MEMORANDUM

NDA:	20-762 S-(b) (4)
Application Type:	(b) (4) Supplement
Sponsor:	Schering-Plough
Drug:	Nasonex™ (Mometasone furoate)
Submission Date:	March 19, 2010
Indication:	Treatment of pediatric nasal polyps
Reviewer:	Ying Fan, Ph.D.
Team Leader (acting):	Yun Xu, Ph.D
Memo Date:	May 6, 2010

Introduction

The sponsor Schering-Plough is submitted an (b) (4) supplement to NDA 20-762. NASONEX® (mometasone furoate) Nasal Spray is currently approved for the treatment of nasal polyps in patients 18 years of age and older. This supplemental NDA (b) (4) for the treatment of nasal polyps in patients 6 years to < 18 years of age.

Nasonex (50 mcg intranasal spray) was first approved on October 1, 1997, and is currently approved for the treatment of symptoms of seasonal and perennial allergic rhinitis (SAR and PAR) in patients ≥ 2 years, the prevention of SAR in patients ≥ 12 years, and the treatment of nasal polyps in patients ≥ 18 years. At the time of approval of the nasal polyp indication, a nasal polyp trial in pediatric patients ≥ 6 years was required as a post-marketing commitment (evaluation in children < 6 years was waived due to the low incidence of nasal polyps in this age group).

This submission includes a clinical overview and the clinical study report P04292. This randomized, double blind, placebo controlled trial primarily assessed the safety in the specified population. The primary endpoint was the change from baseline to last visit in the 24-hour urinary free cortisol level.

MF Nasal Spray Nasal Polyps Pediatric Study Design

This study was primarily a safety study. The primary study variable was the change from Baseline to last visit in the 24-hour urinary free cortisol level. A key secondary endpoint was the 24-hour urinary free cortisol level corrected for creatinine. The 24-hour urinary free cortisol measurement is widely accepted and is one of the most sensitive methods for

determining HPA-axis integrity. Other safety assessments included evaluations of adverse events (AEs), vital signs, and laboratory measurements. Physical examinations were to be performed at the screening and Month 4 visits. Efficacy parameters were considered secondary and included change from Baseline in bilateral polyp size (sum of the left and right nasal fossa grades), change from Baseline in each subject-assessed diary symptom score (nasal congestion/obstruction, anterior rhinorrhea/post-nasal drip, loss of sense of smell), and the investigator's evaluation of therapeutic response.

Selection of Doses in the Study
Eligible subjects from the age of 6 years to <12 years received one of the following randomized, double-blind (to treatment but not regimen, ie, QD versus BID) treatment assignments (in a 4:4:1:1 ratio) for the 4-month treatment period:

• MFNS 100 mcg (50 mcg/spray, one spray/nostril) QD
• MFNS 100 mcg (50 mcg/spray, one spray/nostril) BID
• Placebo (one spray/nostril) QD
• Placebo (one spray/nostril) BID

Eligible subjects from the age of 12 years to <18 years received one of the following randomized, double-blind (to treatment but not regimen, ie, QD versus BID) treatment assignments (in a 4:4:1:1 ratio) for the 4-month treatment period:
• MFNS 200 mcg (50 mcg/spray, 2 sprays/nostril) QD
• MFNS 200 mcg (50 mcg/spray, 2 sprays/nostril) BID
• Placebo (2 sprays/nostril) QD
• Placebo (2 sprays/nostril) BID

The MFNS doses of 100 mcg QD for pediatric subjects 6 to <12 years of age and 200 mcg QD for pediatric subjects 12 to <18 years of age are approved doses for allergic rhinitis for this worldwide commercially available drug. The MFNS 100 mcg BID and 200 mcg BID doses were included in this study because the treatment of nasal polyps is generally twice the dose prescribed for allergic rhinitis.

Reviewer's Comments:
The Division of Clinical Pharmacology 2 (DCP2) has reviewed this NDA for filing purpose. This NDA is fileable from a clinical pharmacology perspective.

The (b) (4) dose in this application (nasal polyps) is doubled dose of the approved allergic rhinitis indication down to 2 yrs of age. There is no HPA-axis study with this doubled dose in pediatric patients, If this study is considered as a dedicated HPA-axis study, then the following deficiencies was found with the study design:

1. Measured after 4 months, not after 6 weeks as recommended in the Guidance (*Allergic Rhinitis: Clinical Development Programs for Drug Products*).

2. No PK assessment

3. No positive control.

4. No significant difference between the treatment groups and placebo.

5. The number of subjects is not sufficient.

Based on the discussion on Filing meeting held on May 3, 2010, this study should not be considered as a dedicated HPA-axis study. It should be mainly considered as an (b) (4) safety study (b) (4) the indication of treatment of nasal polyps in patients 6 years to < 18 years of age. Therefore, we do not have comments from clinical pharmacology perspective at this time. Since this study is not considered as a dedicated HPA-axis study, we will not review this study since there is no PK measurement in the study.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20762	SUPPL (b) (4)	SCHERING PLOUGH HEALTHCARE PRODUCTS INC	NASONEX NASAL SPRAY (MOMETASONE FUROATE)

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