CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

205641Orig1s000

RISK ASSESSMENT and RISK MITIGATION REVIEW(S)

Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Final Risk Management Review

Date:	February 20, 2014
Reviewer(s):	Kendra Worthy, Pharm. D., Division of Risk Management (DRISK)
Team Leader	Reema Mehta, Pharm. D., M.P.H., DRISK
Division Director	Claudia Manzo, Pharm. D., DRISK
Drug Name(s):	Asmanex HFA (mometasone furoate)
Therapeutic Class:	Corticosteroid
Dosage form:	metered dose inhaler
Application Type/Number:	NDA 205641
Applicant/sponsor:	Merck
OSE RCM #:	2013-1602

1 INTRODUCTION

This review documents the Division of Risk Management (DRISK) evaluation of the need for a Risk Evaluation and Mitigation Strategy (REMS) for Asmanex HFA [mometasone fuorate (MF)] metered dose inhaler (MDI), NDA 205641.

The application was initially considered a new molecular entity (NME) but was later reclassified as a 505(b)(1) for a non-NME[1].

2 BACKGROUND

Asmanex HFA MDI is a corticosteroid administered by oral inhalation at a dose of 2 inhalations of 100mcg or 200mcg twice daily. MF is considered to have potent anti-inflammatory activity. The proposed indication is for maintenance treatment of asthma as prophylactic therapy in patients 12 years of age and older.

MF has been approved as Asmanex Twisthaler dry powder inhaler (DPI), 110 and 220mcg, since 2005. In 2008, the DPI formulation was subsequently extended to include patients aged 4 years and older.

Dulera HFA (mometasone furoate/ formoterol), a long-acting beta-agonist (LABA), was approved in 2010. It is available as 200mcg/10mcg and 400mcg/10mcg strengths. Dulera HFA was approved with a REMS that was required for the entire LABA class for the risk of asthma-related deaths, intubations, and hospitalizations associated with the use of LABAs. The originally approved REMS consisted of a Medication Guide, a communication plan, and a timetable for submission of assessments. The Agency internally agreed in June 2012 that the REMS for LABAs were no longer required[2]. In 2012, the Agency issued a complete response (CR) for this formulation for a COPD indication.

Upon the approval of Dulera HFA, the Agency requested that the Sponsor consider development of the HFA mometasone monotherapy- to which they agreed[1]; this NDA application is the subject of this review.

3 MATERIALS REVIEWED

- DPARP Clinical Midcycle slides dated November 25, 2013, Kim Witzmann, Medical Officer.
- DRISK REMS Elimination review of Dulera dated May 8, 2013, Yasmin Choudhry, Medical Officer.

4 OVERVIEW OF CLINICAL PROGRAM

[1] DPARP Clinical Midcycle slides dated November 25, 2013, Kim Witzmann, Medical Officer.

[2] DRISK REMS Elimination review of Dulera dated May 8, 2013, Yasmin Choudhry, Medical Officer.

The DPARP medical officer noted that the sponsor identified eight studies in support for the efficacy of Asmanex HFA. The pivotal studies for this application (P04334 and P04431) were the same pivotal trials used for Dulera HFA. The remaining six studies identified by the Sponsor are from the mometasone monotherapy program in the mid-'90s, which utilized the older formulation. The Agency confirmed with the sponsor that the sponsor would not need to submit additional studies for this NDA[3].

4.1 SAFETY CONCERNS

At total of 4015 asthma patients (≥12yo) have received doses of MF across the entire program. There were five total deaths; two from pivotal studies already reviewed, one in the bone mineral density study, and two others from a study in steroid-dependent patients[3]. The medical officer notes that there do not appear to be any significant safety differences between the older and newer formulations of MF. The most common adverse events were influenza, nasopharyngitis, sinusitis, and headache.

5 RISK MANAGEMENT PROPOSED BY APPLICANT

The sponsor did not submit a proposed REMS or proposed risk management plan with this application.

6 DISCUSSION

At the midcycle review, the safety profile of Asmanex HFA was considered acceptable by the clinical reviewer; the clinical reviewer is not recommending a REMS at this time. The safety profile is consistent with the known safety profile for Asmanex Twisthaler and Dulera HFA and no new safety issues were identified.

MF was previously approved under a REMS as part of a combination product with a LABA (Dulera); however, the Agency internally agreed in June 2012 that the REMS for LABAs was no longer required. Furthermore, there are no REMS required for the single entity of MF or any inhalation corticosteroids.

7 CONCLUSION AND RECOMMENDATIONS

In conclusion, at this time, risk mitigation measures beyond professional labeling are not warranted for Asmanex HFA (MF). Asmanex HFA has proven efficacy for maintenance treatment of asthma as demonstrated by the clinical program. The safety profile for Asmanex HFA is consistent with the known safety profile for comparable approved products. Thus, the benefit-risk profile for Asmanex HFA is favorable and the risks can be mitigated through professional labeling.

Should the Division have any concerns or questions, or feel that a REMS may be warranted for this product, please contact DRISK.

[3] DPARP Clinical Midcycle slides dated November 25, 2013, Kim Witzmann, Medical Officer.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

KENDRA C WORTHY
02/19/2014

CLAUDIA B MANZO
02/19/2014
concur