STATISTICAL ANALYSIS PLAN

Drug Utilization of Pirinase Hayfever Relief for Adults 0.05% Nasal Spray for Allergic Rhinitis Symptoms

Document Status: Final

Version: 1.0

Date: 03 May 2018

SIGNATURE PAGE

Author:
Name: PPD **Ph.D.**
Title: Biostatistician
FMD K&L Inc.

PPD
Signature
Date: PPD

Reviewer:
Name: PPD **Ph.D.**
Title: Director, Biostatistics
FMD K&L Inc.

PPD
Signature
Date: PPD

Approval

Sponsor Representative:
PPD
Title: Project Manager
Concentrics Research

PPD
PPD
Date: PPD

TABLE OF CONTENTS

Abbreviation	Term
CI	Confidence Interval
GSKCH	GlaxoSmithKline Consumer Healthcare
HIV	Human Immunodeficiency Virus
MHRA	Medicines and Healthcare Products Regulatory Agency
QR	Quick Response
SAP	Statistical Analysis Plan
SD	Standard Deviation
TLF	Tables, Listings, and Figures

1. INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) has required a post-approval commitment from GlaxoSmithKline Consumer Healthcare (GSKCH) for Pirinase Hayfever Relief for Adults 0.05% Nasal Spray.

Specifically, MHRA has required this study to evaluate consumer compliance with the product labelling of Pirinase Hayfever Relief for Adults 0.05% Nasal Spray over at least 2 allergy seasons for the treatment of seasonal allergic rhinitis including hayfever. The purpose is to obtain real-world information on how consumers are complying with the product labelling. This study will coincide with the launch of Pirinase Hayfever Relief for Adults 0.05% Nasal Spray in the United Kingdom. This Statistical Analysis Plan (SAP) is based on the final study protocol dated March 8, 2016.

1.1 STUDY OBJECTIVES

The objective of this study is to evaluate if consumers comply with key warnings and directions on the outer label for selection and use of Pirinase Hayfever Relief for Adults 0.05% Nasal Spray.

1.1.1 Primary Objective

There are 5 primary objectives of this study, listed as follows:

1. To assess if consumers of the correct age use the product: Ages 18 and older
2. To assess the correct frequency of use: No more than 2 sprays in each nostril per day
3. To assess reduction of dose: If symptoms improve, 1 spray in each nostril per day
4. To assess if a physician is consulted before use: if a woman is pregnant or breastfeeding
5. To assess if a physician is consulted: If symptoms have not improved after using for 7 days, a doctor is consulted

1.1.2 Secondary Objective

The two secondary objective of this study are as follows:

1. To assess if consumers do not use the drug if they are taking medications for Human Immunodeficiency Virus (HIV)
2. To assess if a physician is consulted: Not used more than 1 month continuously without consulting a doctor

1.2 SUMMARY OF THE STUDY DESIGN

This study is an online survey. Consumers who have purchased and used the product will opt into an online survey by scanning a quick response (QR) code on the product package labelling or through an e-mailed invitation to those who have purchased the product at a Boots Pharmacy, which will also include a link to the survey. The study timeframe is February 15, 2016 to March 31, 2018, approximately 2 calendar years so that data from at least 2 allergy seasons for the treatment of seasonal allergic rhinitis including hayfever are included. The entire study is conducted online. There is no study visits. More detailed information of the list of specific tasks for this study is given in protocol.

2. STUDY ENDPOINTS

2.1.1 Primary Endpoints

Primary endpoints are comprised of the proportion of consumers who comply with each of the five primary objective endpoints, namely:

1. Proportion of consumers with 18 years of age or older.
2. Proportion of consumers who don't exceed 2 sprays/nostril per day.
3. Proportion of consumers whose dose is reduced to 1 spray/nostril per day if symptoms improve.
4. Proportion of female consumers who consulted a Doctor before using the drug if pregnant or breastfeeding.
5. Proportion of consumers who consulted a Doctor if symptoms did not improve after 7 days of use.

2.1.2 Secondary Endpoints

Secondary endpoints are comprised of the proportion of consumers who comply with each of the two specified secondary objective endpoints below:

1. Proportion of consumers who don't use the drug because of taking HIV medications.
2. Proportion of consumers who consulted a Doctor if medication is used for more than 1 month continuously.

2.1.3 Exploratory Endpoints

Demographic information collected are listed below:

1. Gender
2. Age
3. Race
4. Education
5. Household purchase information (primary purchaser or other)

Additional profiling information collected are listed below:

1. How long they have had allergies
2. What type of allergies they have
3. Typical allergy symptoms
4. How often do they see their doctor

3. SAMPLE SIZE AND STATISTICAL POWER CONSIDERATIONS

1,537 consumers were planned to complete the survey. No targeting or enrichment for age, gender, and social backgrounds will be conducted. The demographics will be reported for those who choose to enter the online survey. For the threshold of 80% for success, this sample size of 1537 achieves at least 91% power with an assumed compliance rate of 83.3% for each of these five primary endpoints, and the significance level of 0.05 using a two-sided exact binomial test.

4. STATISTICAL ANALYSIS

4.1 GENERAL STATISTICAL CONSIDERATION

All descriptive statistics for continuous variables will be reported using mean, standard deviation (SD), median, minimum and maximum. Categorical variables will be summarized as number and percentage of consumers.

All summary statistics will be reported with the precision as described in Table 1.

Table 1: Reporting Precisions for Summary Statistics

Statistic	Degree of Precision
n	Integer (no decimal digit)
Mean, Median	One more decimal place than the raw data.
Standard deviation	Two more decimal places than the raw data.
Minimum, Maximum	The same as the raw data.
Percentage	One decimal place, except for 100% and 0% where no decimal will be reported (as written here).

4.2 ANALYSIS POPULATION

All consumers set and full analysis set are defined for the purpose of analysis.

4.2.1 All Consumers Set

All consumers set includes all consumers who scanned QR code or clicked on survey link.

4.2.2 Full Analysis Set

The full analysis set is defined as all consumers who signed the Participation Agreement and did not answer "yes" to Q1A, Q1B, Q1C or left these questions blank.

4.2.3 Protocol Deviations

Not Applicable.

4.3 DISPOSITION

A disposition of consumers includes the count and the percentage of consumers in each of the following categories:

- All consumers set (consumers who clicked the survey)
  - All consumers who started the survey (consumers who responded to any of screening questions).
    - Incomplete screening (consumers who started the survey but didn't answer all screening questions)
    - Screen Fails (consumers who answered all screening questions [QA, QB, Participation Agreement, and Q1A, Q1B, Q1C] but did not qualify for the study)
    - Full analysis set
      - Consumers who answered any of the questions from 2 to 10
      - Consumers who answered any of the questions from 11 to 12

Listing of consumers who are not included in the full analysis set will be generated.

4.4 DEMOGRAPHICS

Demographics (gender, age, age group, race, education, household purchase information) will be summarized in all consumers set population using descriptive statistics. Continuous demographic such as age will be summarized with continuous descriptive statistics: mean, standard deviation (SD), median, minimum and maximum. Categorical variables including gender, age group, and race will be analyzed using discrete summary statistics (frequency and percentage).

Listing of demographic information will be generated for full analysis set.

4.5 PRIMARY ANALYSES

Primary endpoints (defined in Section 2.1.1) will be analyzed individually in full analysis set, and no adjustment for multiple comparisons will be performed. The compliance rate

for each of the five primary endpoints will be reported and its two-sided 95% confidence limit will be computed by using the Clopper-Person exact method. The endpoint will have met the threshold for success if the lower bound of the 2-sided 95% exact confidence interval (CI) is at least 80%.

Listing of consumers for each of primary endpoints will be reported in full analysis set.

4.6 SECONDARY ANALYSES

Secondary endpoints (defined in Section 2.1.2) will be analyzed individually in full analysis set, and no adjustment for multiple comparisons is performed. The compliance rate for each of the secondary endpoints will be reported and its two-sided 95% confidence limit will be computed by using the Clopper-Pearson exact method. There are no success thresholds set for secondary endpoints.

Listing of consumers for each of secondary endpoints will be reported in full analysis set.

4.7 EXPLORATORY ANALYSES

Descriptive summary will be provided for the following exploratory endpoints for the full analysis set, how long they have had allergies, what type of allergies they have, typical allergy symptoms, and how often they see their doctor.

Listing of consumers for exploratory endpoints above will be reported in full analysis set.

5. STATISTICAL SOFTWARE

All statistical analyses will be performed using SAS 9.4 version.

6. HANDLING MISSING DATA

The online survey will provide an audit trail so that data entry can be further reviewed or investigated, if needed. Programmed edit checks will be generated automatically, as the data is being entered into the system (e.g. the consumer will be restricted from proceeding in the survey until the previous question is answered). There will be no formal query resolution and no imputation for any missing data. Missing data will be excluded from the analysis.

7. PROGRAMMING SPECIFICATIONS

The rules for programming derivations and dataset specifications are provided in separate database specification documentations.

8. MOCK TABLES, LISTINGS AND FIGURES (TLF)

The study TLF shells will be provided in a separate document that will display content and format of all tables and listings in detail. There are no figures planned.