PROFESSIONAL INFORMATION

SCHEDULING STATUS

S3

1 NAME OF THE MEDICINE

GLYCOSTOM 0,2 mg/ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of GLYCOSTOM contains 0,2 mg glycopyrronium bromide.

Contains 9,0 mg of sodium chloride per ml.

Sugar free.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection.

A clear, colourless solution free from visible particles and visual fibres.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

In anaesthesia: GLYCOSTOM 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 anaesthesia and intubation.

GLYCOSTOM 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 nondepolarizing muscle relaxants.

4.2 Posology and method of administration

Posology

Adults:

Preanaesthetic medicine: The recommended dose of GLYCOSTOM 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 anaesthesia or at the time the preanaesthetic narcotic and/or sedative is administered.

Intraoperative medicine: GLYCOSTOM may be used during surgery to counteract anaesthetic induced or vagal traction reflexes with the associated arrhythmias (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 etiology of the arrhythmia, and the surgical or anaesthetic manipulations necessary to correct parasympathetic imbalance should be performed.

Reversal of neuromuscular blockade: The recommended dose of GLYCOSTOM is 0,2 mg (1,0 ml) for each 1,0 mg of neostigmine or 5,0 mg of pyridostigmine. 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.

Paediatric population

The recommended dosage range of GLYCOSTOM 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) GLYCOSTOM intravenously for each 1,0 mg of neostigmine or 5,0 mg of pyridostigmine.

Method of administration

GLYCOSTOM is for intravenous or intramuscular injection. For instructions on dilution of the medicine before administration, see section 6.6.

4.3 Contraindications

- Hypersensitivity to glycopyrronium bromide or to any of the excipients of GLYCOSTOM (see section 6.1).
- Angle-closure glaucoma.
- Myasthenia gravis (large doses of quaternary ammonium compounds can block the nicotinic receptors).
- Paralytic ileus.
- Pylorus stenosis.
- Prostatic enlargement.
- Combinations of cholinesterase inhibitors and antimuscarinics such as neostigmine plus GLYCOSTOM should be avoided in patients with extended QT intervals (see section 4.5).

4.4 Special warnings and precautions for u se

Because GLYCOSTOM causes tachycardia, caution is advised in patients with glaucoma, asthma, hypertension, dysrhythmia, cardiac disorder and hyperthyroidism and it is recommended to measure the pulse rate if the patient report very fast or very slow heart rate.

Should be used with caution to patients with increased temperature, as GLYCOSTOM inhibits sweating, and it is recommended to measure the temperature at regular time points.

Should be used with caution to patients with renal insufficiency, prostatic hypertrophy, diarrhoea, ulcerative colitis, parkinsonism, and asthma.

Patients diagnosed with one/some of the mentioned diseases should be informed to tell the doctor if specific symptoms arise.

Duration of effect of GLYCOSTOM may be prolonged in patients with renal impairment since glycopyrrolate is excreted mostly in urine as unchanged medicine (see section 5.2). Dose adjustment can be needed in patients with renal impairment.

GLYCOSTOM contains less than 1 mmol (23 mg) sodium per ml, i.e., sodium free.

4.5 Interaction with other medicines and other forms of interaction

The intravenous administration of any anticholinergic in the presence of cyclopropane anaesthesia can result in ventricular dysrhythmias; therefore, caution should be observed if GLYCOSTOM must be used during cyclopropane anaesthesia. If the injection is given in small incremental doses of 0,1 mg or less, the likelihood of producing ventricular arrhythmias is reduced.

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.

The simultaneous use of two or more of these may increase the risk of side effects such as dry mouth, urinary retention, and constipation. Concurrent use can also lead to confusion in the elderly.

Anticholinergic medicines can delay the absorption of other medicines given at the same time.

The simultaneous use of anticholinergic medicines and digoxin tablets that dissolve slowly can lead to that digoxin levels will be higher in serum.

Domperidone/Metoclopramide: counteracting effect on gastrointestinal activity.

Ketoconazole: Reduced absorption of Ketoconazole.

Levodopa: Absorption of levodopa may decrease.

Memantine: The effect may be amplified during simultaneous use.

Use with other medicines during anaesthesia

Glycopyrrolate as in GLYCOSTOM 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 anaesthetics (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).

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of glycopyrronium bromide in pregnant women. Animal studies are insufficient with respect to reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of GLYCOSTOM during pregnancy.

Breastfeeding

Glycopyrronium bromide is excreted in human milk, but at therapeutic doses of GLYCOSTOM no effects on the breastfed newborns/infants are anticipated.

Fertility

There are no data on how glycopyrronium bromide affects human fertility.

4.7 Effects on ability to drive and use machines

GLYCOSTOM is used in anaesthesia. Patients are not expected to drive or use machines under the influence of the medicine. Administration of GLYCOSTOM may cause drowsiness, visual disturbances and other effects that impair the ability to drive and use machines. These activities should not be performed until the patient is recovered from these undesirable effects.

4.8 Undesirable effects

a. Summary of the safety profile

Adverse reactions listed by System Organ Class. Frequencies are defined using the

following convention: frequent; less frequent; frequency unknown (cannot be estimated from the available data).

b. Tabulated summary of adverse reactions

MedDRA system organ class	**Frequency**	**Adverse reactions**
Immune system disorders	Less frequent	Severe allergic reaction, anaphylaxis, pseudoanaphylaxis
	Frequency unknown	Hypersensitivity, angioedema
Psychiatric disorders	Less frequent	Mental confusion, nervousness, insomnia
Nervous system disorders	Frequent	Drowsiness
	Less frequent	Headache, mental excitement (especially in the elderly), drowsiness, dizziness, giddiness, loss of taste
Eye disorders	Frequent	Visual disturbances
	Less frequent	Blurred vision due to mydriasis, increased ocular tension, photophobia
Cardiac disorders	Less frequent	Bradycardia, tachycardia, palpitations, dysrhythmias
Respiratory, thoracic and mediastinal disorders	Less frequent	Reduced bronchial secretions
	Frequency unknown	Nasal congestion
Gastrointestinal disorders	Less frequent	Nausea, vomiting, constipation, bloated feeling, dry mouth

MedDRA system organ class	Frequency	Adverse reactions
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 administration site conditions	Frequent	Anaphylactic reaction
	Less frequent	Weakness, pharmacologic idiosyncrasies
	Frequency unknown	Malaise

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

Symptoms

Peripheral anticholinergic effects.

Treatment

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

GLYCOSTOM known to have been administered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Quaternary ammonium antimuscarinic

ATC Code: A03AB02

Pharmacological classification: A 5.4 Cholinolytics (anticholinergics)

Glycopyrronium bromide 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.

Glycopyrronium bromide antagonizes muscarinic symptoms (e.g., bronchorrhoea, bronchospasm, bradycardia, and intestinal hypermotility) induced by cholinergic medicines such as the anticholinesterases.

5.2 Pharmacokinetic properties

Absorption

After intravenous administration, the serum concentration drops rapidly and less than 10 % is found in the serum 5 minutes after the dose is given. The effect persists for approx. 4 hours.

After intramuscular injection, maximum plasma concentration is achieved within 30 minutes and maximum effect is achieved after approximately 30-45 minutes. Vagal blockage lasts for 2 - 3 hours and the inhibitory effect on salivary secretion continues for 7 - 8 hours.

Glycopyrronium bromide is absorbed faster if injected into the deltoid muscle than if injected into gluteal muscles or vastus lateralis.

Distribution

Glycopyrronium does not cross the blood-brain barrier, and cerebrospinal fluid levels of Glycopyrronium bromide are below the detection level for up to one hour after therapeutic dosing.

Elimination

Glycopyrrolate is mostly excreted unchanged in urine, faeces, or bile.

Following intravenous or intramuscular administration, 50 % of Glycopyrronium bromide is excreted in the urine after 3 hours in non-uremic patients. Renal elimination is significantly prolonged in patients with uremia. Significant amounts are excreted via the bile. 85 % is excreted in the urine within 48 hours Approx. 80 % of the excreted amount is unchanged Glycopyrronium bromide or its active metabolites. Although the half-life of Glycopyrronium bromide is within 75 minutes, quantifiable levels may remain for up to 8 hours after administration.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid (for pH adjustment)

Sodium chloride

Water for injection

6.2 Incompatibilities

This medicine must not be mixed with other medicines except those mentioned in section 6.6.

6.3 Shelf life

24 months.

Chemical and physical in-use stability has been demonstrated for 48 hours at 25 °C.

From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Store at or below 25 ^{o}C.

For storage conditions after dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

1 ml glass ampoules with a green dot.

Pack size: 10 x 1 ml ampoules per cardboard carton.

6.6 Special precautions for disposal and other handling

To be mixed with isotonic sodium chloride, 5 % or 10 % glucose solution. The pH must not exceed 6,0 in the diluted solution.

7 HOLDER OF CERTIFICATE OF REGISTRATION

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8 REGISTRATION NUMBER

57/5.4/0729

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

8 July 2025

10 DATE OF REVISION OF THE TEXT

Not applicable