RECORD OF TELEPHONE CONVERSATION

Submission Information

Application Type	BLA
STN	125614/0.0
Review Office	OVRR
Applicant	GlaxoSmithKline Biologicals / Lic. # 1617
Product	Zoster Vaccine Recombinant, Adjuvanted

Telecon Details

Telecon Date/Time	05-OCT-2017 11:50 PM
Author	NAIK, RAMACHANDRA
FDA Originated?	Yes
Communication Categories	IR - Information Request
Telecon Summary	Comments on the post-licensure Targeted Safety Study
FDA Participants	Ramachandra Naik, Carmen Collazo-Custodio and Michael Smith
Applicant Participants	Jody Gould and Norris Pyle

Telecon Body: CBER's IR e-mail message pasted below.

RECORD OF TELEPHONE CONVERSATION

From: Naik, Ramachandra
Sent: Thursday, October 05, 2017 11:50 PM
To: 'Jody Gould' <jody.a.gould@gsk.com>
Cc: Collazo, Carmen <Carmen.Collazo@fda.hhs.gov>; Smith, Michael (CBER) <Michael.Smith2@fda.hhs.gov>; Norris Pyle <norris.h.pyle@gsk.com>
Subject: STN 125614/0 Shingrix BLA: Comments on the Targeted Safety Study

Dear Dr. Gould,

Thank you for your responses regarding the Targeted Safety Study (TSS), submitted in amendment 47 (dated 9/26/2017). We find your responses generally acceptable, but have the following comments:

1. Please revise the TSS to identify and capture cases of optic ischemic neuropathy (OIN). The reasons for this are that OIN adverse events (AEs) were imbalanced in the trial data; the arteritic and non-arteritic subtypes were not differentiated; ICD-10 codes for OIN do not differentiate between arteritic and non-arteritic subtypes; and a negative biopsy for temporal arteritis does not exclude arteritic pathology due to possible skip lesions.[1] It would be acceptable to conduct sub-analyses looking at the OIN subtypes, if these data are available.

    a. Please clarify how you will identify OIN as an MAE. Will this include identifying individuals with OIN ICD-10 initial visit codes (H47.01X)?

    b. You identified 42 days after vaccination as the risk window for OIN MAE, but in the clinical trial data, one of the three cases occurred on day 48. We recognize that you will conduct sensitivity analyses utilizing different risk windows, but we recommend that you utilize a longer risk window (e.g., 60 days).

2. Please include a glossary in your protocol to define terms such as “case definition” (utilized for adjudicating cases based on medical chart data) and “claims-based, or electronic healthcare database case definition or algorithm” (for identifying cases of interest in the database).

3. We agree with your decision to not exclude individuals with previous Zostavax vaccination because of the difficulty of identifying these individuals with available data over long periods of time in a healthcare database, and we agree with your decision to include individuals in the study population who are continuously registered in the selected database(s) for at least 1 year, and for whom a medical history is available for at least 12 months before the date of vaccination with HZ/su (1st dose). Please specify if any clean window (a prespecified time period prior to vaccination wherein there should be no claims with the outcome of interest) or exclusion criteria will be used in this study to

help ensure that incident cases are identified, and possible confounders are removed, based on available information during the study's data observation period. For example, will you identify patients having a previous diagnosis of OIN, a Zostavax vaccination, or a diagnosis of herpes zoster within the year prior to vaccination? Such criteria should be equally applied to all study arms.

4. Taking into consideration your proposed feasibility assessment, please provide the following milestones to CBER by October 11, 2017: the dates of final protocol submission, study completion, and final report submission.

We request that you convey whether you agree with our comments by October 11, 2017, with the understanding that the protocol would be submitted after approval.

References:

Docken, PW. Diagnosis of giant cell (temporal) arteritis. In: UpToDate, Trobe , J and Matteson EL (Ed), UpToDate, Waltham, MA, 2017.

*****

Please confirm receipt of this message. Let us know if you have any questions or need additional information.
Regards,
Ram

Ramachandra S. Naik, Ph.D.
Chemist (Regulatory) / Regulatory Project Manager
Center for Biologics Evaluation and Research
Office of Vaccines Research and Review
U.S. Food and Drug Administration
Tel: 301-796-2640
ramachandra.naik@fda.hhs.gov