Rituxan

Description

Rituxan (rituximab)

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 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
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
1. Waldenström’s macroglobulinemia
2. Steroid refractory chronic graft vs. host disease
3. Immune thrombocytopenic purpura
4. Thrombotic thrombocytopenic purpura
5. Refractory autoimmune hemolytic anemia
6. Leptomeningeal metastases
7. Primary central nervous system lymphoma
8. Hodgkin’s lymphoma

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 methylprednisolone) + Rituxan
7. Pentostatin, cyclophosphamide, Rituxan) (PCR)
8. CFAR (cyclophosphamide, fludarabine, alemtuzumab, Rituxan)
9. OFAR (oxaliplatin, fludarabine, cytarabine, Rituxan)
10. Lenalidomide + Rituxan

Related policies
Arzerra, Gazyva, Imbruvica, Kyprolis, Pomalyst, Revlimid, Treanda/Bendeka, Velcade, Zydelig

Policy
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Rituxan may be considered medically necessary in patients 18 years of age or older for the treatment of Non-Hodgkin’s Lymphoma, B-Cell, CD20-Positive, which include Chronic Lymphocytic Leukemia, follicular lymphoma, diffuse large B-cell lymphoma, Burkitt lymphoma, gastric MALT lymphoma, non-gastric MALT lymphoma, nodal marginal zone lymphoma, mantle cell lymphoma, AIDS-Related B-cell lymphomas, post-transplant lymphoproliferative disorder, primary cutaneous B-cell lymphoma, splenic marginal zone lymphoma, hairy cell leukemia or Castleman’s disease, rheumatoid arthritis, granulomatosis with polyangiitis (formerly Wegener’s granulomatosis), microscopic polyangiitis, Waldenström’s macroglobulinemia, steroid refractory chronic graft vs. host disease, immune thrombocytopenic purpura, thrombotic thrombocytopenic purpura, refractory autoimmune hemolytic anemia, leptomeningeal metastases, primary central nervous system lymphoma or Hodgkin’s lymphoma and if the conditions indicated below are met.

Rituxan may be considered investigational in patients less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age
18 years of age or older

Diagnoses

Patient must have ONE of the following:
1. Non-Hodgkin Lymphomas (NHL), B-Cell, CD20-Positive with ONE of the following indications:
   a. Follicular lymphoma
   b. Diffuse large B-cell lymphoma
   c. Burkitt lymphoma
   d. Gastric MALT lymphoma
   e. Non-gastric MALT lymphoma
   f. Nodal Marginal Zone lymphoma
   g. Mantle cell lymphoma
   h. AIDS-Related B-cell lymphomas
   i. Post-transplant lymphoproliferative disorder
   j. Primary cutaneous B-cell lymphoma
   k. Splenic marginal zone lymphoma
   l. Hairy Cell Leukemia
   m. Castleman’s disease

2. Chronic Lymphocytic Leukemia (CLL)

3. Rheumatoid arthritis (RA)
   a. Moderately- to severely-active RA
   b. Inadequate treatment response, intolerance, or contraindication to one or more tumor necrosis factor (TNF) antagonist therapies

4. Microscopic polyangiitis (MPA)
   a. Currently taking a glucocorticoid

5. Granulomatosis with polyangiitis (formerly Wegener’s granulomatosis)
   a. Currently taking a glucocorticoid

6. Waldenström’s macroglobulinemia

7. Steroid refractory chronic graft vs. host disease

8. Immune thrombocytopenic purpura

9. Thrombotic thrombocytopenic purpura

10. Refractory autoimmune hemolytic anemia

11. Leptomeningeal metastases

12. Primary central nervous system lymphoma

13. Hodgkin’s lymphoma

AND NONE of the following for ALL indications:
   a. Used in combination with any other biologic DMARD or targeted synthetic DMARD
   b. Use of a live vaccines, (Non-live vaccines should be administered at 4 weeks prior to a course of Rituxan)
c. Severe, active infections

Prior – Approval Renewal Requirements

Age 18 years of age or older

Diagnoses

Patient must have ONE of the following:

1. Non-Hodgkin Lymphomas (NHL), B-Cell, CD20-Positive with ONE of the following indications:
   a. Follicular lymphoma
   b. Diffuse large B-cell lymphoma
   c. Burkitt lymphoma
   d. Gastric MALT lymphoma
   e. Non-gastric MALT lymphoma
   f. Nodal Marginal Zone lymphoma
   g. Mantle cell lymphoma
   h. AIDS-Related B-cell lymphomas
   i. Post-transplant lymphoproliferative disorder
   j. Primary cutaneous B-cell lymphoma
   k. Splenic marginal zone lymphoma
   l. Hairy Cell Leukemia
   m. Castleman’s disease
2. Chronic Lymphocytic Leukemia (CLL)
3. Rheumatoid arthritis (RA)
4. Microscopic polyangiitis (MPA)
   a. Currently taking a glucocorticoid
5. Granulomatosis with polyangiitis (formerly Wegener's granulomatosis)
   a. Currently taking a glucocorticoid
6. Waldenström’s macroglobulinemia
7. Steroid refractory chronic graft vs. host disease
8. Immune thrombocytopenic purpura
9. Thrombotic thrombocytopenic purpura
10. Refractory autoimmune hemolytic anemia
11. Leptomeningeal metastases
12. Primary central nervous system lymphoma
13. Hodgkin’s lymphoma

AND NONE of the following for ALL indications:

a. Used in combination with any other biologic DMARD or targeted synthetic DMARD

b. Use of a live vaccines, (Non-live vaccines should be administered at 4 weeks prior to a course of Rituxan)

c. Severe, active infections

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval Renewal Limits

Duration 12 months

Rationale

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

Section: Prescription Drugs  Effective Date: January 1, 2018
Subsection: Antineoplastic Agents  Original Policy Date: July 29, 2011
Subject: Rituxan  Page: 8 of 9


Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
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<tbody>
<tr>
<td>February 2012</td>
<td>Added Methotrexate (MTX) is required unless there is intolerance to MTX, contraindication to MTX or failure on MTX.</td>
</tr>
<tr>
<td>September 2012</td>
<td>Annual editorial and reference update</td>
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<tr>
<td></td>
<td>Deleted requirement of concurrent fludarabine and cyclophosphamide therapy for CLL (NCCN guidelines include many other concurrent therapies)</td>
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<tr>
<td>December 2012</td>
<td>Added indication for thrombotic thrombocytopenic purpura.</td>
</tr>
<tr>
<td>March 2013</td>
<td>Added exclusion of concomitant TNFI therapy or other biologic DMARD</td>
</tr>
<tr>
<td></td>
<td>Added exclusion of live vaccine within two weeks.</td>
</tr>
<tr>
<td>September 2013</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>March 2014</td>
<td>Annual editorial review</td>
</tr>
<tr>
<td>September 2014</td>
<td>Annual editorial review</td>
</tr>
<tr>
<td>December 2014</td>
<td>Annual editorial review and reference update</td>
</tr>
<tr>
<td>March 2015</td>
<td>Addition of Revlimid (lenalidomide) to combination therapy and defined</td>
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5.21.10

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NHL categories

June 2015  Annual review
December 2015  Annual review and reference update
Revised RA statement: Inadequate treatment response, intolerance, or contraindication to one or more tumor necrosis factor (TNF) antagonist therapies

June 2016  Annual editorial review and reference update
Change of NOT using a Tumor Necrosis Factor (TNF) antagonist and NOT using any of the following: Abatacept (Orencia), Tocilizumab (Actemra), Anakinra (Kineret), Tofacitinib (Xeljanz) to not to be used in combination with any other biologic DMARD or targeted synthetic DMARD
Addition of indications: leptomeningeal metastases, primary central nervous system lymphoma, Hodgkin’s lymphoma and Castleman’s disease
Policy number change from 5.04.10 to 5.21.10

June 2017  Annual editorial review and reference update
Addition of the age requirement to all indications

December 2017  Annual Editorial review
Updated renewal section

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2017 and is effective on January 1, 2018.