Ruxience™ (rituximab-pvvr) – New biosimilar approval

- On July 23, 2019, Pfizer announced the FDA approval of Ruxience (rituximab-pvvr), a biosimilar to Genentech/Biogen's Rituxan® (rituximab).

  — Ruxience is the second FDA-approved biosimilar to Rituxan.
  — Teva/Celltrion's Truxima® (rituximab-abbs) was the first biosimilar to Rituxan and was approved on November 28, 2018. Teva/Celltrion's launch plans for Truxima are pending.

- Ruxience, Truxima and Rituxan share the following indications:

  — Treatment of adult patients with Non-Hodgkin's lymphoma (NHL):
    - Relapsed or refractory, low grade or follicular, CD20-positive B-cell NHL as a single agent
    - Previously untreated follicular, CD20-positive, B-cell NHL in combination with first line chemotherapy and, in patients achieving a complete or partial response to a rituximab product in combination with chemotherapy, as single-agent maintenance therapy
    - Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy
    - Previously untreated diffuse large B-cell, CD20-positive NHL in combination with (cyclophosphamide, doxorubicin, vincristine, and prednisone) (CHOP) or other anthracycline-based chemotherapy regimens
  — Previously untreated and previously treated CD20-positive chronic lymphocytic leukemia (CLL) in combination with fludarabine and cyclophosphamide.

- Ruxience and Rituxan also share the indication of granulomatosis with polyangiitis (GPA) (Wegener's Granulomatosis) and microscopic polyangiitis (MPA) in adult patients in combination with glucocorticoids.

- In addition, Rituxan is indicated for the treatment of adult patients with rheumatoid arthritis and pemphigus vulgaris.

- A biosimilar product is a biological agent that is considered highly similar to an already-approved biological drug, known as the reference product. Biological products are generally derived from a living organism and can come from many sources, including humans, animals, microorganisms or yeast.

  — A biosimilar product must show no clinically meaningful differences in terms of safety and effectiveness from the reference product. Only minor differences in clinically inactive components are allowable in biosimilar products.
  — In addition, a biosimilar product may only be approved for the indication(s) and condition(s) that have been FDA approved for the reference product, and must have the same

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mechanism(s) of action, route(s) of administration, dosage form(s) and strength(s) as the reference product.

- Ruxience has been approved as a biosimilar, ***not*** as an interchangeable product.
- The approval of Ruxience is based on a review of analytical, non-clinical, pharmacokinetic and clinical data confirming that Ruxience is highly similar to Rituxan.
- Similar to Rituxan and Truxima, Ruxience carries a boxed warning for fatal infusion-related reactions, severe mucocutaneous reactions, hepatitis B virus reactivation and progressive multifocal leukoencephalopathy.
- Other warning and precautions of Ruxience include tumor lysis syndrome, infections, cardiovascular adverse reactions, renal toxicity, bowel obstruction and perforation, immunization, embryo-fetal toxicity, and concomitant use with other biologic agents and disease modifying anti-rheumatic drugs in GPA and MPA.
- The most common adverse reactions (≥ 25%) with Ruxience use in NHL were infusion-related reactions, fever, lymphopenia, chills, infection and asthenia.
- The most common adverse reactions (≥ 25%) with Ruxience use in CLL were infusion-related reactions and neutropenia.
- The most common adverse reactions (≥ 15%) with Ruxience use in GPA and MPA were infections, nausea, diarrhea, headache, muscle spasms, anemia, and peripheral edema. Another important adverse reaction was infusion-related reactions.
- The recommended dose of Ruxience is given by intravenous infusion and varies by indication:

Indication	Dose	Duration
Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL	375 mg/m^2	Once weekly for 4 or 8 doses
Retreatment for relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL		Once weekly for 4 doses
Previously untreated, follicular, CD20-positive, B-cell NHL		Administer on day 1 of each cycle of chemotherapy, for up to 8 doses
Non-progressing, low-grade, CD20-positive, B-cell NHL, after first-line CVP chemotherapy		Following completion of 6 to 8 cycles of CVP chemotherapy, administer once weekly for 4 doses at 6-month intervals for a maximum of 16 doses
Diffuse large B-cell NHL		Administer on day 1 of each cycle of chemotherapy for up to 8 infusions
CLL	375 mg/m^2 the day prior to the initiation of FC chemotherapy, then 500 mg/m^2 on day 1 of cycles 2-6 (every 28 days)	--
Active GPA/MPA	375 mg/m^2	Once weekly for 4 weeks

    - Refer to the Ruxience drug label for further dosing recommendations, glucocorticoid dosing and maintenance treatment for GPA/MPA.

- Pfizer's launch plans for Ruxience are pending. Ruxience will be available as 100 mg/10 mL and 500 mg/50 mL solution is single-dose vials.