Submitted by:

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Date of Request: 05-August-2020

NCCN Guidelines Panel: Multiple Myeloma

On behalf of GlaxoSmithKline (GSK), this letter is a formal request to the NCCN Multiple Myeloma Guidelines Panel to review the enclosed data for inclusion of *Blenrep* (belantamab mafodotin-blmf) as a monotherapy treatment for adult patients with previously treated multiple myeloma. This request is based on the DREAMM-2 (NCT03525678) trial, which was published in the *Lancet Oncology* and presented at the American Society of Clinical Oncology Virtual Meeting on May 29th, 2020.[1,2] *Blenrep* was approved by the US Food and Drug Administration (FDA) on August 5th, 2020.[3]

Specific Changes Requested in the Guidelines:

We respectfully request the following update:

- For Therapy for Previously Treated Multiple Myeloma on page MYEL-F (3 of 3): under Preferred Regimens, addition of *Blenrep* as a monotherapy option for patients with previously treated multiple myeloma.

FDA Clearance: *Blenrep* is a B-cell maturation antigen (BCMA)-directed antibody and microtubule inhibitor conjugate currently indicated as monotherapy for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior therapies including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent.[3] This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

Rationale:

Our submission is based on the recent FDA approval and the DREAMM-2 (NCT03525678) trial which demonstrated the efficacy and safety of belantamab mafodotin 2.5 mg/kg in patients with relapsed or refractory multiple myeloma (RRMM) who were refractory to an immunomodulatory drug, proteasome inhibitor and refractory/intolerant to an anti-CD38 monoclonal antibody.[1,2]

Currently, the standard-of-care treatment options for patients with multiple myeloma include immunomodulatory agents, proteasome inhibitors, and anti-CD38 monoclonal antibodies.[4] Patients refractory to agents in all three of these classes have an especially poor prognosis, with a median overall survival between 5.6 and 9.2 months.[4-7] With each subsequent therapy, the likelihood of response and length of survival decreases.[6] Therefore, novel therapies are needed for patients who have exhausted available treatment options.[4] In the current treatment landscape for multiple myeloma, there are no FDA-approved BCMA-targeted therapies.

Blenrep is the first approved BCMA-targeted therapy for the treatment of relapsed or refractory multiple myeloma.[3] Findings from the ongoing DREAMM-2 trial demonstrate deep and durable responses in patients with heavily pretreated multiple myeloma consistent with the daratumumab-refractory sub-population in the first-time-in-human DREAMM-1 trial.[8,9] At 13 months, overall response was achieved in 31 (32%) of 97 patients, with more than half (18/31) of responders achieving a very good partial response (VGPR) or better. Additionally, the duration of response estimate was 11 months, median progression-free survival was 2.7 months, and the overall survival estimate was 13.7 months.[2] The safety profile observed in the DREAMM-2 study was consistent with previously reported data; no new safety signals were identified.[2,8-10] Belantamab mafodotin has a safety profile that is mainly characterized by corneal events, thrombocytopenia, and anemia. Dose reductions (35%) and dose delays (54%) were effective in managing adverse events (AEs) and allowed patients to remain on treatment, as demonstrated by a low

discontinuation rate (9%). Although keratopathy (microcyst-like corneal epithelial changes on eye exam with or without symptoms) observed on eye examination was common (68 [72%] of 95 patients), few patients permanently discontinued treatment due to corneal events (3%). Seventeen patients experienced a decline in visual acuity to 20/50 or worse at least once during or after the treatment period. The median duration of this decline was 21.5 days and 82% of patients recovered by the last assessment. No permanent loss of vision has been reported as of the 13-month follow-up.

In order to assist patients and prescribing physicians with appropriate risk management related to corneal events during treatment with belantamab mafodotin, GSK developed a comprehensive Risk Evaluation and Mitigation Strategy (REMS) program, including a Communication Plan and Elements to Assure Safe Use (ETASU).[3] Corneal events represent a novel type of AE for physicians who treat patients with multiple myeloma. However, collaboration between the eye care professional and the oncologist, reflected in the DREAMM program and formalized in the REMS, allows the eye care professional to identify these findings in a timely manner so the oncologist can adjust the belantamab mafodotin regimen appropriately.

In summary, belantamab mafodotin demonstrated deep and durable responses in a highly refractory patient population with a manageable safety profile, as demonstrated by the majority of responders achieving a VGPR or better, a long duration of response and low rates of discontinuation due to AEs. Additionally, the recent Oncologic Drugs Advisory Committee voted 12-0 in favor of belantamab mafodotin's positive risk/benefit profile. Your consideration of this submission is greatly appreciated. If any questions arise or if you require any additional information, please do not hesitate to contact Ji Chung, PharmD, RPh at ji.8.chung@gsk.com.

Sincerely,

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The following data disclosures are submitted in support of this proposed change.

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3. Prescribing Information for Blenrep (belantamab mafodotin-blmf).
4. Mikhael J. Treatment options for triple-class refractory multiple myeloma. *Clin Lymphoma Myeloma Leuk.* 2020;20(1):1–17. https://doi.org/10.1016/j.clml.2019.09.621.
5. Chari A, Vogl DT, Graviatopoulou M, et al. Oral selinexor-dexamethasone for triple-class refractory multiple myeloma. *N Engl J Med.* 2019;381:727–38. https://doi.org/10.1056/NEJMoa1903455.
6. Gandhi UH, Cornell RF, Lakshman A, et al. Outcomes of patients with multiple myeloma refractory. *Leukemia* 2019;33:2266–75. https://doi.org/10.1038/s41375-019-0435-7.
7. Pick M, Vainstein V, Goldschmidt N, et al. Daratumumab resistance in frequent in advanced-stage multiple myeloma patients irrespective of CD38 expression and is related to dismal prognosis. *Eur J Haematol.* 2018;100(5):494–501. https://doi.org/10.1111/ejh.13046.
8. Trudel S, Lendvai N, Popat R, et al. Antibody–drug conjugate, GSK2857916, in relapsed/refractory multiple myeloma: an update on safety and efficacy from dose expansion phase I study. *Blood Cancer Journal.* 2019;9(4):37. doi:http://dx.doi.org/10.1038/s41408-019-0196-6.
9. Trudel S, Lendvai N, Popat R, et al. Targeting B-cell maturation antigen with GSK2857916 antibody-drug conjugate in relapsed or refractory multiple myeloma (BMA117159): a dose escalation and expansion phase 1 trial. *Lancet Oncol.* 2018;19(12):1641-1653. doi:http://dx.doi.org/10.1016/S1470-2045(18)30576-X.
10. Farooq AV, Degli Esposti S, Popat R, et al. Corneal Epithelial Findings in Patients with Multiple Myeloma Treated with Antibody-Drug Conjugate Belantamab Mafodotin in the Pivotal, Randomized, DREAMM-2 Study. *Ophthalmol Ther.* 2020. doi:http://dx.doi.org/10.1007/s40123-020-00280-8.