RATIONALE FOR INCLUSION IN PA PROGRAM

Background
Rituxan is a monoclonal antibody that is manufactured through biotechnology methods rather than by the human body's own immune system. The drug works by greatly reducing the number of specific immune cells in the blood, known as B-cells. The drug binds 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. With the targeted mechanism of action of Rituxan to B-cells, it is used in the treatment of chronic lymphocytic leukemia (CLL), a slowly progressing blood and bone marrow cancer, that arises from a group of white blood cells known as B-cells, in the treatment of CD20 positive, Non-Hodgkin’s Lymphoma (NHL), which is a type of cancer that occurs in B-cells, and in the treatment of rheumatoid arthritis (RA) which B-cells are believed to play an important role in RA (1-4).

Regulatory Status
FDA-approved indication: Rituxan is a CD20-directed cytolytic antibody indicated for the treatment of patients with: (1)

1. Non-Hodgkin’s Lymphoma (NHL)
2. Chronic lymphocytic leukemia (CLL)
3. 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.
4. Granulomatosis with Polyangiitis (GPA) (Wegener’s Granulomatosis) and Microscopic Polyangiitis (MPA) in combination with glucocorticoids.

Limitations of use:
Rituxan is not recommended for use in patients with severe, active infections (1).

Rituxan has several boxed warnings regarding fatal infusion reactions, tumor lysis syndrome (TLS), severe mucocutaneous reactions, and progressive multifocal leukoencephalopathy (PML) resulting in death (1).

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 in patients with
**RITUXAN**
(rituximab)

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).

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

Rituxan infusions should be discontinued in patients that develop serious or life-threatening cardiac arrhythmias. Perform cardiac monitoring during and after all infusions of Rituxan for patients who develop clinically significant arrhythmias, or who have a history of arrhythmia or angina (2).

The safety of immunization with live viral vaccines following Rituxan therapy has not been studied and vaccination with live virus vaccines is not recommended (1).

In patients with lymphoid malignancies, during treatment with Rituxan monotherapy, obtain complete blood counts (CBC) and platelet counts prior to each Rituxan course. During treatment with Rituxan and chemotherapy, obtain 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 Rituxan therapy. The duration of cytopenias caused by Rituxan can extend months beyond the treatment period (1).

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

**Other Non-Hodgkin’s Lymphomas (2)**
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
Rituxan 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 + Rituxan
2. Bendamustine, Rituxan (BR)
3. CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituxan
4. HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine) + Rituxan
5. Dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + Rituxan
6. HDMP (high-dose methylpredisolone) + Rituxan
7. Pentostatin, cyclophosphamide, Rituxan (PCR)
8. CFAR (cyclophosphamide, fludarabine, alemtuzumab, Rituxan)
9. OFAR (oxaliplatin, fludarabine, cytarabine, Rituxan)
10. Lenalidomide + Rituxan
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Summary
Rituxan is a monoclonal antibody that is manufactured through biotechnology methods rather than by the human body's own immune system. The drug works by greatly reducing the number of specific immune cells in the blood, known as B-cells. The drug binds 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 is therefore used to treat diseases which are characterized by excessive numbers of B cells, overactive B cells, or dysfunctional B cells. This includes non-hodgkin lymphoma (NHL), chronic lymphocytic leukemia (CLL), rheumatoid arthritis (RA), microscopic polyangiitis (MPA), and granulomatosis with polyangiitis (1-4).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Rituxan (rituximab) while maintaining optimal therapeutic outcomes.

References