Budesonide/formoterol Easyhaler®: Dose consistency under simulated real-life conditions

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INTRODUCTION

Easyhaler® is a multi-dose Dry Powder Inhaler (DPI) for asthma and COPD patients designed to be simple and easy to use. Budesonide/formoterol (BF) Easyhaler has been developed and introduced to the market in order to complement the Easyhaler® product portfolio. Based on in vitro studies and in vivo pharmacokinetic data, BF Easyhaler products, BG4/5, 150/4/5 and 300/4/5, were shown to be therapeutically equivalent with the corresponding Symbicort® Turbohaler® products. We tested the in vitro drug delivery characteristics, delivered dose (DD) accuracy and the particle dose (FPD) of new BF Easyhaler® multidose DPI (Orion Corporation Orion Pharma, Finland) under simulated real-life conditions.

AIMS

The studies aimed to confirm in vitro drug delivery characteristics, DD and FPD of BF Easyhaler as a function of inhaler life and after the exposure to stress tests (moisture, dropping, vibration and freezing/thawing).

METHODS

We used commercially available BF Easyhaler products containing 80/4.5, 150/4.5 and 300/4.5 pg per dose of budesonide and formoterol. A total of 12 Inhalers from two batches of all strengths were used when confirming the dosing, through the inhaler; three Inhalers for DD and FPD, respectively. Four Inhalers from one batch of all strengths were used when studying the effect of moisture; two Inhalers for DD and FPD. Six Inhalers from one batch of middle strength were used to study the effect of freezing/thawing; three Inhalers for DD and FPD. Another four Inhalers from one batch of all strengths were used to study the effect of dropping (includes the end of labelled amount of doses); two Inhalers for DD and FPD. Finally, a total of 8 Inhalers from two batches of all strengths were used to study the effect of vibration; two Inhalers for DD and FPD.

Delivered dose

The DD from each inhaler was determined by using sampling apparatus and procedure described in the European Pharmacopoeia. Four times an air was drawn through the inhaler at a flow rate corresponding 4 kPa pressure drop across the inhaler. The amount of active drug collected into the sampling apparatus was determined by high performance liquid chromatography (HPLC).

Fine Particle Dose (FPD)

FPD (λ=3 μm) was determined by using a next generation Impactor (NGI) equipped with a preseparator according to the procedure described in the European Pharmacopoeia. For each Inhaler 4 times an air was discharged into the NGI at flow rate corresponding 4 kPa pressure drop across the inhaler.

RESULTS

Delivered Dose and Fine Particle Dose

DD and FPD doses analyzed through Easyhaler life time remained stable (Fig. 1), enabling patients to inhale the correct dose throughout the container life. The effect of moisture on DD and FPD is shown on Fig. 1. Further, freezing and thawing did not affect either DD or FPD results (Fig. 1). Dropping the device from one meter height did not influence DD (Fig 2); of either budesonide or formoterol. Similar results were obtained for FPD (results presented as NGI stage by stage in Fig 3); and no breakages of the Inhaler occurred. Vibration of the inhaler did not influence DD (Fig 2) or either budesonide or formoterol. Virtually identical results were obtained for FPD (results presented as NGI stage by stage in Fig 3).

CONCLUSIONS

• DD and FPD remain stable through inhaler life.
• Environmental moisture, dropping, vibration and freezing/thawing did not affect the performance.
• DD and FPD doses are not affected by moisture and freeze-thaw cycles.
• Dropping and vibration do not affect DD or FPD, or result in breakage of the Inhaler.
• In vivo performance of Budesonide/Formoterol Easyhaler confirms reliable dosing.
• Easyhaler is shown to be a robust in dosing accuracy and is a viable inhaler for treatment of patients with asthma and COPD.

REFERENCES

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