PRogitine®

(phentolamine mesylate) Ampoules, 10 mg/mL
Alpha-adrenoreceptor blocker

DESCRIPTION
ROGITINE is m-[N-(2-Imidazolin-2-ylmethyl)-p-toluidino] phenol.

ACTIONS
ROGITINE (phentolamine mesylate) produces an alpha-adrenoreceptor 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
1. Prevention and control of hypertensive episodes in patients with pheochromocytoma, preoperatively and during surgical excision.
2. Prevention of dermal necrosis and sloughing, following intravenous administration or extravasation of norepinephrine.
3. Diagnosis of pheochromocytoma (ROGITINE test).

CONTRAINDICATIONS
Myocardial infarction, history of myocardial infarction, coronary insufficiency, angina or other evidence suggestive of coronary artery disease.
Hypotension.
Known hypersensitivity to phentolamine or related compounds. Known hypersensitivity to sulfites.

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 ROGITINE (phentolamine mesylate), usually in association with marked hypotensive episodes with shock-like states which occasionally occur.
The presence of sulfites in ROGITINE ampoules can, especially in patients with bronchial asthma, lead to isolated hypersensitivity reactions, which may become manifest as an acute asthma attack, or shock, or clouding of consciousness.
For screening tests in patients with hypertension, the generally available urinary assay of catecholamines or other biochemical assays have largely supplanted the ROGITINE 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 ROGITINE 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 ROGITINE (phentolamine mesylate) 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, ROGITINE should be used with caution in patients with gastritis or peptic ulcer.
Use caution in administering ROGITINE to patients with renal impairment; since the drug is primarily excreted by the kidney, a reduction in dosage may be necessary.

Pregnancy and Nursing
Animal studies indicate that high doses of ROGITINE 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.

Effects on ability to drive or use of machines
ROGITINE may cause central nervous system 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 injections, 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.

DOSAGE AND ADMINISTRATION
1. *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 2-5 mg of ROGITINE (phentolamine mesylate) intravenously 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 i.v. ROGITINE as indicated to help prevent or control paroxysms of hypertension, respiratory depression, convulsions, or other effects of epinephrine intoxication. (Post-operatively, norepinephrine may be given to control the hypotension which commonly follows complete removal of a pheochromocytoma.)
2. *Prevention of dermal necrosis and sloughing following intravenous administration or extravasation of norepinephrine.*
   Infiltrate ROGITINE mesylate (5 to 10 mg in 10 mL saline) into the area of extravasation within 12 hours.
3. *Diagnosis of pheochromocytoma (ROGITINE 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:
   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 $t_{1/2}$ 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 has normal blood pressure.
   Procedure:
   i. Keep patient at rest in the supine position throughout the test, preferably in a quiet, darkened room. Delay ROGITINE injection until blood pressure is stabilized, as evidenced by blood pressure readings taken every 10 minutes for at least one-half hour.
   ii. The dose for adults is 5 mg; for children, 1 mg.
   iii. Insert the syringe needle into vein, delay injection until pressor response to venipuncture has subsided.
   iv. Inject ROGITINE 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 ROGITINE. 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.

b. *Intramuscular*
   If the intramuscular test for pheochromocytoma is preferred, preparation is the same as for the intravenous test. The dose for adults is 5 mg intramuscularly; for children, 3 mg. Record blood pressure every 5 minutes for 30 to 45 minutes following intramuscular 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.

OVERDOSAGE
Death has occurred following use of ROGITINE (phentolamine mesylate) 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 ROGITINE 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 i.v. infusion, can be considered the pharmacological antagonist. The effect of ROGITINE 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 b.p..
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 i.v. infusion. Treat hypoglycemia with i.v. glucose until compensated.

HOW SUPPLIED
Ampoules (1 mL) containing 10 mg phentolamine mesylate, 0.5 mg sodium metabisulphite PH, 35.0 mg glucose, and water up to 1 mL. Available in boxes of 5 ampoules.
ROGITINE ampoule is incompatible with alkaline solutions. Store at 2 to 8 °C. Do not freeze. Protect from heat and light.

Manufactured and distributed by:
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