**INDICATION & IMPORTANT SAFETY INFORMATION**

**Indication**

GAZYVA® (obinutuzumab), in combination with chlorambucil, is indicated for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL).

GAZYVA® (obinutuzumab), in combination with bendamustine followed by GAZYVA monotherapy, is indicated for the treatment of patients with follicular lymphoma (FL) who relapsed after, or are refractory to, a rituximab-containing regimen.

GAZYVA® (obinutuzumab), in combination with chemotherapy followed by GAZYVA monotherapy in patients achieving at least a partial remission, is indicated for the treatment of adult patients with previously untreated stage II bulky, III or IV follicular lymphoma (FL).

**Important Safety Information**

**BOXED WARNINGS: HEPATITIS B VIRUS REACTIVATION AND PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY**

- Hepatitis B Virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, can occur in patients receiving CD20-directed cytolytic antibodies, including GAZYVA. Screen all patients for HBV infection before treatment initiation. Monitor HBV positive patients during and after treatment with GAZYVA. Discontinue GAZYVA and concomitant medications in the event of HBV reactivation.

- Progressive Multifocal Leukoencephalopathy (PML) including fatal PML, can occur in patients receiving GAZYVA.

**Contraindications**

- GAZYVA is contraindicated in patients with known hypersensitivity reactions (e.g. anaphylaxis) to obinutuzumab or to any of the excipients, or serum sickness with prior obinutuzumab use.

Please see the accompanying full Prescribing Information for additional Important Safety Information, including BOXED WARNINGS.
Additional Important Safety Information

ClL

- The most common Grade 3 to 4 adverse reactions (incidence ≥10%) observed in patients with CLL in the GAZYVA containing arm were neutropenia, infusion reactions, and thrombocytopenia.
- The most common adverse reactions (incidence ≥10%) observed in patients with CLL in the GAZYVA containing arm were infusion reactions, neutropenia, thrombocytopenia, anemia, pyrexia, cough, nausea, and diarrhea.
- Adverse reactions rates and laboratory abnormalities from the Stage 2 phase are consistent with the rates in Stage 1. In addition to the adverse reactions observed in Stage 2, in Stage 1 back pain (5% vs. 2%), anemia (12% vs. 10%) and cough (10% vs. 7%) were observed at a higher incidence in the GAZYVA treated patients. The incidence of Grade 3 to 4 back pain (<1% vs. 0%), cough (0% vs. <1%) and anemia (5% vs. 4%) was similar in both treatment arms. With regard to laboratory abnormalities, in Stage 1 hyperkalemia (33% vs. 18%), creatinine increased (30% vs. 20%) and alkaline phosphatase increased (18% vs. 11%) were observed at a higher incidence in the GAZYVA treated patients. The incidence of Grade 3 to 4 back pain (<1% vs. 0%), cough (0% vs. <1%) and anemia (5% vs. 4%) was similar in both treatment arms. With regard to laboratory abnormalities, in Stage 1 hyperkalemia (33% vs. 18%), creatinine increased (30% vs. 20%) and alkaline phosphatase increased (18% vs. 11%) were observed at a higher incidence in patients treated with GAZYVA with similar incidences of Grade 3 to 4 abnormalities between the two arms.

Relapsed/Refractory NHL

- The GADOLIN study evaluated safety in 392 patients with relapsed or refractory NHL, including FL (81%), small lymphocytic lymphoma (SLL) and marginal zone lymphoma (MZL) (a disease for which GAZYVA is not indicated) who did not respond to or progressed within 6 months of treatment with rituximab product or a rituximab product-containing regimen. In patients with follicular lymphoma, the profile of adverse reactions was consistent with the overall NHL population.
- The most common Grade 3 to 4 adverse reactions (incidence ≥10%) observed in the GAZYVA containing arm were neutropenia, thrombocytopenia and infusion reactions.
- The most common adverse reactions (incidence ≥10%) in the GAZYVA containing arm were infusion reactions, neutropenia, nausea, fatigue, cough, diarrhea, constipation, pyrexia, thrombocytopenia, vomiting, upper respiratory tract infection, decreased appetite, arthralgia, sinusitis, anemia, asthenia and urinary tract infection.
Additional Important Safety Information (cont)

Relapsed/Refractory NHL (cont)

- During the monotherapy period with GAZYVA, Grade 3 to 4 adverse reactions included neutropenia (10%), and anemia, febrile neutropenia, thrombocytopenia, sepsis, upper respiratory tract infection, and urinary tract infection (all at 1%)
- During the monotherapy period with GAZYVA, the most common adverse reactions (incidence ≥5%) were cough (15%), upper respiratory tract infections (12%), neutropenia (11%), sinusitis (10%), diarrhea (8%), infusion related reactions (8%), nausea (8%), fatigue (8%), bronchitis (7%), arthralgia (7%), pyrexia (6%), nasopharyngitis (6%), and urinary tract infections (6%)

Previously Untreated NHL

- A randomized, open-label multicenter trial (GALLIUM) evaluated the safety of GAZYVA as compared to rituximab product in 1385 patients with previously untreated follicular lymphoma (86%) or marginal zone lymphoma (14%)
- Serious adverse reactions occurred in 50% of patients on the GAZYVA arm and 43% of patients on the rituximab product arm. Fatal adverse reactions were reported during treatment in 3% in the GAZYVA arm and 2% in the rituximab product arm, most often from infections in the GAZYVA arm. During treatment and follow-up combined, fatal adverse reactions were reported in 5% of the GAZYVA arm and 4% of the rituximab product arm, with infections and second malignancies being leading causes. In the GAZYVA arm, fatal infections occurred in 2% of patients compared to <1% in the rituximab product arm
- Neutropenia, infusion related reactions, febrile neutropenia and thrombocytopenia were the most common Grade 3 to 5 adverse reactions (incidence ≥5%) observed more frequently in the GAZYVA arm
- Throughout treatment and follow-up, the most common adverse reactions (incidence ≥20%) observed at least 2% more in the GAZYVA arm were infusion related reactions, neutropenia, upper respiratory tract infection, cough, constipation and diarrhea
- During the monotherapy period, the common adverse reactions (incidence ≥10%) observed at least 2% more with GAZYVA were upper respiratory infection (40%), cough (23%), musculoskeletal pain (20%), neutropenia (19%) and herpesvirus infection (13%)

You are encouraged to report side effects to Genentech and the FDA. You may contact Genentech by calling 1-888-835-2555. You may contact the FDA by visiting www.fda.gov/medwatch, or calling 1-800-FDA-1088.

Please see the accompanying full Prescribing Information for additional Important Safety Information, including BOXED WARNINGS.