VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

Glycopyrronium Bromide 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 (heart) muscle, the sinoatrial node (part of the heart), the atrioventricular node (part of the heart), exocrine glands (such as sweat glands) and to a limited degree in the autonomic ganglia.

Thus it diminishes the volume and free acidity of gastric secretions and controls excessive secretions in the throat and top of the lungs. Glycopyrronium Bromide helps to prevent symptoms of over-secretion of mucus in the lungs.

The highly polar quaternary ammonium group of Glycopyrronium Bromide limits its passage across lipid membranes, and as such the drug is not likely to be present in the brain., in contrast to Atropine Sulphate and Scopolamine Hydrobromide, which are non-polar tertiary amines which penetrate lipid barriers easily.

Glycopyrronium Bromide 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 this causes a slowing of the gastric secretions in the stomach) and the anti-sialagogue effects (the reduction in the amount of mucus) persist up to 7 hours, periods longer than for atropine. With, intravenous injection, the onset of action is generally evident within one minute.

It is used as an adjuvant in anaesthesiology to offset some of the other more undesirable effects associated with other aesthetic products.

VI.2.2 Summary of treatment benefits

Glycopyrronium Bromide has been tested in various Clinical Trials worldwide to be effective in each of the indications stated above.

VI.2.3 Unknowns relating to treatment benefits

Based on the currently available data, no gaps in knowledge about efficacy in the target population were identified, that would warrant post-authorisation efficacy studies. Furthermore, there is no evidence to suggest that treatment results would be different in any subgroup of the target population, for any of the indications, taking into account factors such as age, sex, race or organ impairment.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	**What is known**	**Preventability**
Risk of loss of vision in patients with narrow angle glaucoma	In common with other antimuscarinics glycopyrronium bromide may cause risk of loss of vision in patients with narrow angle glaucoma; and the mechanism has been shown to block end plate nicotinic receptors resulting in the effect.	The SmPC covers such possible events and this will be monitored to ensure the warnings are adequate to prevent such occurrences. The PIL instructs patients to inform their doctor or pharmacist if they have had any adverse reaction following administration

Risk	What is known	Preventability
Worsening of symptoms in patients with myasthenia gravis	In common with other antimuscarinics glycopyrronium bromide may cause worsening of symptoms in patients with myasthenia gravis to occur; and the mechanism has been shown to block end plate nicotinic receptors resulting in the effect.	The SmPC covers such possible events and this will be monitored to ensure the warnings are adequate to prevent such occurrences. The PIL instructs patients to inform their doctor or pharmacist if they have had any adverse reaction following administration
Developing or worsening of symptoms in patients with coronary heart disease; congestive heart failure; cardiac arrhythmias; hypertension and thyrotoxicosis	In common with other antimuscarinics glycopyrronium bromide may cause worsening of symptoms in patients with cardiac or thyroid problems to occur; and the mechanism has been shown to block end plate nicotinic receptors resulting in the effect.	The SmPC covers such possible events and this will be monitored to ensure the warnings are adequate to prevent such occurrences. The PIL instructs patients to inform their doctor or pharmacist if they have had any adverse reaction following administration
Risk of ventricular arrhythmias if used during inhalation anaesthesia	In common with other antimuscarinics glycopyrronium bromide may cause arrhythmias in patients to occur.	The SmPC covers such possible events and this will be monitored to ensure the warnings are adequate to prevent such occurrences. The PIL instructs patients to inform their doctor or pharmacist if they have had any adverse reaction following administration
Inhibition of sweating: risk for patients with fever	In common with other antimuscarinics glycopyrronium bromide may cause an inhibition of sweating in patients to occur; and the mechanism has been shown to block end plate nicotinic receptors resulting in the effect.	The SmPC covers such possible events and this will be monitored to ensure the warnings are adequate to prevent such occurrences. The PIL instructs patients to inform their doctor or pharmacist if they have had any adverse reaction following administration
Use in patients with QT prolongation	Since glycopyrronium bromide may affect heart rate rhythm due to its anti-muscarinic effects, any patients with a pre-existing cardiac condition or patients with existing QT prolongation should be considered prior to the administration of the product.	The SmPC covers such possible events and this will be monitored to ensure the warnings are adequate to prevent such occurrences. The PIL instructs patients to inform their doctor or pharmacist if they have had any adverse reaction following administration
Risk of drug-drug interaction including potential effect with other anti-cholinergic and other anti-muscarinic drugs (such as antiparkinsonism agents), phenothiazines, tricyclic antidepressants, disopyramide, procainamide, quinidine, antihistamines, or narcotic analgesics such as meperidine	Since glycopyrronium bromide may interact with existing anti-cholinergic or anti muscarinic drugs, caution should be considered prior to the administration of the product	The SmPC covers such possible events and this will be monitored to ensure the warnings are adequate to prevent such occurrences. The PIL instructs patients to inform their doctor or pharmacist if they have had any adverse reaction following administration

Important potential risks

Risk	What is known
Risk of incompatibility with drugs used in anaesthetic practice	Since glycopyrronium bromide may interact with existing anti-cholinergic or anti-muscarenic drugs caution should be considered prior to the administration of the product with other anaesthetics.
Hypersensitivity reactions (anaphylactic reactions)	If the patient is allergic to any of the components of the product then it should not be taken

Missing information

Risk	What is known
Use in Pregnancy	Very limited information is available concerning pre-clinical or clinical exposure in pregnancy which is why the information is regarded as missing.
Use in children	Very limited information is available concerning clinical exposure in children which is why the information is regarded as missing. The term children covers a wide age group and a better understanding of children in the ages of 0 – 2 years and 3 – 11 would be useful in optimising the dosing and making this clear within the SPC.
Reproductive toxicity	Since glycopyrronium bromide may have an effect in pre-clinical models caution should be considered prior to the administration of the product in pregnancy.

VI.2.5 Summary of additional risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them.
An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

No additional risk minimisation activities are required. Routine pharmacovigilance activities are considered sufficient to monitor the benefit-risk profile of the product and detect any safety concerns.

VI.2.6 Planned post authorisation development plan (if applicable)

There are no studies in the post authorisation development plan.

VI.2.7 Summary of changes to the risk management plan over time

N/A