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# OLODATEROL

## ▼STRIVERDI®, ▼RESPIMAT® FOR COPD

dtbn
DRUG ASSESSMENT REPORT
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## Nothing to puff up with pride


### ABSTRACT

**Olodaterol is a new long-acting beta2-agonists for control of asthma.**

**It has only been actively compared with formoterol in terms of improvement of lung function in a small 6-week study, without any significant differences found.**

**Its safety profile seems to be similar to that of other LABA.**

**Data supporting its effectiveness when used alone are very limited.**


### CLASSIFICATION

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

### Indications[1]

It is indicated as a maintenance bronchodilator treatment in patients with chronic obstructive pulmonary disease (COPD).

### Mechanism of action and pharmacokinetics[1]

Olodaterol is a long-acting beta2-agonists (LABA) with a fast onset of action and a duration of action of at least 24 hours.

### Posology and administration[1]

The recommended dose of olodaterol is 5mcg administered in 2 puffs once daily at the same time. The recommended dose should not be exceeded.

### Clinical efficacy

The clinical development of olodaterol included ten randomized, double-blind, placebo-controlled phase III trials,[2,3] four pivotal 48-week randomized clinical trials (RCTs) (n=3104),[4,5] four 6-week RCTs (n=429) to evaluate its bronchodilating profile and two 6-week RCTs (n=308) to evaluate its effect on endurance time during exercise.

In pivotal RCTs, the patients had moderate to very severe COPD and were allowed to continue their usual therapy, which primarily consisted of corticosteroids and tiotropium. The primary endpoints were FEV AUC (0-3 h) and FEV (12-24 h) as compared to placebo. Although statistically significant differences were obtained in pulmonary function between groups in the two endpoints, only differences in FEV AUC (0-3 h) were clinically relevant. The Transitional Dyspnea Index (TDI) was also included in two pivotal RCTs, but no statistically significant differences were observed.[5] Although patients treated with olodaterol used less rescue medication,[4] differences were not clinically relevant in terms of quality of life.[5] Both variables were used as secondary endpoints. Exacerbations could not be assessed due to the design and duration of the RCTs.

Some RCTs included an arm that received either formoterol[5] or tiotropium,[6] but the effects of these substances on lung function were not directly compared with those of olodaterol. The exception was a small 6-week trial assessing the effects of olodaterol on lung function vs formoterol, but no statistically significant differences were observed.[7] In placebo-controlled studies, olodaterol was not proven to be superior to formoterol and tiotropium in improving lung function. No comparative studies were conducted assessing other variables of clinical interest. Finally, olodaterol has not been compared directly with indacaterol, the only once-daily LABA.[8]

### Safety

#### Adverse reactions[1]

The most frequent adverse reactions included nasopharyngitis, dizziness, hypertension, rash and arthralgia. Intensity was generally mild to moderate. Although the systemic effects of LABA are generally mild, they may cause musculoskeletal tremor, insommia, palpitations, tachycardia, hypokalemia, hyperglycemia, and lengthened QTc interval.[10] Given that safety data on olodaterol are limited, it should be used with caution in risk patients.

*It does not improve dyspnoea, exacerbations, or quality of life*

#### Contraindications[1]

Hypersensitivity to olodaterol or to any of its excipients.

#### Special warnings and precautions for use[1]

Olodaterol should not be used in asthma or as a rescue therapy. If paradoxical bronchospasm occurs olodaterol therapy should be discontinued immediately and alternative therapy substituted.

LABAs may cause hyperglycemia and hypokalemia which can provoke adverse cardiovascular effects. Olodaterol should not be administered concomitantly with other medicinal products causing hypokalemia.

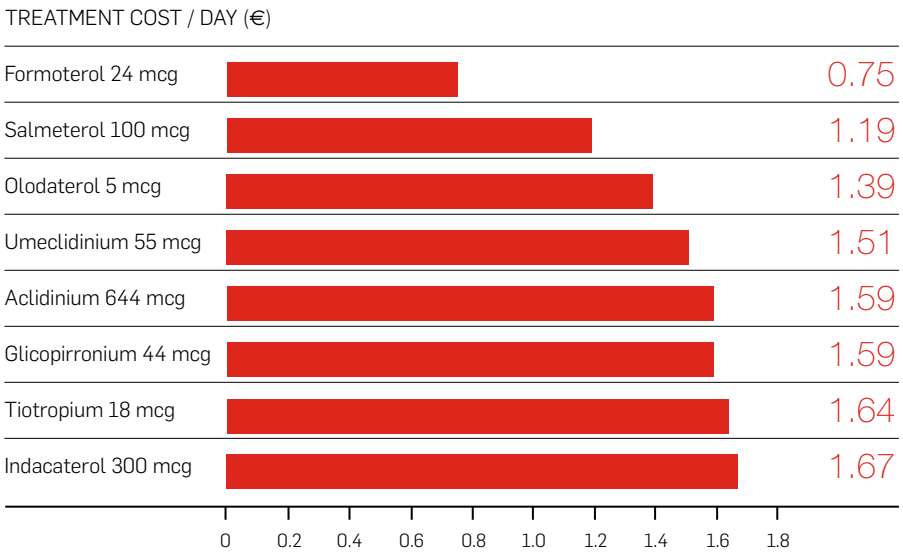
#### Usage in special situations[1]

**Pregnancy and breast-feeding:** No data available.

**Renal impairment:** Dose adjustment is not required in patients with mild or moderate renal impairment. Olodanerol should be administered with caution in patients with severe renal impairment.

**Liver impairment:** Dose adjustment is not required in patients with mild or moderate liver impairment. Olodanerol should be administe-

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.




red with caution in patients with severe liver impairment.

**Advanced age:** dose adjustment is not required.

**Patients < 18 years:** no recommendations have been published on the use of olodanerol in patients aged < 18 years.

### Drug interactions[1]

Olodanerol should only be used concomitantly with beta-blockers (including eyedrops) if there are compelling reasons for their use. In this setting, cardioselective beta-blockers could be considered, although they should be administered with caution.

Concomitant treatment with xanthine derivatives, steroids, or diuretics (other than potassium sparing ones) may potentiate any hypokalemic effect of adrenergic agonists.

## Place in therapeutics

The goal of drug therapy for stable COPD is relieving asthma symptoms, reducing the frequency and severity of exacerbations, and improving quality of life and tolerance to exercise. Treatment choice should be made on a case-by-case basis and consists of a dose-escalation scheme in accordance with the severity of symptoms and the risk of exacerbations, and by weighing adverse effects, patient's preferences and response, and the cost of the devices used.[10]

Inhaled bronchodilators are the base of drug therapy for COPD. Short-acting bronchodilators are primarily used on demand to rapidly control asthma symptoms. In patients with permanent symptoms, the treatment of choice are long-acting bronchodilators -either LABA or anticholinergics (LAMA)- alone. Concomitant use of LABA and inhaled corticosteroids is only indicated in patients with frequent exacerbations and $FEV_1$ < 50%. There is no sufficient evidence supporting the superiority of LAMA over LABA, nor a specific combination of LAMA/LABA over other combinations or over CI/LABA combinations. The effectiveness and safety of triple therapy LAMA/LABA/CI has not been investigated yet.[10]

Olodaterol is another LABA for maintenance therapy of COPD. Compared to placebo, olodaterol only improves lung function within the first hours, without statistically significant differences with formoterol and tiotropium vs placebo. Olodaterol has not been demonstrated to yield clinically relevant results in relation to dyspnea and quality of life. No direct comparative studies have been conducted comparing olodaterol vs indacaterol, the only once-daily LABA. Nevertheless, there is scant evidence on the use of olodaterol alone, as it has been used concomitantly with other medical products in clinical trials.

In light of the above, and considering that other more widely-used LABA are already available, olodaterol does not offer any therapeutic advance for the treatment of COPD.

## Presentations

Striverdi Respimat® (Boehringer Ingelheim España) 2.5mcg inhalation solution providing 60 puffs (30 medicinal doses) (€41.68)

## References

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