Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Glycopyrrolate Injection USP 200 micrograms/ml, 1 ml & 3 ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of solution contains 200 micrograms (0.2 mg) of Glycopyrronium Bromide.

For excipients, see 6.1.

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

Glycopyrrolate Injection is for intravenous or intramuscular injection.

Premedication :

Adults 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 profound and prolonged antisialogogue 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 antisialogogue 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 - 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 - 15 micrograms/kg (0.01 to 0.015mg/kg) intravenously with 50 micrograms/kg (0.05mg/kg) neostigmine or equivalent dose of pyridostigmine. Glycopyrrolate 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. Glycopyrrolate may be administered simultaneously from the same syringe with the anticholinesterase; greater cardiovascular stability results from this method of administration.

4.3 Contraindications

Hypersensitivity to glycopyrrolate.

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

Administration of anticholinergic agents during inhalation anaesthesia can result in ventricular arrhythmias.

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

Not relevant, as Glycopyrrolate Injection is intended for pre-operative or intra-operative use.

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

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. The effect of glycopyrrolate on secretory organs is particularly marked and prolonged and good control of salivary and pharyngeal secretions can be obtained with doses which do not produce marked changes in heart rate. Gastric secretions are, similarly, reduced by glycopyrrolate.

Glycopyrrolate Injection has been used successfully as an adjunct to reversal by neostigmine when atropine has been used as the pre-operative anticholinergic.

The use of glycopyrrolate as a pre-operative anticholinergic is associated with less effect on the cardiovascular system, compared to atropine.

The use of Glycopyrrolate 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.

Greater cardiovascular stability results from simultaneous administration of glycopyrrolate and neostigmine methylsulphate from the same syringe.

5.2 Pharmacokinetic properties

Quaternary ammonium anticholinergic agent, highly ionised at physiological pH with resulting poor penetration of brain and placental barriers. Excretion is through bile and urine as unchanged drug.

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

Glycopyrrolate 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.

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

6.3 Shelf Life

2 years.
Once opened, use immediately.

6.4 Special precautions for storage

Keep the container in the outer carton. Do not store above 25°C.

6.5 Nature and contents of container

1 ml and 3 ml clear glass ampoules, glass type I Ph. Eur. borosilicate glass packed in cardboard cartons to contain 5 or 10 ampoules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

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

7 MARKETING AUTHORISATION HOLDER

Antigen Pharmaceuticals Ltd.
Roscrea
Co. Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER

PA 73/126/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 08 October 1992

Date of last renewal: 08 October 2002

10 DATE OF REVISION OF THE TEXT

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