

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Robinul Injection

Glycopyrronium Bromide 200 micrograms in 1ml Solution for Injection.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml of injection contains 200 micrograms (0.2mg) of glycopyrronium bromide (glycopyrrolate).

3. PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless, sterile solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

1. To protect against the peripheral muscarinic actions of anticholinesterases such as neostigmine and pyridostigmine, used to reverse residual neuromuscular blockade produced by non-depolarising muscle relaxants.
2. As a pre-operative antimuscarinic agent to reduce salivary tracheobronchial and pharyngeal secretions and to reduce the acidity of the gastric contents.
3. As a pre-operative or intra-operative antimuscarinic to attenuate or prevent intra-operative bradycardia associated with the use of suxamethonium or due to cardiac vagal reflexes.

4.2. Posology and method of administration

Robinul Injection is for intravenous or intramuscular injection.

Premedication: Adults and older patients: 200 to 400 micrograms (0.2mg to 0.4mg) intravenously or intramuscularly before the induction of anaesthesia.

Alternatively, a dose of 4 to 5 micrograms/kg (0.004 to 0.005mg/kg) up to a maximum of 400 micrograms (0.4mg) may be used. Larger doses may result in profound and prolonged antisialagogue effect which may be unpleasant for the patient.

Children: 4 to 8 micrograms/kg (0.004 to 0.008mg/kg) up to a maximum of 200 micrograms (0.2mg) intravenously or intramuscularly before the induction of anaesthesia. Larger doses may result in profound and prolonged antisialagogue effect which may be unpleasant for the patient.

Intra-operative use: Adults and older patients: A single dose of 200 to 400 micrograms (0.2 to 0.4mg) by intravenous injection should be used. Alternatively, a single dose of 4 to 5 micrograms/kg (0.004 to 0.005mg/kg) up to a maximum of 400 micrograms (0.4mg) may be used. This dose may be repeated if necessary.

Children: A single dose of 200 micrograms (0.2mg) by intravenous injection should be used. Alternatively, a single dose of 4 to 8 micrograms/kg (0.004 to 0.008mg/kg) up to a maximum of 200 micrograms (0.2mg) may be used. This dose may be repeated if necessary.

Reversal of residual non-depolarising neuromuscular block:

Adults and older patients: 200 micrograms (0.2mg) intravenously per 1000 micrograms (1mg) neostigmine or the equivalent dose of pyridostigmine. Alternatively, a dose of 10 to 15 micrograms/kg (0.01 to 0.015mg/kg) intravenously with 50 micrograms/kg (0.05mg/kg) neostigmine or equivalent dose of pyridostigmine. Robinul may be administered simultaneously from the same syringe with the anticholinesterase; greater cardiovascular stability results from this method of administration.

Children: 10 micrograms/kg (0.01mg/kg) intravenously with 50 micrograms/kg (0.05mg/kg) neostigmine or the equivalent dose of pyridostigmine. Robinul may be administered simultaneously from the same syringe with the anticholinesterase; greater cardiovascular stability results from this method of administration.

4.3. Contraindications

Apart from established hypersensitivity to glycopyrrolate, there are no absolute contra-indications to Robinul.

4.4. Special warnings and precautions for use

Because of the increase in heart rate produced by the administration of anticholinergics, use with caution in patients with coronary artery disease; congestive heart failure; cardiac arrhythmias; hypertension; thyrotoxicosis. This product should be used very cautiously in pyrexial patients due to inhibition of sweating.

Large doses of quaternary ammonium anticholinergic compounds have been shown to block end plate nicotinic receptors. This should be considered before using glycopyrrolate in patients with myasthenia gravis.

It is known that the administration of anticholinergic agents during inhalation anaesthesia can result in ventricular arrhythmias.

4.5. Interaction with other medicinal products and other forms of interaction

Anticholinergic agents may delay absorption of other medicaments given concomitantly.

Excessive cholinergic blockade can occur if Robinul Injection is given concomitantly with belladonna alkaloids or other synthetic anticholinergic agents (such as antiparkinsonism agents), phenothiazines, tricyclic antidepressants, disopyramide, procainamide, quinidine, antihistamines, or narcotic analgesics such as meperidine.

Concurrent administration of anticholinergics and corticosteroids may result in increased intraocular pressure.

Concurrent use of anticholinergic agents with slow-dissolving tablets of digoxin may cause increased serum digoxin levels.

4.6. Pregnancy and lactation

Although reproduction studies in rats and rabbits revealed no teratogenic effects from glycopyrrolate, safety in human pregnancy and lactation has not been established. 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. The significance of this for man is not clear.

4.7. Effects on ability to drive and use machines

Do not operate or drive heavy machinery unless the drug has been shown not to interfere with mental or physical ability.

4.8. Undesirable effects

Robinul may produce the following effects which are extensions of its fundamental pharmacological actions: dry mouth, difficulty in micturition, disturbances in visual accommodation, tachycardia, palpitation, inhibition of sweating. However the use of Robinul Injection as a preoperative anticholinergic is associated with less effect on the cardiovascular system compared to atropine.

4.9. Overdose

Since glycopyrrolate is a quaternary ammonium agent, symptoms of overdosage are peripheral rather than central in nature. To combat peripheral anticholinergic effects, a quaternary ammonium anticholinesterase such as neostigmine methylsulphate may be given in a dose of 1000 micrograms (1.0mg) for each 1000 micrograms (1.0mg) of glycopyrrolate known to have been administered by the parenteral route.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Glycopyrrolate is a quaternary ammonium antimuscarinic agent and like other anticholinergic agents, it 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 sinoatrial 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 sulphate and scopolamine hydrobromide, which are non-polar tertiary amines which penetrate lipid barriers easily.

Robinul Injection has been used successfully as an adjunct to reversal by neostigmine when atropine has been used as the preoperative anticholinergic. The use of Robinul Injection as an adjunct to reversal by neostigmine of non-depolarising muscle relaxants is associated with less initial tachycardia and better protection against the cholinergic effects of neostigmine compared to reversal with a mixture of neostigmine and atropine.

5.2. Pharmacokinetic properties

Glycopyrrolate is rapidly diminished and/or excreted after intravenous administration. The terminal elimination phase is relatively slow with quantifiable levels remaining up to 8 hours after administration. Peak effects occur approximately 30 to 45 minutes after intramuscular administration. The vagal blocking effects persist for 2 to 3 hours and the antisialagogue effects persist up to 7 hours, periods longer than for atropine. With intravenous injection, the onset of action is generally evident within one minute.

5.3. Preclinical safety data

No further relevant information other than that which is included in other sections of the Summary of Product Characteristics.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sodium Chloride
Dilute Hydrochloric Acid
Water for Injections

6.2. Incompatibilities

Robinul Injection has been shown to be physically compatible with the following agents commonly used in anaesthetic practice: Butorphanol, Lorazepam, Droperidol and Fentanyl Citrate, Levorphanol Tartrate, Pethidine Hydrochloride, Morphine Sulphate, Neostigmine, Promethazine and Pyridostigmine.

Robinul Injection has been shown to be physically incompatible with the following agents commonly used in anaesthetic practice: Diazepam, Dimenhydrinate, Methohexitone Sodium, Pentazocine, Pentobarbitone Sodium, Thiopentone Sodium.

6.3. Shelf life

5 years.

6.4. Special precautions for storage

Do not store above 25°C.

6.5. Nature and contents of container

Robinul Injection 1ml and 3ml is presented in clear One point cut (OPC) glass ampoules, packed in cardboard cartons to contain 10 x 1ml; 10 x 3ml and 3 x 3ml ampoules.

6.6. Instructions for use/handling

Keep out of reach and sight of children.

If only part of an ampoule is used, discard the remaining solution.

7. MARKETING AUTHORISATION HOLDER

Anpharm Ltd.
Roscrea
Co. Tipperary
Ireland.

8. MARKETING AUTHORISATION NUMBER(S)

PL 15372/0004

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

1 July 1997

10 DATE OF REVISION OF THE TEXT

March 2009