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Federal Employee Program

RITUXIMAB

Rituxan (rituximab), **Riabni** (rituximab-arrx), Ruxience (rituximab-pvvr), Truxima (rituximab-abbs)

Preferred products: Riabni, Rituxan

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Rituxan (rituximab) and its biosimilars are monoclonal antibodies that are manufactured through biotechnology methods rather than by the human body's own immune system. The drugs work by greatly reducing the number of specific immune cells in the blood, known as B-cells. The drugs bind to a particular protein, the CD20 antigen, on the surface of normal and malignant B-cells, making it easier for the patient's immune system to attack the cancer cell as if it were a foreign pathogen. The targeted mechanism of action of Rituxan and its biosimilars are used in the treatment of the following: chronic lymphocytic leukemia (CLL), CD20 positive, Non-Hodgkin's Lymphoma (NHL), rheumatoid arthritis (RA), Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis), Microscopic Polyangiitis (MPA) and active pemphigus vulgaris (1-7).

Regulatory Status

FDA-approved indications: Rituxan and its biosimilars are CD20-directed cytolytic antibodies indicated for the treatment of patients with: (1-4)

1. Adult patients with Non-Hodgkin's Lymphoma (NHL)
2. Pediatric patients aged 6 months and older with mature B-cell Non-Hodgkin's Lymphoma (NHL) and mature B-cell acute leukemia
    a. Diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma, Burkitt-like lymphoma, or mature B-cell acute leukemia
3. Adult patients with Chronic lymphocytic leukemia (CLL)
4. Rheumatoid arthritis (RA) in combination with methotrexate in adult patients with moderately-to severely-active rheumatoid arthritis who have had an inadequate response to one or more TNF antagonist therapies
5. Granulomatosis with Polyangiitis (GPA) (Wegener's Granulomatosis) and Microscopic Polyangiitis (MPA) in adult and pediatric patients 2 years of age and older in combination with glucocorticoids.
6. Moderately to severely active pemphigus vulgaris (PV) in adult patients

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Limitations of Use:

Rituxan and its biosimilars are not recommended for use in patients with severe, active infections (1-4).

Rituxan and its biosimilars have several boxed warnings regarding fatal infusion reactions, Hepatitis B virus (HBV) reactivation, severe mucocutaneous reactions, and progressive multifocal leukoencephalopathy (PML) resulting in death (1-4).

Acute renal failure, hyperkalemia, hypocalcemia, hyperuricemia, or hyperphosphatemia from tumor lysis, some fatal, can occur within 12-24 hours after the first infusion of Rituxan or its biosimilars in patients with non-Hodgkin lymphoma (NHL). Patients at high risk for tumor lysis syndrome should be administered aggressive intravenous hydration, anti-hyperuricemic agents, and their renal function should be monitored (1-4).

Serious, including fatal, bacterial, fungal, and new or reactivated viral infections can occur during and following the completion of therapy of Rituxan or its biosimilars. Discontinue Rituxan or its biosimilars for serious infections and institute appropriate anti-infective therapy (1-4).

Rituxan and its biosimilars should be discontinued in patients that develop serious or life-threatening cardiac arrhythmias. Perform cardiac monitoring during and after all infusions of Rituxan or its biosimilars for patients who develop clinically significant arrhythmias, or who have a history of arrhythmia or angina (1-4).

The safety of immunization with live viral vaccines following Rituxan and its biosimilars have not been studied and vaccination with live virus vaccines is not recommended (1-4).

In patients with lymphoid malignancies, during treatment with Rituxan or its biosimilars as monotherapy, obtain complete blood counts (CBC) and platelet counts prior to each rituximab course. During treatment with Rituxan or its biosimilars in combination with chemotherapy, obtain

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CBC and platelet counts at weekly to monthly intervals and more frequently in patients who develop cytopenias. In patients with rheumatoid arthritis, granulomatosis with polyangiitis (GPA), or microscopic polyangiitis (MPA), obtain CBC and platelet counts at two to four month intervals during rituximab therapy. The duration of cytopenias caused by Rituxan or its biosimilars can extend months beyond the treatment period (1-4).

Off-Label Uses:

There are a number of important off-label uses for the use of Rituxan (rituximab) and its biosimilars that are supported by the medical literature. The inclusion of the following conditions is based on the studies cited.

Other Non-Hodgkin's Lymphomas (5)

1. Burkitt lymphoma
2. Gastric MALT lymphoma
3. Non-gastric MALT lymphoma
4. Nodal Marginal Zone lymphoma
5. Mantle cell lymphoma
6. AIDS-Related B-cell lymphomas
7. Post-transplant lymphoproliferative disorder
8. Primary cutaneous B-cell lymphoma
9. Splenic marginal zone lymphoma
10. Hairy Cell Leukemia
11. Castleman's disease

Other Conditions (5-12)

1. Waldenström's macroglobulinemia
2. Steroid refractory chronic graft vs. host disease
3. Immune thrombocytopenic purpura
4. Thrombotic thrombocytopenic purpura

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5. Refractory autoimmune hemolytic anemia
6. Leptomeningeal metastases
7. Primary central nervous system lymphoma
8. Hodgkin's lymphoma
9. Refractory systemic lupus erythematosus (SLE)
10. Refractory myasthenia gravis (MG)

Rituxan or its biosimilars as monotherapy or in conjunction with various chemotherapy agents as well as other monoclonal antibodies is supported by clinical trial data and NCCN guideline recommendations. The following chemoimmunotherapy regimens are used for either first-line therapy or relapsed/refractory therapy depending on the results of genetic testing and comorbidities in affected patients: (5)

1. Alemtuzumab + rituximab
2. Bendamustine, rituximab (BR)
3. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + rituximab
4. HyperCVAD (cyclophosphamide,vincristine,doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine) + rituximab
5. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + rituximab
6. HDMP (high-dose methylpredisolone) + rituximab
7. Pentostatin, cyclophosphamide, rituximab) (PCR)
8. CFAR (cyclophosphamide, fludarabine, alemtuzumab, rituximab)
9. OFAR (oxaliplatin, fludarabine, cytarabine, rituximab)
10. Lenalidomide + rituximab

Summary

Rituxan (rituximab) and its biosimilars are monoclonal antibodies that are manufactured through biotechnology methods rather than by the human body's own immune system. The drugs work by greatly reducing the number of specific immune cells in the blood, known as B-cells. The drugs

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bind to a particular protein, the CD20 antigen, on the surface of normal and malignant B-cells, making it easier for the patient's immune system to attack the cancer cell as if it were a foreign pathogen. Rituxan and its biosimilars are therefore used to treat diseases which are characterized by excessive numbers of B cells, overactive B cells, or dysfunctional B cells (1-6).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Rituxan and its biosimilars while maintaining optimal therapeutic outcomes.

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