PHENTOLAMINE - UNIEZ468598HBV)</td>
<td>PHENTOLAMINE MESYLATE</td>
<td>5 mg in 1 mL</td>
</tr>
</tbody>
</table>

**Inactive Ingredients**

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>MANNITOL (UNII: 3OWL53L36A)</td>
<td>25 mg in 1 mL</td>
</tr>
</tbody>
</table>

**Packaging**

<table>
<thead>
<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NDC:0143-9564-10</td>
<td>10 in 1 BOX</td>
<td>11/04/2015</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>NDC:0143-9564-01</td>
<td>1 mL in 1 VIAL; Type 0: Not a Combination Product</td>
<td>11/04/2015</td>
<td></td>
</tr>
</tbody>
</table>

**Marketing Information**

<table>
<thead>
<tr>
<th>Marketing Category</th>
<th>Application Number or Monograph Citation</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANDA</td>
<td>ANDA040235</td>
<td>05/15/1998</td>
<td></td>
</tr>
</tbody>
</table>

**Labeler** - West-Ward Pharmaceuticals Corp (001230762)

Revised: 12/2018