1.3.1.1 PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S3

PROPRIETARY NAME AND DOSAGE FORM

ROBINUL 1 ml INJECTABLE

ROBINUL 2 ml INJECTABLE

COMPOSITION

ROBINUL 1 ml INJECTABLE contains: Glycopyrrolate 0,2 mg per 1 ml

ROBINUL 2 ml INJECTABLE contains: Glycopyrrolate 0,4 mg per 2 ml

Excipients:

Chlorbutanol (preservative) 0,5 % *m/v,* water for injection

CATERGORY AND CLASS

A 5.4. Cholinolytics (anticholinergics)

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Glycopyrrolate, like other anticholinergic (antimuscarinic) medicines, 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 secretion and controls excessive pharyngeal, tracheal and bronchial secretions. Glycopyrrolate antagonizes muscarinic symptoms (e.g. bronchorrhoea, bronchospasm, bradycardia, and intestinal hypermotility) induced by cholinergic medicine 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 and can penetrate lipid barriers easily.

Pharmacokinetic properties

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 antisialagogue effects persist up to 7 hours, a period longer than for atropine. With intravenous injection, the onset of action is generally evident within one minute.

INDICATIONS

In anaesthesia:

ROBINUL INJECTABLE is indicated for use as a pre-operative 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 anaesthesia and intubation.

ROBINUL INJECTABLE protects against the peripheral muscarinic effects (e.g. bradycardia and excessive secretions) of cholinergic medicines such as neostigmine and pyridostigmine given to reverse the neuromuscular blockade due to nondepolarising muscle relaxants.

CONTRAINDICATIONS

ROBINUL INJECTABLE is contraindicated in patients with hypersensitivity to glycopyrrolate or to any of the excipients in ROBINUL INJECTABLE (see COMPOSITION).

WARNINGS AND SPECIAL PRECAUTIONS

Because ROBINUL INJECTABLE causes tachycardia, extreme caution is advised in patients with existing tachycardia, thyrotoxicosis, coronary artery disease, cardiac dysrhythmias, hypertension, congestive heart failure and cardiac insufficiency.

As ROBINUL INJECTABLE inhibits sweating, patients with increased temperature (especially children) should be observed closely.

Caution is advised when ROBINUL INJECTABLE is used in patients with prostatic hypertrophy, paralytic ileus, pyloric stenosis and closed angle glaucoma.

Anticholinergic medicines such as ROBINUL INJECTABLE can cause ventricular dysrhythmias when administered during inhalation anaesthesia especially in association with the halogenated hydrocarbons. Caution should be observed if ROBINUL INJECTABLE is used during halogenated anesthesia. If given in small incremental doses of 0,1 mg or less, the likelihood of producing ventricular dysrhythmias is reduced.

Quaternary ammonium compounds in large doses have been shown to block end plate nicotinic receptors. This should be considered before using ROBINUL INJECTABLE in patients with myasthenia gravis.

The renal elimination of glycopyrrolate is considerably prolonged in patients with uraemia. ROBINUL INJECTABLE should therefore be used with caution in such patients.

Effects on ability to drive and use machines

Since adverse reactions such as dizziness, mental confusion and blurred vision have been

reported in patients receiving ROBINUL INJECTABLE.

Patients should not drive, use machinery or perform any tasks that require concentration, until they are certain that ROBINUL INJECTABLE does not adversely affect their ability to do so (see SIDE EFFECTS).

INTERACTIONS

Antimuscarinic interactions

There is an increased risk of antimuscarinic side effects in patients taking medicines with antimuscarinic effects such as MAOIs, amantadine, clozapine, tricyclic antidepressants and nefopam.

Use with other medicines during anaesthesia

Glycopyrrolate as in ROBINUL INJECTABLE has been used clinically with at least the following medicines: a barbiturate (sodium thiopental), narcotic analgesics (morphine, alphaprodine hydrochloride, fentanyl), sedative/tranquiliser (droperidol, diazepam), gaseous anaesthetics (nitrous oxide), volatile liquid anesthetics (diethyl ether, halothane, methoxyflurane, enflurane), parenteral anesthetics (ketamine), peripherally-acting skeletal muscle relaxants (succinylcholine, gallamine, d-tubocurarine, pancuronium), cholinergic medicines (neostigmine, pyridostigmine) and other anticholinergics (atropine).

Chemical incompatibilities

Known chemical incompatibilities include the following injectables: sodium bicarbonate, diazepam, sodium pentobarbital, various phenothiazine, dimenhydrinate and chloramphenicol.

ROBINUL INJECTABLE is also incompatible with alkalis.

The stability of ROBINUL INJECTABLE, when mixed with infusion solutions and additives, is

questionable above a pH of 6, owing to ester hydrolysis.

HUMAN REPRODUCTION

The safety of ROBINUL INJECTABLE in pregnancy and lactation has not been established.

Pregnancy

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.

Lactation

Glycopyrrolate may be excreted in breast milk.

DOSAGE AND DIRECTIONS FOR USE

ROBINUL INJECTABLE may be administered intramuscularly, intravenously or subcutaneously, without dilution, in the following indications:

Adults :

Pre-anaesthetic medication : The recommended dose of ROBINUL INJECTABLE is **0,004 mg (0,02 ml) per kilogram of body mass** by intramuscular injection, given 30 minutes to one hour prior to the anticipated time of induction of anesthesia or at the time the preanaesthetic narcotic and/or sedative is administered.

Intra-operative medication: ROBINUL INJECTABLE may be used during surgery to counteract anesthetic induced or vagal traction reflexes with the associated dysrhythmias (e.g. bradycardia). It should be administered intravenously as single dose of **0,1 mg (0,5 ml)** and repeated as needed, at intervals of 2 to 3 minutes. The usual attempts should be made to determine the aetiology of the dysrhythmia, and the surgical or anesthetic manipulations necessary to correct

parasympathetic imbalance should be performed.

Reversal of neuromuscular blockade: The recommended dose of ROBINUL INJECTABLE is **0,2 mg(1,0 ml) for each 1,0 mg of neostigmine or 5,0 mg of pyridostigmine.** In order to minimise the appearance of cardiac side effects, these substances may be administered simultaneously by intravenous injection and may be mixed in the same syringe.

Children: The recommended dosage range of ROBINUL INJECTABLE in children up to **12 years** of age, is **0,004 mg to 0,008 mg (0, 02 ml to 0, 04 ml) intramuscularly per kilogram of body mass.** For intraoperative use and for reversal of neuromuscular blockade, **the paediatric dose is 0, 2 mg (1, 0 ml) ROBINUL INJECTABLE intravenously for each 1, 0 mg of neostigmine or 5, 0 mg of pyridostigmine.**

Compatibility with other medicines:

Chemical compatibility – ROBINUL INJECTABLE is chemically compatible for mixing and injection with the following:

5 % and 10 % glucose in water or saline; meperidine injection; morphine sulphate; fentanyl plus droperidol injection; hydroxyzine injection. ROBINUL INJECTABLE may be administered via the tubing of a running infusion of physiological saline or lactated Ringer's solution.

Chemical incompatibilities:

See INTERACTIONS

SIDE EFFECTS

Immune system disorders

Less frequent: Severe allergic reaction, anaphylaxis, pseudoanaphylaxis

Psychiatric disorders

Less frequent: Mental confusion, nervousness, insomnia

Nervous system disorders

Less frequent: Headache, mental excitement (especially in the elderly), drowsiness, dizziness, giddiness, loss of taste

Eye disorders

Less frequent: Blurred vision due to midriasis, increased ocular tension, photophobia

Cardiac disorders

Less frequent: Bradycardia, tachycardia, palpitation, dysrhythmias

Respiratory, thoracic and mediastinal disorders

Less frequent: Reduced bronchial secretions

Gastrointestinal disorders

Less frequent: Nausea, vomiting, constipation, bloated feeling, dry mouth

Skin and subcutaneous tissue disorders

Less frequent: Decreased sweating, urticaria, flushing, dryness of the skin

Renal and urinary disorders

Less frequent: Urinary hesitancy and retention

Reproductive system and breast disorders

Less frequent: Impotence, suppression of lactation

General disorders and administrative site conditions

Less frequent: Weakness, pharmacologic idiosyncrasies

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENTS

Symptoms

Since ROBINUL INJECTABLE is a quaternary ammonium medicines, symptoms of overdosage are peripheral rather than central in nature (see SIDE EFFECTS).

Treatment

To combat peripheral anticholinergic effects, a quaternary ammonium anticholinesterase such as neostigmine methylsulphate may be given in a dose of 1, 0 mg for each 1, 0 mg of ROBINUL

INJECTABLE known to have been administered.

IDENTIFICATION

ROBINUL INJECTABLE is a clear, colourless liquid.

PRESENTATION

ROBINUL 1 ml INJECTABLE is filled into a 1 ml clear glass ampoule with a break ring and is available in boxes of 10 and 100.–

ROBINUL 2 ml INJECTABLE is filled into a 2 ml clear glass ampoule with a break ring and is available in boxes of 10 and 100.–

Not all packs and pack sizes are necessarily marketed.

STORAGE INSTRUCTIONS

Store at or below 25 °C, protected from light.

Keep in original packaging until required for use.

REGISTRATION NUMBER

ROBINUL1 ml INJECTABLE : J/5.4/50

ROBINUL 2 ml INJECTABLE : W/5.4/129

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead 2191

DATE OF PUBLICATION OF THE PROFFESSIONAL INFORMATION FOR HUMAN USE

ROBINUL 1 ml INJECTABLE: 25 April 1977

ROBINUL 2 ml INJECTABLE: 16 August 1988

Date of the most recent amendment to the professional information as approved by the Authority: 09 April 2020

Botswana:	S2
ROBINUL 1 ml INJECTABLE:	BOT0500744
ROBINUL 2 ml INJECTABLE:	BOT0500743

Namibia:	NS1
ROBINUL 1 ml INJECTABLE:	04/5.4/0144
ROBINUL 2 ml INJECTABLE:	04/5.4/0143

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