PACKAGE INSERT

Pr Phentolamine Mesylate Injection Sandoz Standard

SANDOZ

5 mg/mL

THERAPEUTIC CLASSIFICATION
Alpha-adrenoreceptor Blocker

ACTIONS AND CLINICAL PHARMACOLOGY

Phentolamine 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.

INDICATIONS

Phentolamine Mesylate Injection Sandoz Standard, is indicated in the following:

- Prevention and control of hypertensive episodes in patients with pheochromocytoma, preoperatively and during surgical excision.
- Prevention of dermal necrosis and sloughing following intravenous administration or extravasation of norepinephrine.
- Diagnosis of pheochromocytoma (phentolamine test).

CONTRAINDICATIONS

Phentolamine mesylate is contraindicated in the following:

- Myocardial infarction, history of myocardial infarction, coronary insufficiency, angina or other evidence suggestive of coronary artery disease.
- Hypotension.
- Hypersensitivity to phentolamine or related compounds.

WARNINGS

Blood pressure must be monitored for appropriate selection of patients, dosage, and duration of therapy. Myocardial infarction, cerebrovascular spasm, and cerebrovascular occlusion have been reported to occur following the administration of phentolamine, usually in association with marked hypotensive episodes with shock-like states which occasionally occur.

For screening tests in patients with hypertension, the generally available urinary assay of catecholamines or other biochemical assays have largely supplanted the phentolamine test and other pharmacological tests for reasons of accuracy and safety. None of the chemical or pharmacological tests are infallible in the diagnosis of pheochromocytoma. The phentolamine 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

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

Due to its stimulatory effect on the gastrointestinal tract, including gastric secretion, phentolamine should be used with caution in patients with gastritis or peptic ulcer.

Use caution in administering phentolamine to patients with renal impairment; since the drug is primarily excreted by the kidney, a reduction in dosage may be necessary.

Pregnancy and Lactation

Animal studies indicate that high doses of phentolamine to pregnant rats and mice resulted in slightly decreased growth and slight skeletal immaturity in the fetuses. At very high doses a slightly lower rate of implantation was found in the rat. There are no studies in pregnant or nursing women. The use of phentolamine is therefore not recommended unless the potential benefits justify the potential risks.

Occupational Hazards

Phentolamine may cause central nervous symptoms, e.g. dizziness, which may impair the patient's reactions. Patients must therefore be warned against engaging in activities that require quick reactions, such as driving motor vehicles or operating machines.

Drug Interactions

See **DOSAGE AND ADMINISTRATION**, **Diagnosis of Pheochromocytoma, Preparation.**

ADVERSE REACTIONS

Orthostatic hypotension and tachycardia occur frequently. Acute and prolonged hypotensive episodes and cardiac arrhythmias have been reported (see **WARNINGS**). In addition, weakness, dizziness, flushing, nasal stuffiness, nausea, vomiting, diarrhea, anorexia, abdominal discomfort, conjunctival infections, sedation, anginal pain, and precordial pain may occur.

Priapism, penile hematoma and fibrosis have been reported following local injection. Neither the route of administration nor this use are approved or recommended.

OVERDOSAGE: SYMPTOMS AND TREATMENT

Death has occurred following use of phentolamine 5 mg for diagnostic purposes; fatal reactions do not appear to be related to the presence/absence of pheochromocytoma. A 47 year old man survived 440 mg infused in one day.

Symptoms

The main clinical manifestations of overdosage with phentolamine are arterial hypotension, tachycardia, cardiac stimulation, arrhythmias, increase in systemic venous capacity, and possibly shock. These effects may be accompanied by headache, hyperexcitability and visual disturbances, sweating, increased gastric motility, vomiting and diarrhea, hypoglycemia.

Treatment

Severe hypotension should be treated by discontinuing treatment with phentolamine and maintaining the patient in the supine position with the feet raised.

Norepinephrine, cautiously titrated in continuous IV infusion, can be considered the pharmacological antagonist. The effect of phentolamine may wear off in a short time and administration of norepinephrine may have to be adjusted accordingly. Do not use epinephrine since this may cause a further fall in blood pressure.

The ECG should be monitored when a pressor agent is used because major arrhythmias may occur. Should excessive cardiac stimulation and hypertensive crisis arise, administer a beta blocking agent by slow IV infusion. Treat hypoglycemia with IV glucose until compensated.

DOSAGE AND ADMINISTRATION

Prevention or control of hypertensive episodes in the patient with pheochromocytoma, preoperatively and during surgical excision.

For use in preoperative reduction of elevated blood pressure, inject 2 to 5 mg of Phentolamine Mesylate Injection Sandoz Standard IV or IM 1 or 2 hours before surgery (and repeat if necessary). For children, use the minimum effective dose e.g. 1 mg for a child over 8 years old.

During surgical removal of pheochromocytoma, repeat IV Phentolamine Mesylate Injection Sandoz Standard as indicated to help prevent or control paroxysms of hypertension, respiratory depression, convulsions, or other effects of epinephrine intoxication. (Postoperatively, norepinephrine may be given to control the hypotension which commonly follows complete removal of a pheochromocytoma).

Prevention of dermal necrosis and sloughing following IV administration or extravasation of norepinephrine.

Infiltrate Phentolamine Mesylate Injection Sandoz Standard (5 to 10 mg in 10 mL saline) into the area of extravasation within 12 hours.

Diagnosis of pheochromocytoma (phentolamine 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.

Intravenous

Preparation: Review the CONTRAINDICATIONS, WARNINGS, and PRECAUTIONS. Withhold all medication such as sedatives, analgesics, and all other medication unless deemed essential (e.g. digitalis and insulin) for at least 24 hours (preferably 48 to 72 hours) prior to the test. Special precautions should be taken with agents that have a long half-life and may interact with phentolamine (e.g. guanethidine, reserpine and antidepressants). Withhold antihypertensive drugs until blood pressure returns to the untreated, hypertensive level. Do not perform test on a patient who is normotensive.

Procedure

- Keep patient at rest in the supine position throughout the test, preferably in a quiet, darkened room. Delay Phentolamine Mesylate Injection Sandoz Standard until blood pressure is stabilized, as evidenced by blood pressure readings taken every 10 minutes for at least one-half hour.
- Phentolamine Mesylate Injection Sandoz Standard contains phentolamine mesylate 5 mg dissolved in 1 mL of sterile water for injection. Dose for adults is 5 mg; for children, 1 mg.
- Insert the syringe needle into vein, delay injection until pressor response to venipuncture has subsided.
- Inject Phentolamine Mesylate Injection Sandoz Standard rapidly. Record blood pressure immediately after injection, at 30-second intervals for the first 3 minutes, and at 60-second intervals for the next 7 minutes.

Interpreting the Test

Positive response, suggestive of pheochromocytoma, is indicated by a drop in blood pressure of more than 35 mm Hg systolic and 25 mm Hg diastolic pressure. A typical positive response may be a drop of 60 mm Hg systolic and 25 mm Hg diastolic. Maximal depressor pressure effect usually is evident within 2 minutes after injection. Return to pre-injection pressure commonly occurs within 15 to 30 minutes, but may return more rapidly.

If blood pressure falls to a dangerous level, treat patient as outlined under **OVERDOSAGE**.

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

Negative response is indicated when the blood pressure is unchanged, elevated, or is reduced less than 35 mm Hg systolic and 25 mm Hg diastolic after injection of Phentolamine Mesylate Injection Sandoz Standard. A negative response to this test does not exclude the diagnosis of pheochromocytoma, especially in patients with paroxysmal hypertension in whom the incidence of false negative responses is high.

Intramuscular

If the IM test for pheochromocytoma is preferred, preparation is the same as for the IV test. Dose for adults is 5 mg IM, for children, 3 mg. Record blood pressure every 5 minutes for 40 to 45 minutes following IM injection. Positive response is indicated by a drop in blood pressure of 35 mm Hg systolic and 25 mm Hg diastolic or greater within 20 minutes following injection.

AVAILABILITY OF DOSAGE FORMS

Each mL of Phentolamine Mesylate Injection Sandoz Standard contains: phentolamine mesylate 5 mg, dextrose 3.5%, sodium metabisulfite 0.6 mg, glacial acetic acid, anhydrous sodium acetate, sodium hydroxide and/or methanesulfonic acid to adjust pH and water for injection.

Phentolamine Mesylate Injection Sandoz Standard is available in 1 mL vials, boxes of 10.

Refrigerate between 2 and 8°C.
Protect from light and heat.
Discard unused portion.

Do not use if the solution becomes discoloured.

LATEX-FREE STOPPER – Stopper contains no dry natural rubber.

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