

**CENTER FOR DRUG EVALUATION AND RESEARCH**

*APPLICATION NUMBER:*

**17-558**

**APPROVED LABELING**

Package Insert

Date: December 1974

*PK*  
FEB 6 1975

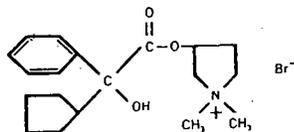
## Robinul® Injectable **APPROVED**

brand of  
**Glycopyrrolate\*, NF**  
(anticholinergic for use in anesthesia)

Each 1 ml contains:  
Glycopyrrolate, NF ..... 0.2 mg  
Water for Injection, USP ..... q.s.  
Chlorobutanol, USP (preservative) ..... 0.5%

For intramuscular, intravenous or subcutaneous administration.

**Description:** Robinul (glycopyrrolate) Injectable is a synthetic anticholinergic agent. It is a quaternary ammonium compound with the following chemical structure:



Unlike atropine, glycopyrrolate is completely ionized at physiological pH values.

Robinul (glycopyrrolate) Injectable is a clear colorless liquid.

**Actions:** Glycopyrrolate, like other anticholinergic (antimuscarinic) agents, inhibits the action of acetylcholine on structures innervated by postganglionic cholinergic nerves and on smooth muscles that respond to acetylcholine but lack cholinergic innervation. These peripheral cholinergic receptors are present in the autonomic effector cells of smooth muscle, cardiac muscle, the sino-atrial node, the atrioventricular node, exocrine glands, and, to a limited degree, in the autonomic ganglia. Thus, it diminishes the volume and free acidity of gastric secretions and controls excessive pharyngeal, tracheal, and bronchial secretions.

Glycopyrrolate antagonizes muscarinic symptoms (e.g., bronchorrhea, bronchospasm, bradycardia, and intestinal hypermotility) induced by cholinergic drugs such as the anticholinesterases.

The highly polar quaternary ammonium group of glycopyrrolate limits its passage across lipid membranes, such as the blood-brain barrier, in contrast to atropine sulfate and scopolamine hydrobromide, which are non-polar tertiary amines which penetrate lipid barriers easily.

Peak effects occur approximately 30 to 45 minutes after subcutaneous or intramuscular administration. The vagal blocking effects persist for 2 to 3 hours and the antisialogogue effects persist up to 7 hours, periods longer than for atropine. With intravenous injection, the onset of action is generally evident within one minute.

**Indications in Anesthesia:** Robinul (glycopyrrolate) Injectable is indicated for use as a preoperative antimuscarinic to reduce salivary, tracheobronchial, and pharyngeal secretions; to reduce the volume and free acidity of gastric secretions; and, to block cardiac vagal inhibitory reflexes during induction of anesthesia and intubation. Glycopyrrolate protects against the peripheral muscarinic effects (e.g., bradycardia and excessive secretions) of cholinergic agents such as neostigmine and pyridostigmine given to reverse the neuromuscular blockade due to nondepolarizing muscle relaxants.

**Contraindications:** There are no absolute contraindications to the use of Robinul Injectable in conjunction with anesthesia except known hypersensitivity to glycopyrrolate.

**Warnings:** This drug should be used with great caution, if at all, in patients with glaucoma or asthma.

**Precautions:** *Usage in Pregnancy.* The use of any drug in pregnancy, lactation, or in the childbearing age requires that the potential benefits of the drug be weighed against the possible hazards to mother and child. Reproduction studies in rats and rabbits revealed no teratogenic effects from glycopyrrolate. However, diminished rates of conception and of survival at weaning were observed in rats, in a dose-related manner. Studies in dogs suggest that this may be due to diminished seminal secretion which is evident at high doses of glycopyrrolate.

Use with caution in patients with: myasthenia gravis; coronary artery disease; congestive heart failure; cardiac arrhythmias; hypertension.

The intravenous administration of any anticholinergic in the presence of cyclopropane anesthesia can result in ventricular arrhythmias; therefore, caution should be observed if Robinul (glycopyrrolate) Injectable must be used during cyclopropane anesthesia. If the drug is given in small incremental doses of 0.1 mg or less, the likelihood of producing ventricular arrhythmias is reduced.

Investigate any tachycardia before giving glycopyrrolate since an increase in the heart rate may occur.

**Adverse Reactions:** Anticholinergics produce certain effects most of which are extensions of their fundamental pharmacological actions. Adverse reactions to anticholinergics in general may include dry mouth; urinary hesitancy and retention; blurred vision due to mydriasis; increased ocular tension; tachycardia; palpitation; decreased sweating; loss of taste; headache; nervousness; drowsiness; weakness; dizziness; insomnia; nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling; severe allergic reaction or drug idiosyncrasies including anaphylaxis; urticaria and other dermal manifestation; some degree of mental confusion and/or excitement, especially in elderly persons.

**Dosage and Administration:** Robinul (glycopyrrolate) Injectable may be administered subcutaneously, intramuscularly, or intravenously without dilution.

**Adults: Preanesthetic Medication.** The recommended dose of Robinul (glycopyrrolate) Injectable is .002 mg (.01 ml) per pound of body weight by intramuscular injection, given 30 minutes to one hour prior to the anticipated time of induction of anesthesia or at the time the preanesthetic narcotic and/or sedative are administered.

**Intraoperative Medication.** Robinul (glycopyrrolate) Injectable may be used during surgery to counteract drug-induced or vagal traction reflexes with the associated arrhythmias (e.g., bradycardia). It should be administered intravenously as single doses of 0.1 mg (0.5 ml) and repeated, as needed, at intervals of 2-3 minutes. The usual attempts should be made to determine the etiology of the arrhythmia, and the surgical or anesthetic manipulations necessary to correct parasympathetic imbalance should be performed.

**Reversal of Neuromuscular Blockade.** The recommended dose of Robinul (glycopyrrolate) Injectable is 0.2 mg (1.0 ml) for each 1.0 mg (1.0 ml) of neostigmine or the equivalent dose of pyridostigmine. In order to minimize the appearance of cardiac side effects, the drugs may be administered simultaneously by intravenous injection and may be mixed in the same syringe.

**Children:** The recommended dosage range, when used as preanesthetic medication in children up to 12 years of age, is .002 mg to .004 mg intramuscularly per pound of body weight. For intraoperative use and for reversal of neuromuscular blockade, the pediatric dose is 0.2 mg (1.0 ml) Robinul Injectable intravenously for each 1.0 mg (1.0 ml) of neostigmine or the equivalent dose of pyridostigmine.

**Compatibility With Other Agents: Chemical compatibility.** Robinul (glycopyrrolate) Injectable is chemically compatible for mixing and injection with the following: 5% and 10% glucose in water or saline; Demerol® (meperidine) Injectable; morphine sulfate; Innovar® (fentanyl plus droperidol) Injectable; Vistaril® (hydroxyzine) Injectable; Prostigmin® (neostigmine) Injectable; Mestinon® (pyridostigmine) Injectable. Robinul Injectable may be administered via the tubing of a running infusion of physiological saline or lactated Ringer's solution.

Known chemical incompatibilities include the following injectables: sodium bicarbonate; Valium® (diazepam); sodium pentobarbital; various phenothiazines; Dramamine® (dimenhydrinate), and chloramphenicol.

**Drug Interaction During Anesthesia.** Glycopyrrolate has been used clinically with at least the following medications: a barbiturate (sodium thiopental); narcotic analgesics (morphine, alphaprodine hydrochloride, fentanyl); sedative/tranquilizers (droperidol, diazepam); gaseous anesthetics (nitrous oxide); volatile liquid anesthetics (diethyl ether, halothane, methoxyflurane, enflurane); parenteral anesthetics (ketamine); peripherally-acting skeletal muscle relaxants (succinylcholine, gallamine, d-tubocurarine, pancuronium); cholinergic agents (neostigmine, pyridostigmine); and other anticholinergics (atropine).

There are no known unique or unanticipated drug-drug interactions with other agents except that Robinul (glycopyrrolate) Injectable should be used with caution if at all during cyclopropane anesthesia (see Precautions).

**Management of Overdosage:** To combat peripheral anticholinergic effects, a quaternary ammonium anticholinesterase such as neostigmine methylsulfate may be given in a dose of 1.0 mg for each 1.0 mg of Robinul (glycopyrrolate) Injectable known to have been administered.

**How Supplied:** Robinul (glycopyrrolate) Injectable is available in 1 ml, 5 ml, and 20 ml vials (NDC 0031-7890).

Manufactured to the specifications of A. H. ROBINS COMPANY, INC., Richmond, Va. 23220, by TAYLOR PHARMACAL COMPANY, Decatur, Ill. 62525.

\*U.S. Patent No. 2,956,062

**A-H-ROBINS**

A. H. ROBINS COMPANY RICHMOND, VIRGINIA 23220

December 1974

Printed in U.S.A.

Robininul<sup>®</sup> Injectable  
BRAND OF  
glycopyrrolate  
FIVE/1ml AMPULS

LOT NO.

**Robinul<sup>®</sup> Injectable**  
BRAND OF  
glycopyrrolate / Robins

\* U. S. Patent No. 2,956,062

Manufactured for  
A. H. ROBINS COMPANY / RICHMOND, VA. 23220

A-H-ROBINS

Robininul<sup>®</sup> Injectable  
BRAND OF  
glycopyrrolate  
FIVE/1ml AMPULS

7890-87  
1ml-174

ORIG  
17-258

5 ml NDC 0031-7890-93  
MULTIPLE DOSE VIAL  
**Robinul<sup>®</sup> Injectable**  
BRAND OF  
glycopyrrolate\*  
0.2 mg/ml

Water for injection, U.S.P. q.s.  
Chlorobutanol (preservative) 0.5%  
For I. M., I. V. or S. C. use.

CAUTION: Federal law prohibits  
dispensing without prescription.

MANUFACTURED FOR  
A. H. ROBINS COMPANY  
RICHMOND, VA. 23220

A-H-ROBINS

LOT NO.

A-H-ROBINS

A-H-ROBINS

7890-93  
5ml-174

NDC 0031-7890-93  
5 ml/MULTIPLE DOSE VIAL  
**ROBINUL<sup>®</sup> INJECTABLE**  
GLYCOPYRROLATE . . . 0.2 mg/ml  
water for injection, U.S.P. . . . q.s.  
chlorobutanol (preservative) . . . 0.5%

For intramuscular, intravenous, or  
subcutaneous administration.  
USUAL DOSE: 0.1 mg (0.5 ml) at  
four hour intervals, three or four  
times daily.

CAUTION: Federal law prohibits  
dispensing without prescription.

Consult directions before use.  
Mfd. for A. H. Robins Co.  
Richmond, Virginia 23220

Lot No.

1 ml Ampul NDC 0031-7890-  
**ROBINUL<sup>®</sup> INJECTABLE**  
GLYCOPYRROLATE . . . 0.2 mg/ml  
Water for injection, U.S.P. . . . q.s.  
chlorobutanol (preservative) . . . 0.5%  
For I.M., I.V. or S.C. use.  
CAUTION: Federal law prohibits  
dispensing without prescription.  
Mfd. for A. H. Robins Co.  
Richmond, Virginia 23220

FIVE / 1 ml AMPULS

NDC 0031-7890-87

# Robinul<sup>®</sup> Injectable

BRAND OF

**glycopyrrolate\***

**0.2 mg/ml**

Water for Injection, U.S.P.  
Chlorobutanol (preservative)

q.s.  
0.5%

For intramuscular, intravenous, or  
subcutaneous administration.

USUAL DOSE: 0.1 mg (0.5 ml) at four hour  
intervals, three or four times daily. Consult  
directions before use.

CAUTION: Federal law prohibits dispensing  
without prescription.

AH-ROBINS

For intramuscular,  
intravenous, or  
subcutaneous  
administration.

USUAL DOSE: 0.1 mg  
(0.5 ml) at four hour  
intervals, three or four  
times daily. Consult  
directions before use.

Robinul<sup>®</sup>  
Injectable  
BRAND OF  
glycopyrrolate

\*U.S. Patent No. 2,956,062

AH-ROBINS

AH-ROBINS