

INTERNAL DRAFT

SUMMARY OF PRODUCT CHARACTERISTICS

Product Summary

1. Trade Name of the Medicinal Product

Glycopyrrolate Injection U.S.P. 200 micrograms/ml, 1ml & 3ml.

2. Qualitative and Quantitative Composition

Each ml of solution contains 200 micrograms of glycopyrrolate U.S.P.

3. Pharmaceutical Form

Clear, colourless, sterile solution intended for parenteral administration to human beings.

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 and volume 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, cardiac vagal reflexes or that associated with the use of the non-depolarising relaxants atracurium and vecuronium.

4.2. Posology and Method of Administration

For intravenous or intramuscular use.

A.) PremedicationAdults and older Patients

200 to 400 micrograms (0.2 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 a marked and prolonged antisialogogue action 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 a marked and prolonged antisialogogue action which may be unpleasant for the patient.

B.) Intra-operative UseAdults 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 - 0.005mg/kg) up to a maximum of 400 micrograms (0.4mg) may be used. This dose may be repeated as necessary.

Children

When indicated, a single dose of 200 micrograms (0.2mg) by intravenous injection should be used. Alternatively, a single dose of 4 to 8 micrograms per 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 non-depolarising neuromuscular blockAdults and Older Patients

200 micrograms (0.2mg) intravenously per 1000 micrograms (1mg) neostigmine or the equivalent dose of pyridostigmine. Alternatively, a dose of 10 - 15 micrograms/kg (0.01 to 0.015mg/kg) intravenously with 50 micrograms/kg (0.05mg/kg) of neostigmine or the equivalent dose of pyridostigmine.

Glycopyrrolate may be mixed with either neostigmine or pyridostigmine in the same syringe and administered simultaneously; 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 equivalent doses of pyridostigmine. Glycopyrrolate may be mixed in the same syringe as neostigmine or pyridostigmine and administered simultaneously; greater cardiovascular stability results from this method of administration.

4.3. Contra-indications

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

4.4. Special Warnings and Precautions for Use

Because of the increased heart rate produced by the administration of anticholinergics, glycopyrrolate should be administered with care in patients with coronary artery disease;

congestive heart failure; cardiac dysrhythmias; hypertension; thyrotoxicosis. Extreme care must be observed if it is necessary to use glycopyrrolate in pyrexial patients due to the inhibition of sweating.

Quaternary ammonium compounds in large dose have been shown to block the nicotinic muscle end plate receptors. This must be evaluated prior to its administration in patients with myasthenia gravis.

Anticholinergic drugs can cause ventricular arrhythmias when administered during inhalation anaesthesia especially in association with the halogenated hydrocarbons.

4.5. Interactions with other Medicaments and other forms of Interaction

The effects of glycopyrrolate may be enhanced by the concurrent administration of other drugs with antimuscarinic properties.

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

Although disturbances in visual accommodation may occur which might affect a patient's ability to drive and use machines, the conditions under which glycopyrrolate is administered would generally preclude any opportunity to drive or operate machines.

4.8. Undesirable Effects

Glycopyrrolate 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.

4.9. Overdose

Because glycopyrrolate is a quaternary ammonium compound, symptoms of overdosage are peripheral rather than central in nature. To treat peripheral anticholinergic effects, a quaternary ammonium anticholinesterase such as neostigmine methyl sulphate 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.

Pharmacological Properties

5.1. Pharmacodynamic Properties

Glycopyrrolate has a specific effect on salivary and sweat gland activity with little effect on pupil size, visual accommodation or heart rate. At a dose of 0.2mg intramuscularly, sweat gland activity and salivation are markedly inhibited for over 6 hours.

Absorption from the intramuscular site of administration is almost complete and as rapid, as that following intravenous (I.V.) administration. As would be anticipated from a quaternary ammonium compound, oral absorption is poor and erratic.

Glycopyrrolate is a superior drug when compared with atropine. A dose of 0.4mg I.M. inhibits salivation by over 90% and produces only slight slowing of the heart rate. Atropine has been shown in doses of 2.0mg I.M. to inhibit salivation by approximately 80% but produces a rise in heart rate of greater than 80%.

5.2. Pharmacokinetic Properties

Studies involving radio-labelled glycopyrrolate (200ug intravenously) show that the initial distribution phase is extremely rapid, approximately 90% of the radio-activity disappeared from plasma within five minutes and being rapidly excreted in bile and urine.

Approximately 10 - 20% is absorbed from the gastro-intestinal tract and is excreted in bile and urine as unchanged drug and metabolites. Like all quaternary ammonium compounds, it penetrates the blood brain barrier only poorly.

5.3. Preclinical Safety Data

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

Pharmaceutical Particulars

6.1. List of Excipients

Sodium Chloride B.P.
Dilute Hydrochloric Acid B.P.
Water for Injections B.P.

6.2. Incompatibilities

Glycopyrrolate 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.

Glycopyrrolate is incompatible with alkalis, these include the following agents used in anaesthetic practice: diazepam, dimenhydrinate, methohexitone sodium, pentazocine, pentobarbitone sodium, propofol, thiopentone sodium.

6.3. Shelf Life

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

6.4. Special Precautions for Storage

Protect from light.
Store in a cool dry place.

6.5. Nature and Contents of Container

1ml and 3ml clear glass ampoules, glass type I, Ph. Eur. borosilicate glass packed in cardboard cartons to contain 10 x 1ml or 10 x 3ml ampoules.

6.6. Instruction for Use/Handling

For I.M. and I.V. Injection.
Use as directed by the physician.
Keep out of reach of children.
If only part used, discard the remaining solution.

Administrative Data

7. Marketing Authorisation Holder

Antigen International Limited
Roscrea
Co. Tipperary
Ireland

8. Marketing Authorisation Number

PL 02848/0159.

9. Date of First Authorisation/Renewal of Authorisation

5 November 1991

10. Date of (Partial) Revision of the Text

23 October 1996