Gazyva® (obinutuzumab) – Expanded indication and new warning

- On November 16, 2017, Genentech announced the FDA approval of Gazyva (obinutuzumab), in combination with chemotherapy followed by Gazyva monotherapy in patients achieving at least a partial remission, for the treatment of adult patients with previously untreated stage II bulky, III or IV follicular lymphoma (FL).

- Gazyva is also indicated in combination with Leukeran® (chlorambucil), for the treatment of patients with previously untreated chronic lymphocytic leukemia; and in combination with bendamustine (Bendeka™, Treanda®) followed by Gazyva monotherapy, for the treatment of patients with FL who relapsed after, or are refractory to, a rituximab (Rituxan®, Rituxan Hycela™)-containing regimen.

- FL is the most common slow-growing (indolent) form of non-Hodgkin's lymphoma (NHL), accounting for about one in five cases of NHL. It is estimated that > 14,000 new cases of FL will be diagnosed in the U.S. in 2017.

    - FL is considered incurable and characterized by periods of remission and relapse. The disease typically becomes harder to treat each time it returns, and early progression can be associated with poor long-term prognosis.

- The expanded indication for Gazyva was approved based on an open-label study of 1,202 patients with previously untreated stage II bulky, III or IV FL. Patients were randomized to receive either Gazyva or rituximab in combination with chemotherapy for 6 – 8 cycles. Patients with at least partial response to combination therapy received monotherapy with Gazyva or rituximab until disease progression or for a maximum of two years.

    - Fewer number of events occurred in the Gazyva-treated group vs. rituximab-treated group (18% vs. 23%; HR = 0.72 [95% CI: 0.56, 0.93]; p = 0.0118)

- Gazyva carries a boxed warning for hepatitis B virus reactivation and progressive multifocal leukoencephalopathy.

- The *Contraindications* and the *Warnings and Precautions* sections of the Gazyva drug label were also updated with information regarding hypersensitivity reactions including serum sickness.

    - Hypersensitivity reactions have been reported in patients treated with Gazyva. Signs of immediate-onset hypersensitivity included dyspnea, bronchospasm, hypotension, urticaria and tachycardia. Late-onset hypersensitivity diagnosed as serum sickness has also been reported, with symptoms that include chest pain, diffuse arthralgia and fever.
    - Hypersensitivity reactions may be difficult to clinically distinguish from infusion related reactions. However, hypersensitivity very rarely occurs with the first infusion and, when observed, often occurs after previous exposure.
    - If a hypersensitivity reaction is suspected during or after an infusion, the infusion must be stopped and treatment permanently discontinued. Patients with known hypersensitivity reactions to Gazyva, including serum sickness, must not be retreated.

- The most common adverse reactions (≥ 10% and ≥ 2% in the Gazyva-treated arm) with Gazyva use in previously untreated NHL were infusion reactions, neutropenia, upper respiratory tract infection, cough, constipation, diarrhea, headache, herpesvirus infection, arthralgia, insomnia, pneumonia, thrombocytopenia, decreased appetite, alopecia and pruritus.

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- The recommended dosage of Gazyva for previously untreated FL is 1,000 mg intravenously on days 1, 8 and 15 of cycle 1, 1,000 mg on day 1 of cycles 2 – 6 or cycles 2 – 8, and then 1,000 mg every 2 months for up to 2 years.

- Consult the drug label for recommendations about combination chemotherapy and for all other indications.