

Mid-Cycle Communication, November 21, 2014 – BEXSERO

Application type and number: BL STN 125546/0

Product name: BEXSERO, Meningococcal Group B Vaccine

Proposed indication: Active immunization to prevent invasive meningococcal disease caused by Neisseria meningitidis serogroup B in individuals 10 through 25 years of age

Applicant: Novartis Vaccines and Diagnostics, Inc.

Meeting type: Mid-Cycle Communication

Meeting date & time: November 21, 2014, 1:00 PM

CBER Attendees:

Margaret Bash, M.D., M.P.H.	Review Committee Chair
Edward Wolfgang	Lead Regulatory Project Manager
Kirk Prutzman, Ph.D.	Regulatory Project Manager
Ramachandra Naik, Ph.D.	Regulatory Project Manager
Anuja Rastogi, M.D.	Clinical Reviewer
Loris McVittie, Ph.D.	Deputy Director, OVRD/DVRPA
Elizabeth Sutkowski, Ph.D.	Chief, OVRD/DVRPA/RRB3

Contractor (PDUFA V)

Christopher Sese Consultant, Eastern Research Group

Novartis Attendees:

Rino Rappuoli, Global Head Research & Development
Manish Vyas, Global Head Regulatory Affairs
Jim Wassil, Global Product Lead
Sue Fekete, Head of Regulatory Affairs North America
Patricia Stoehr, Director Regulatory Affairs, Meningitis Franchise
Janne Udal, Senior Group Manager, Regulatory CMC

Discussion Summary:

The items the Review Committee Chair informed Novartis of are presented below.

1. Status of issues identified and their resolution
 - o Information Requests (IRs)
 - CBER indicated that they have sent a number of information requests. Novartis has responded to most of them (amendments 3 through 26) and CBER review of the responses is ongoing.
 - CBER noted that they are awaiting official responses to some of the IRs listed by date sent below:
 - 11/6/2014 -----(b)(4)----- test: validation data for the detection of unspecified impurities)
 - 11/13/2014 (Carton & Container labeling)
 - 11/17/2014 (timeline to submit the ----(b)(4)--- specification reassessment data for - -----(b)(4)-----

- 11/20/14 (request to submit concurrent testing letters for the drug substance samples of the bulk OMV and three recombinant proteins (rp) to sample custodian)
- CBER stated that they may have additional information requests to send to Novartis concerning endotoxin specifications and other issues (the specifics of which were not for discussion at this time). These comments should be sent to Novartis sometime early next week or when available.
- CBER added that additional IRs may be sent since many reviews are still ongoing.
- Labeling
 - CBER noted that they have provided comments on the carton/container labeling on November 13, 2014.
 - CBER informed Novartis that they are reviewing the package insert and expect to have initial comments sent in early to mid-December.

2. Status of safety concerns

- CBER stated that they have not identified any safety concerns that would preclude approval.

3. Risk management

- CBER asked Novartis to provide an update on whether they have any plans for monitoring safety of the vaccine, e.g., routine surveillance, review of safety data from ongoing studies, any studies regarding co-administration with routinely administered vaccines, etc. CBER indicated that they would soon be conferring with Novartis separately regarding their plans to evaluate safety during pregnancy.

4. Miscellaneous items

- Meetings update
 - CBER stated that a late cycle meeting for this submission is tentatively scheduled for 1:00 PM on January 23, 2014, and asked Novartis to check their availability. CBER reiterated that they have determined that an Advisory Committee meeting will not be necessary for this application.
- Projected milestones
 - CBER stated that the official milestones for a priority review remain the same; however, because of the urgent public health need for a vaccine against invasive

meningococcal group B disease, CBER is making efforts to expedite the review of the BLA as much as possible.

- Post-marketing issues
 - CBER mentioned that post-marketing requirements and post-marketing commitments are being discussed internally and will be communicated to Novartis when ready. Novartis was informed that they will be asked to provide their commitment to conduct these studies and the proposed dates related to the studies, where relevant.
 - CMC issues
 - Novartis was informed that written agreements with timelines will be needed from Novartis concerning specific CMC issues that are needed but considered non-critical for approval. Future discussions between CBER and Novartis will be scheduled.

Meeting ended.