CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761049Orig1s000

PHARMACOLOGY REVIEW(S)

MEMORANDUM

Date: February 23, 2016
From: Alexander H. Putman, PhD
Nonclinical Reviewer
Division of Hematology Oncology Toxicology for Division of Oncology Products 2
Through: Whitney S. Helms, PhD
Nonclinical Supervisor
Division of Hematology Oncology Toxicology for Division of Oncology Products 2
To: BLA #761049: Avelumab (BAVENCIO)
Re: Nonclinical Review

Avelumab is a programmed death ligand 1 (PD-L1) blocking antibody indicated for the treatment of patients with metastatic Merkel cell carcinoma (MCC). The nonclinical review is complete and has been added to the Multi-disciplinary Review and Evaluation, which will be uploaded to DARRTS when it is finalized. Refer to the Multi-disciplinary Review and Evaluation for additional details. A post-marketing commitment was requested to conduct an animal study that will measure the effect of PD-L1 inhibition on the magnitude of the primary and recall antibody responses to antigen challenge. There are no nonclinical issues that would prevent approval of this application.

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/s/

ALEXANDER H PUTMAN
02/23/2017

WHITNEY S HELMS
02/23/2017

PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR NDA/BLA or Supplement

BLA Number: 761049 **Applicant:** EMD Serono, Inc. **Stamp Date:** 7/6/2016

Drug Name: Avelumab **BLA Type:** Standard

On **initial** overview of the BLA application for filing:

	Content Parameter	Yes	No	Comment
1	Is the pharmacology/toxicology section organized in accord with current regulations and guidelines for format and content in a manner to allow substantive review to begin?	X		
2	Is the pharmacology/toxicology section indexed and paginated in a manner allowing substantive review to begin?	X		
3	Is the pharmacology/toxicology section legible so that substantive review can begin?	X		Appears to be acceptable.
4	Are all required (*) and requested IND studies (in accord with 505 b1 and b2 including referenced literature) completed and submitted (carcinogenicity, mutagenicity, teratogenicity, effects on fertility, juvenile studies, acute and repeat dose adult animal studies, animal ADME studies, safety pharmacology, etc)?	X		
5	If the formulation to be marketed is different from the formulation used in the toxicology studies, have studies by the appropriate route been conducted with appropriate formulations? (For other than the oral route, some studies may be by routes different from the clinical route intentionally and by desire of the FDA).	X		Appears to be acceptable.
6	Does the route of administration used in the animal studies appear to be the same as the intended human exposure route? If not, has the applicant submitted a rationale to justify the alternative route?	X		
7	Has the applicant submitted a statement(s) that all of the pivotal pharm/tox studies have been performed in accordance with the GLP regulations (21 CFR 58) or an explanation for any significant deviations?	X		Appears to be acceptable.
8	Has the applicant submitted all special studies/data requested by the Division during pre-submission discussions?	X		

PHARMACOLOGY/TOXICOLOGY FILING CHECKLIST FOR NDA/BLA or Supplement

	Content Parameter	Yes	No	Comment
9	Are the proposed labeling sections relative to pharmacology/toxicology appropriate including human dose multiples expressed in either mg/m2 or comparative serum/plasma levels) and in accordance with 201.57?	X		
10	Have any impurity – etc. issues been addressed? (New toxicity studies may not be needed.)		X	This is a review issue.
11	Has the applicant addressed any abuse potential issues in the submission?	Not applicable		
12	If this NDA/BLA is to support a Rx to OTC switch, have all relevant studies been submitted?	Not applicable		

IS THE PHARMACOLOGY/TOXICOLOGY SECTION OF THE APPLICATION FILEABLE? - YES

Please identify and list any potential review issues to be forwarded to the Applicant for the 74-day letter.

None

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/s/

ALEXANDER H PUTMAN
11/08/2016

WHITNEY S HELMS
11/14/2016