GLYCOPYRRONIUM BROMIDE

▼Seebri Breezhaler®, ▼Enurev Breezhaler® in COPD.

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ABSTRACT

Glycopyrronium bromide is an inhaled long-acting muscarinic antagonist (LAMA) approved for the relief of symptoms in adult patients with Chronic Obstructive Pulmonary Disease (COPD).

The only head-to-head trial published to date showed non-inferiority vs tiotropium but not superiority.

The average change with respect to baseline FEV_1 trough was 103 mL (glycopyrronium) *vs* 99 mL (tiotropium), but there was no clinical relevance (120 mL).

Safety profile remains inconclusive given the short duration of the trials, the chronic nature of the disease and lack of data with regard to its cardiovascular safety profile.

Indications[1]

Glycopyrroium bromide is indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD).

Mechanism of action[1]

Glycopyrromium is a long-acting muscarinic antagonist. It acts by blocking the bronchoconstrictor effect of acetylcholine on smooth muscle cells thus dilating the respiratory airways.

Posology and administration[1]

The recommended dose consists of an inhalation of the contents of a capsule (liberating a dose of 44 mcg of glycopyrronium) once daily by employing the Breezhaler inhaler, preferably at the same time every day.

Clinical efficacy

Two trials have been published comparing glycopyrronium compared to placebo (GLOW1[2], GLOW2[3]) to evaluate lung function. Glycopyrronium proved significantly more effective than placebo in FEV_1 trough values after 12 weeks of treatment, although clinical relevance remained uncertain (difference with glycopyrronium of 108 mL in GLOW1 and 97mL in GLOW2).

Only one head-to-head non-inferiority trial lasting 12 weeks has been published (GLOW5[5]) which compared the efficacy and safety profile of glycopyrronium (50 mcg once daily) to tiotropium (18 mcg once daily). There were 657 participants (73.8% men) in the trial with an average age of 63.5 years.

The results showed "non-inferiority" of glycopyrronium vs tiotropium, with average changes with respect to baseline values in FEV_1 trough of 103 mL (glycopyrronium) and 99 mL (tiotropium), but with no clinical relevance (120 mL according to the EMA criteria).

With regard to the rate of exacerbations, reductions were similar in both groups under glycopyrronium or tiotropium, with annual rates of 0.38 and 0.35 respectively, although longer trials (at least one year) are necessary to make an adequate evaluation.[5]

Safety

Adverse reactions

The most frequent adverse reactions described in clinical trials include: nasopharyngitis, insomnia, cefalea, dry mouth, gastroenteritis and urinary tract infections.[1]

The trials also describe cases of atrial fibrillation at higher rates in the groups under glycopyrronium compared to the groups under placebo.[3,7]

No more effective than tiotropium and unknown long-term safety profile

The safety profile of glycopyrronium seems similar to that of tiotropium with a similar incidence of overall adverse reactions (40.4% vs 40.6%, respectively). However, it should be taken into account that the only comparative trial was of short duration and does not allow for an adequate evaluation of the long-term safety profile.[5]

The EMA Risk Management Plan recommends post-marketing surveillance to monitor both cardiovascular and cerebrovascular events associated to glycopirronium.[7]

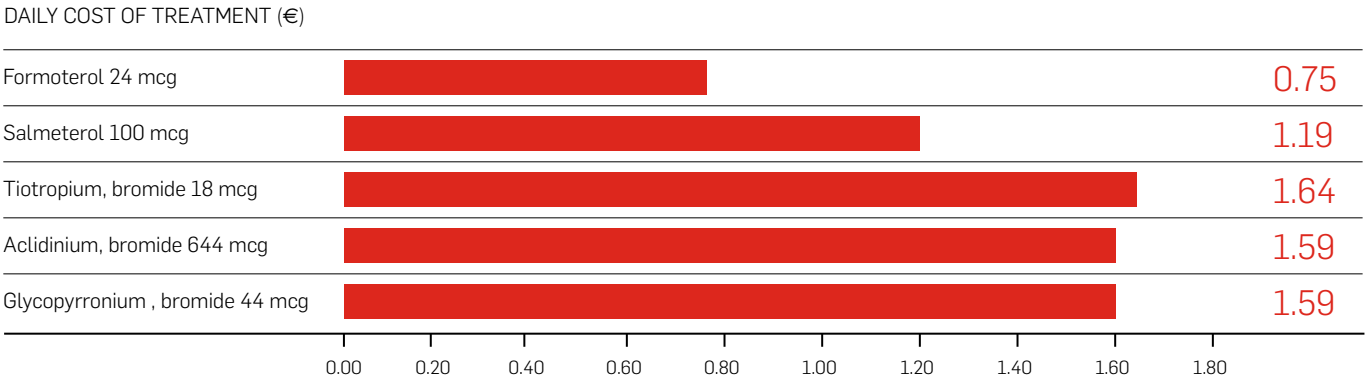
Contraindications[1]

Glycopyrronium bromide is contraindicated in cases of hypersensitivity to the active substance or to any of the excipients. As it contains lactose, patients with hereditary intolerance to galactose, Lapp lactase deficiency or problems with the absorption of glucose or galactose should not take this drug.

CLASSIFICATION

4	IMPORTANT THERAPEUTIC INNOVATION
3	MODEST THERAPEUTIC INNOVATION
2	SOME ADDED VALUE IN SPECIFIC SITUATIONS
1	**NO THERAPEUTIC INNOVATION**
0	INSUFFICIENT EVIDENCE

The qualification assigned to the drug was agreed by the Drug Assessment Committees of Andalusia, Basque Country, Catalonia Institute of Health, Aragon and Navarre. The current report is based on the available information and is susceptible to be updated according to the latest evidence. Let us remind the reader about the importance of notifying the Pharmacovigilance Centre when there are suspicions of adverse reactions to drugs.



Warnings and precautions[1]

Glycopyrronium bromide should be used with precaution in patients suffering from narrow angle glaucoma, urinary retention and with a history of cardiovascular disease.

Use in special situations[1]

Pregnancy and breastfeeding. There is no available information. Renal failure: it may be used in cases of mild to moderate renal failure. Liver impairment: no information. Children: there are no recommendations for specific use in children under 18 years.

Interactions[1]

Concomitant use of glycopyrronium bromide with other anticholinergic agents is not recommended.

EMA Risk Management Plan[7]

The EMA considers the need to carry out a post-marketing safety trial on cardio and cerebrovascular events in order to clarify the safety profile of this drug. It also considers the need for adequate representation in clinical trials of elderly patients with comorbidities or either liver or renal impairment.

Place in therapeutics

Pharmacological management of COPD is focused on reducing symptoms and/or complications. After diagnosis, treatment should be initiated progressively in relation to the severity of the obstruction and the patient's symptom profile, where bronchodilation represents the first step in the management of the disease. Inhaled bronchodilators such as long-acting ß2-agonists (LABA) and long-acting muscarinic antagonists (LAMA) constitute the basis of symptomatic management of COPD patients and permanent symptoms.[8,9]

Glycopyrronium bromide is a new LAMA for the management of COPD. There is one only head-to-head trial (GLOW5)[5] in which glycopyrronium has shown non inferiority but not superiority vs tiotropium on trough FEV1 change.

Currently, the long-term profile of glycopyrronium is still not defined as the duration of the trials was not long enough for evaluation. Taking into account the potential for adverse cardiovascular reactions, and having excluded patients with cardio and cerebrovascular risk from the trials, the EMA has recommended post-marketing follow-up. At present we are still awaiting results.

Therefore taking into account the available data on efficacy and safety this agent cannot be considered as a first line option for the management of COPD.

Presentations

Seebri breezhaler®(Novartis), Enurev breezhaler® (Ferrer) 44 mcg 30 capsules+inhaler (47.61 €)

References

A complete report on Glycopyrronium bromide can be found at: www.bit.navarra.es

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