



BLA 761440/Original 2

**COMPLETE RESPONSE**

GlaxoSmithKline LLC  
Attention: Hayley Karpick, PharmD, RPh  
Associate Director, Global Regulatory Affairs  
1250 South Collegeville Road, UP 4400  
Collegeville, PA 19426

Dear Dr. Karpick:

Please refer to your biologics license application (BLA) received September 23, 2024, and your amendments, under section 351(a) of the Public Health Service Act for Blenrep (belantamab mafodotin-blmf) injection.

We acknowledge receipt of your major amendment dated July 22, 2025, which extended the goal date by three months.

BLA 761440 provides for the use of Blenrep (belantamab mafodotin-blmf) for the following indications which, for administrative purposes, we have designated as follows:

- BLA 761440/Original 1 – treatment of adult patients with relapsed or refractory multiple myeloma in combination with bortezomib and dexamethasone in patients who have received at least two prior lines of therapy, including a proteasome inhibitor and an immunomodulatory agent.
- BLA 761440/Original 2 – (b) (4)

The subject of this action letter is BLA 761440/Original 2. A separate action letter will be issued for BLA 761440/Original 1.

All future submissions to BLA 761440/Original 2 should specify the BLA number and the original number to which each submission pertains.

We have completed the review of BLA 761440/Original 2, as amended, and have determined that we cannot approve this application in its present form. We have described below our reasons for this action and, where possible, our recommendations to address these issues.

The Agency has determined that the results of Study 207499 (DREAMM-8) do not support a favorable benefit-risk assessment, given the significant safety and tolerability concerns, the lack of demonstration of an overall survival benefit, and the limited applicability to the U.S. patient population.

While the DREAMM-8 trial met its primary endpoint of progression free survival, benefit was not established for the key secondary endpoint of overall survival. There were high rates of ocular toxicity, including high grade events, and high rates of dose modifications, the majority of which were due to ocular toxicity. These toxicity and tolerability issues raise concerns regarding the safety and appropriateness of the intended dosage of belantamab mafodotin.

Additionally, there are substantial concerns regarding the applicability of the DREAMM-8 study results to the current U.S. patient population with relapsed or refractory multiple myeloma. The control arm is not an approved regimen in the U.S. and there was limited U.S. enrollment in DREAMM-8

To support resubmission of the BLA, you must address these deficiencies by conducting further dose optimization to identify a dosage of belantamab mafodotin in combination with pomalidomide and dexamethasone that has an acceptable safety and tolerability profile. You must also provide randomized efficacy and safety data for belantamab mafodotin in combination with pomalidomide and dexamethasone in patients with relapsed or refractory multiple myeloma that are applicable to the U.S. population and support a favorable benefit-risk assessment. We recommend you request a meeting with the Agency to discuss any planned trials to support a sBLA resubmission.

### **SAFETY UPDATE**

When you respond to the above deficiencies, include a safety update as described at 21 CFR 601.2. The safety update should include data from all nonclinical and clinical studies/trials of the product under consideration regardless of indication, dosage form, or dose level.

- (1) Describe in detail any significant changes or findings in the safety profile.
- (2) When assembling the sections describing discontinuations due to adverse events, serious adverse events, and common adverse events, incorporate new safety data as follows:
  - Present new safety data from the studies/clinical trials for the proposed indication using the same format as in the original submission.
  - Present tabulations of the new safety data combined with the original application data.

- Include tables that compare frequencies of adverse events in the original application with the retabulated frequencies described in the bullet above.
  - For indications other than the proposed indication, provide separate tables for the frequencies of adverse events occurring in clinical trials.
- (3) Present a retabulation of the reasons for premature trial discontinuation by incorporating the drop-outs from the newly completed trials. Describe any new trends or patterns identified.
- (4) Provide case report forms and narrative summaries for each patient who died during a clinical trial or who did not complete a trial because of an adverse event. In addition, provide narrative summaries for serious adverse events.
- (5) Describe any information that suggests a substantial change in the incidence of common, but less serious, adverse events between the new data and the original application data.
- (6) Provide updated exposure information for the clinical studies/trials (e.g., number of subjects, person time).
- (7) Provide a summary of worldwide experience on the safety of this product. Include an updated estimate of use for product marketed in other countries.
- (8) Provide English translations of current approved foreign labeling not previously submitted.

## **OTHER**

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 601.3(b). If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 601.3(c). You may also request an extension of time in which to resubmit the application. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

You may request a meeting or teleconference with us to discuss what steps you need to take before BLA 761440/Original 2 may be approved. If you wish to have such a meeting, submit your meeting request as described in the draft guidance for industry *Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products*.<sup>1</sup>

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<sup>1</sup> When final, this guidance will represent the FDA's current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

If you have any questions, contact

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Sincerely,

*{See appended electronic signature page}*

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Center for Drug Evaluation and Research

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**This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.**  
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/s/  
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