

MOMETASONE FUROATE

▼Asmanex Twisthaler® for asthma management

It is inhaled, but does not aspire...
for something more

Indications¹

Maintenance treatment of persistent asthma.

Mechanism of action¹

Mometasone furoate is a topical corticoid with local anti-inflammatory effects.

Dosage and administration¹

Mild to moderate persistent asthma: the initial recommended dose for the majority of patients is 400 mcg once daily. Clinical data available show that better control of asthma is obtained when the drug is applied at night time. Some patients reach an adequate control with 400 mcg daily in two doses (200 mcg/12h). In some patients dose reduction to 200 mcg daily at night time proves effective for management. **Severe asthma:** the initial recommended dose is 400 mcg/12 h (maximum dose recommended).

Once symptoms are under control, it should be adjusted to the minimum effective dose.

It should not be used as a rescue medication for the relief of acute symptoms and should be used regularly to maintain the therapeutic benefits even when the patient is asymptomatic.

In patients accustomed to the Turbuhaler® device, the use of Twisthaler® Turb may produce errors in dosage as they are very similar but function differently, and if used in the same way the dose may be duplicated.

Clinical efficacy

The majority of the studies were carried out in patients over 12 years with mild to moderate persistent asthma under previous therapy with inhaled corticoids and with a duration of between 4 and 12 weeks.⁸⁻¹² They all were trials studying superiority except for one non-inferiority trial.¹²

The primary endpoint evaluated in the majority of the studies was the forced expiratory volume in one second (FEV₁) with respect to baseline values, expressed in absolute values (mL) or in percentage (%). Only in the non-inferiority trial was maximum expiratory flow (MEF) measured. In the majority of the studies there was no predefined difference to establish clinical relevance.

Momethasone was compared to budesonide in two multicenter RCTs.^{9,10} In both studies a statistically significant improvement was found

though of questionable clinical relevance in regard to the change in FEV₁ with respect to baseline values. Momethasone 200 mcg/12h or 400 mcg once daily was compared to budesonide 400 mcg/12h. FEV₁ values obtained were 160±30 mL and 160±30 mL compared to 60±30 mL.⁹ Analogously, differences were observed between momethasone 440 mcg once daily and budesonide 400 mcg once daily (190±40 mL compared to 30±40 mL, respectively).¹⁰ It should be taken into account that this last study was designed to detect a difference of 200 mL in the average variation of FEV₁ with respect to baseline values, and the dose of budesonide was not equipotential. On the other hand, the scarce effect obtained with budesonide FEV₁ (30 y 60 mL) is remarkable.

No advantages vs beclomethasone and budesonide while costing twice as much

In comparison to fluticasone there is one superiority trial¹¹ which did not show statistically significant differences in the primary endpoint (FEV₁) between the total daily doses of 400 mcg and 800 mcg momethasone and 500 mcg fluticasone. There is also a non-inferiority trial¹² where the primary endpoint was the average variation in MEF with respect to baseline values. The results indicate that 400 mcg momethasone-DPI was "not inferior" to 500 mcg fluticasone-DPI, both taken twice daily. However, the low quality of the trial and the analysis performed only by "intention to treat" but not "by protocol" undermines the results which should be interpreted with caution.

Safety

Adverse reactions

In the controlled clinical trials with placebo, oral candidiasis was very frequent (>10%) in the group under therapy with 400 mcg twice



DRUG ASSESSMENT REPORT

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ABSTRACT

Mometasone furoate is an inhaled glucocorticoid indicated in the maintenance treatment of persistent asthma

No advantage has been shown in terms of relevant clinical outcomes with respect to other inhaled corticosteroids.

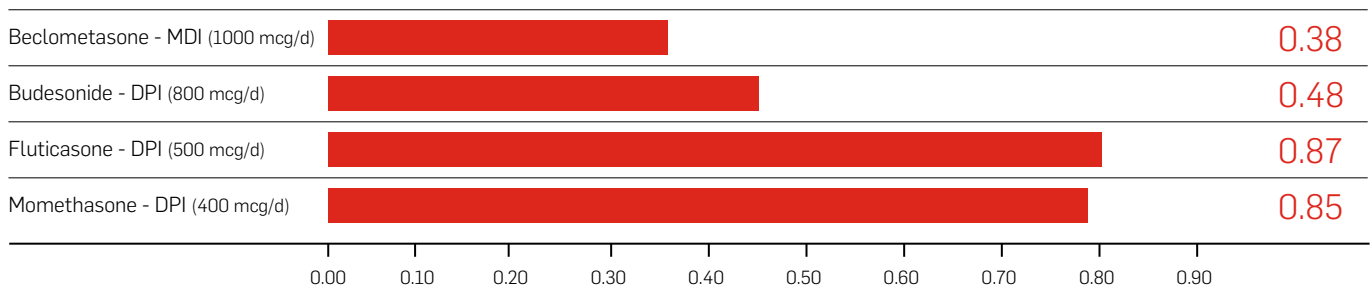
The profile of adverse effects and the administration regimen of mometasone are similar to that of other inhaled corticoids.

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 Navarra. 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.

DAILY COST OF TREATMENT (€)



daily. The incidence of oral candidiasis was related with the increase in dose and the time of exposure.³ Other frequent adverse reactions (1-10%) related to treatment were pharyngitis, cefalea and dysphonia.¹

The incidence of adverse effects related to treatment was lower with mometasone-DPI administered once daily compared to two doses (17-19% vs 20-28%) and increases with the dose.

Contraindications¹

Hypersensitivity to the active substance or to any of the excipients (lactose).

Warnings and precautions¹

- Risk of adrenal insufficiency after switching from oral corticoids to inhaled mometasone. In these cases it is recommended to taper off systemic corticosteroids with precaution.
- Possibility of clinically relevant adrenal suppression especially after prolonged treatment at high doses and at doses higher than recommended. This possibility should be considered during stressful periods or in elective surgery, situations that may require supplementary systemic corticoids.
- Paradoxical bronchospasm may occur in association with mometasone use..
- Avoid use or if necessary employ precaution in patients with active or inactive tuberculosis affecting the respiratory tract, or untreated fungal, bacterial or viral systemic infections or herpes simplex affecting the eye.
- This drug can produce a reduction in the growth rate in children and adolescents.
- Treatment should not be abruptly discontinued.

Use in especial situations¹

Pregnancy and breastfeeding: Given the lack of adequate studies, it should not be used during pregnancy or lactation. **Children:** No information in children under 12 years of age. **Elderly patients over 65 years:** No dose adjustments required.

Interactions¹

There is a possibility of greater systemic exposure to mometasone when administered concomitantly with potent CYP3A4 isoenzyme inhibitors (for example, ketoconazole, itraconazole, nelfinavir, ritonavir).

Place in therapeutics¹

Inhaled corticoids are elective treatments in persistent asthma given their efficacy in both the reduction of symptoms and the improvement of lung function, and also the reduction of exacerbations.

Low-dose corticoids, equivalent to 400 mcg of budesonide, are effective in the majority of patients, although some patients can benefit from higher doses, especially in patients with severe asthma.¹² In the case of beclometasone, budesonide, and fluticasone there is ample evidence on their efficacy and long-term safety while the evidence for mometasone is still more limited.

According to the NICE¹⁹ guidelines on inhaled corticoids in the management of asthma in adults and children over 12 years, it could be reasonable to assume that there are no relevant differences in terms of efficacy among the different inhaled corticoids available both at low and high doses. Low-dose corticoids produce less systemic adverse

effects. If the different inhalers are timely used there is little difference in clinical efficacy. Corticoids at high doses can lead to an increase in the risk of systemic adverse effects that could be related to the pharmacokinetics, the properties of the inhaler and other factors that may affect the deposit of the drug in the lungs.

At equivalent doses there are few differences in efficacy and adverse effects between inhaled corticoids and it is appropriate to use the lowest effective dose.

The available information does not show superiority of mometasone compared to other inhaled corticosteroids in terms of relevant clinical results, and therefore it is recommended to keep using other inhaled corticoids with wider evidence and cheaper price.

Presentations

Asmanex Twisthaler® (Merck Sharp and Dohme) inhalation powder, 200 mcg 60 doses (29.07 €), 400 mcg 60 doses (51.14 €)

References

A complete report on Mometasone furoate can be found at: www.bit.navarra.es