

From: Sweeney, Colleen [<mailto:Colleen.Sweeney@fda.hhs.gov>]
Sent: Monday, August 22, 2016 5:49 PM
To: Margaretten, Nadine
Cc: Steele, Matthew; Khurana, Taruna
Subject: RE: STN: 125592/0 Information Request regarding clinical items

Dear Dr. Margaretten,

We have the following requests for additional information regarding your biologics license application (BLA):

1. The following comments pertain to data from pregnancies that occurred during conduct of studies P012, P014, P001, P015 and P003:
 - a. For each pregnancy that occurred, please provide the amount of time female subjects took the study treatment (MK 82-37 or placebo) while pregnant.
 - b. For each study, please clarify whether female subjects were provided instructions on whether to discontinue the study drug if a pregnancy occurs. If they were, please provide those instructions.
2. We request the following additional analyses of the P001 study results:
 - a. Please perform a sensitivity analysis on the primary efficacy endpoint that imputes missing endpoint values for subjects in both study groups (treatment and control) using the subject-specific baseline Total Combined Rhinitis Score TCRS (at the beginning of the trial) .
 - b. Please provide the sensitivity analysis results (i.e., the treatment differences relative to placebo and the corresponding 95% confidence intervals) for all subjects as well as by age subgroups (<18 years of age, 18-65 years of age, and ≥65 years of age).
 - c. Please provide the results of the analyses (analysis of covariance, longitudinal data analysis, multiple imputation method, and last observation carried forward) shown in Table 11-4 by age subgroups listed above.
 - d. Please provide the 95% confidence intervals of the treatment differences relative to placebo for all of your secondary endpoints by age subgroups listed above.
3. For study P015, you provide an efficacy analysis for the TCRS for different time points in the trial (illustrated in panels 9-5 and 9-6 in the clinical study report). Please provide the percent treatment difference relative to placebo with the corresponding 95% confidence interval for each time point. Please perform a sensitivity analysis as requested in Item #2a for these time points.

Please submit the above information as an amendment to STN 125592/0.

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