Genentech
A Member of the Roche Group

Submitted by:
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Date of request: October 11, 2017
NCCN Guidelines Panel: B-Cell

On behalf of Genentech, Inc., I respectfully request the NCCN B-Cell Guideline Panel to consider the following key enclosed data for:

- **Gazyva® (obinituzumab):** Previously Untreated Follicular Lymphoma

    - Marcus R., Davies A., Ando K., et al. Obinutuzumab for the First-Line Treatment of Follicular Lymphoma. *N Engl J Med* 2017; 377:1331-44.

Specific Changes:

- Please consider the above publication for your updating purposes.

FDA Clearance:

- Gazyva is FDA-approved:
    - in combination with chlorambucil, for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL)
    - in combination with bendamustine followed by Gazyva monotherapy, for the treatment of patients with follicular lymphoma who relapsed after, or are refractory to, a rituximab containing regimen
- Gazyva is not FDA approved for the treatment of previously untreated follicular lymphoma.
- Rituxan is FDA-approved:
    - Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to Rituxan in combination with chemotherapy, as single-agent maintenance therapy.
- Rituxan is not FDA approved in combination with bendamustine for the treatment of previously untreated follicular lymphoma.

Please refer to the product prescribing information for the full FDA-approved indications and safety information.

- Full Gazyva prescribing information available at: http://www.gene.com/download/pdf/gazyva_prescribing.pdf
- Full Rituxan prescribing information available at: https://www.gene.com/download/pdf/rituxan_prescribing.pdf

Rationale:

- Currently, Gazyva is included in the NCCN guidelines as a Category 2A regimen for first-line follicular lymphoma. -Please consider the attached full publication for your updating purpose.

- **Marcus et al**.: The Phase 3 GALLIUM study evaluated the efficacy and safety of Gazyva with chemotherapy followed by maintenance Gazyva versus rituximab with chemotherapy followed by maintenance rituximab in previously untreated follicular lymphoma or marginal zone lymphoma.
    - In patients with follicular lymphoma, treatment with Gazyva plus chemotherapy was associated with a significant improvement in the primary endpoint of investigator-assessed estimated 3-year rate of progression-free survival (PFS) over Rituxan with chemotherapy (80% vs. 73.3% respectively; HR 0.66; 95% CI, 0.51- 0.85; p=0.001).
    - The most common adverse events of any grade in the safety population of patients with follicular lymphoma were infusion related-reactions (59% in the Gazyva arm and 48.9% in the Rituxan arm), nausea (46.9% and 46.6% respectively), and neutropenia (48.6% and 43.6%).
    - There were a total of 81 deaths in the trial. Of these deaths investigators considered 24 in the Gazyva arm and 20 in the Rituxan arm to be due to adverse events.
- The GALLIUM study results were previously submitted in abstract form.
- An additional study which evaluated the use of Gazyva in previously untreated Follicular Lymphoma is listed below.

I hope this information is helpful to you. If you have any questions, please contact me directly at or by email at parekh.krupa@gene.com.

Sincerely,

Krupa Parekh, Pharm.D.

Supplemental References:

1. Grigg A, Dyer MJS, Diaz MG, et al. Safety and efficacy of obinutuzumab with CHOP or bendamustine in previously untreated follicular lymphoma. *Haematologica* 2017;102:765-772.

C#17-M0126