

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

761078Orig1s000

PRODUCT QUALITY REVIEW(S)

Recommendation: Approval

BLA 761078
Review #1
Review Date April 3, 2017

Drug Name/Dosage Form	Bavencio (avelumab)/Injection for infusion
Strength/Potency	200 mg/10 mL
Route of Administration	Intravenous infusion
Rx/OTC Dispensed	Rx
Indication	Treatment of patients with locally advanced or metastatic urothelial cancer (UC) with disease progression on or after platinum-based therapy
Applicant/Sponsor	EMD Serono, Inc.
US agent, if applicable	N/A

Product Overview

Quality Review Team

DISCIPLINE	REVIEWER	BRANCH/DIVISION
Drug Substance	Arulvathani Arudchandran	OBP/DBRRII
Drug Product	Arulvathani Arudchandran	OBP/DBRRII
Facilities	Steve Fong	OPF/DIA
Microbiology	Maria Reyes Candau-Chacon Lakshmi Narasimhan	OPF/DMA
Business Regulatory Process Manager	Truong Quach	OPQ/OPRO
Team Lead	Patrick Lynch	OBP/DBRRII
Application Technical Lead	Patrick Lynch	OBP/DBRRII
Review Chief	Juhong Liu	OBP/DBRRII

Multidisciplinary Review Team

DISCIPLINE	REVIEWER	OFFICE/DIVISION
RPM	Kim Robertson	OHOP/DOP1
Cross-disciplinary Team Lead	V. Ellen Maher	OHOP/DOP1
Medical Officer	Chana Weinstock	OHOP/DOP1
Pharm/Tox	Wei Chen, Todd Palmby	OHOP/DHOT
Clinical Pharmacology	Nan Zheng, Jingyu (Jerry) Yu	OCP/DPM
Statistics	Joyce Cheng, Shenghui Tang	OB/DBV

a. Names

- i. Proprietary Name: Bavencio
- ii. Trade Name: Bavencio
- iii. Non-Proprietary/USAN: avelumab
- iv. CAS name: 1537032-82-8
- v. Common name: MSB0010718C
- vi. INN Name: avelumab
- vii. Compendial Name: N/A
- viii. OBP systematic name: MAb Human (IgG1) ANTI Q9NZQ7 (PD1L1_HUMAN) [MSB0010718C]

b. Pharmacologic category

Human IgG1 λ monoclonal antibody

Submissions Reviewed:

SUBMISSION(S) REVIEWED	DOCUMENT DATE
761078/0000	December 27, 2016

Quality Review Data Sheet**1. LEGAL BASIS FOR SUBMISSION: 351(a)****2. RELATED/SUPPORTING DOCUMENTS:****A. DMFs: N/A****B. Other Documents:**

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
BLA	761049	Cross-referenced for CMC and nonclinical information for avelumab, including Module 2.3, Module 2.4, Module 2.6, Module 3, and Module 4.

3. CONSULTS: N/A

Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

a. Recommendation

The Office of Biotechnology Products, CDER, recommends approval of BLA 761078 for Bavencio (avelumab) manufactured by EMD Serono, Inc. The CMC information for this application, provided by cross-reference to BLA 761049 approved on March 23, 2017, supports the conclusion that the manufacture of Bavencio is well controlled and produces a product that is pure and potent.

b. Action letter language

- Manufacturing location:
 - Drug substance – Merck Serono SA,
Succursale de Corsier-sur-Vevey
Chemin du Fenil, Zone Industrielle B
1804 Corsier-sur-Vevey
Switzerland
 - Drug product – Merck Serono S.A.
Succursale d'Aubonne
Zone Industrielle de l'Ouriettaz
CH-1170 Aubonne
Switzerland
- Fill sized and dosage form – 200 mg/10 mL in single dose vial, Intravenous Injection
- Dating period:
 - Drug product – 24 months; 2-8 °C
 - Drug substance – (b) (4) months; (b) (4) °C
 - Stability option (select one below):
 - For stability protocols:
 - We have approved the stability protocol(s) in your license application for the purpose of extending the expiration dating period of your drug substance and drug product under 21 CFR 601.12.
- Exempt from lot release
 - Yes
 - Rationale if exempted – Bavencio is exempt specified according to 601.2(a)

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

None

II. Summary of Quality Assessments

A. General Summary

BLA 761078 for Bavencio (avelumab) was submitted by EMD Serono on December 27, 2017, for the indication of the treatment of patients with locally advanced or metastatic urothelial cancer (UC) with disease progression on or after platinum-based therapy. A prior BLA 761049 for Bavencio, for the indication of treating patients with metastatic Merkel cell carcinoma (mMCC), was approved on March 23, 2017. Quality Modules 3 and the overall CMC package for BLA 761078 are cross-referenced to the first BLA 761049 for Bavencio. The Office of Biotechnology Products and Office of Pharmaceutical Quality (OPQ) recommended approval of BLA 761049 in February of 2017. Refer to the Executive Summary and ATL Review for BLA 761049, dated February 27, 2017, located in CDER Informatics Platform (Panorama). Data previously submitted under BLA 761049 supports a manufacturing process and control strategy for Bavencio that consistently produces a pure and potent product. As all manufacturing process and controls under BLA 761049 are shared with BLA 761078, these data are adequate to support Bavencio for the UC indication.

B. Environmental Assessment

EMD Serono claims categorical exclusion from submission of an environmental assessment in accordance with 21 CFR 25.15 (a),(d). BLA 761078 includes a statement of compliance that avelumab meets the criteria for exclusion as defined in 21 CFR 25.31(c), and without extraordinary circumstances described in 21 CFR 25.15(d). The categorical exclusion is granted.



**Juhong
Liu**

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**Patrick
Lynch**

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