Reference number(s)
2501-A

STANDARD MEDICARE PART B MANAGEMENT

RITUXAN (rituximab)
RUXIENCE (rituximab-pvvr)
TRUXIMA (rituximab-abbs)
RIABNI (rituximab-arrx)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

Rituxan is indicated for the treatment of pediatric patients aged 6 months and older with previously untreated, advanced stage, CD20-positive diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL), Burkitt-like lymphoma (BLL) or mature B-cell acute leukemia (B-AL) in combination with chemotherapy.

Rituxan, Ruxience, Truxima, and Riabni are indicated for:

1. Non-Hodgkin's Lymphoma (NHL) in adult patients with:
   i. Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent
   ii. 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
   iii. Non-progressing (including stable disease), low-grade, CD20-positive, B-cell NHL, as a single agent after first-line CVP (cyclophosphamide, vincristine, and prednisone) chemotherapy
   iv. Previously untreated diffuse large B-cell, CD20-positive NHL in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) or other anthracycline-based chemotherapy regimens
2. Previously untreated, advanced stage, CD 20-positive, diffuse large B-cell lymphoma (DLBCL), Burkitt lymphoma (BL), Burkitt-like lymphoma (BLL) or mature B-cell leukemia (B-AL in combination with chemotherapy in pediatric patients aged 6 months and older with mature B-cell NHL and mature B-cell acute leukemia.
3. Chronic lymphocytic leukemia (CLL), in combination with fludarabine and cyclophosphamide (FC), for the treatment of adult patients with previously untreated and previously treated CD20-positive CLL.
4. Granulomatosis with Polyangiitis (Wegener's Granulomatosis) and Microscopic Polyangiitis, in combination with glucocorticoids.
5. Rheumatoid Arthritis (RA) in combination with methotrexate in adult patients with moderately-to severely-active RA who have inadequate response to one or more TNF antagonist therapies.

Rituxan is also indicated for:
Pemphigus Vulgaris (PV)
Rituxan is indicated for the treatment of adult patients with moderate to severe pemphigus vulgaris.

B. Compendial Uses

1. B-cell lymphoma
    i. Acquired immunodeficiency syndrome (AIDS)-related B-cell lymphoma
    ii. Burkitt lymphoma
    iii. Castleman's disease
    iv. Diffuse large B-cell lymphoma
    v. High grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
    vi. Histological transformation of indolent lymphomas to diffuse large B-cell lymphoma
    vii. Follicular lymphoma
    viii. Mantle cell lymphoma
    ix. Marginal zone lymphoma (nodal, splenic, gastric/non-gastric MALT)
    x. Post-transplant lymphoproliferative disorder (PTLD)
    xi. Pediatric aggressive mature B-cell lymphomas
    xii. B-cell lymphoblastic lymphoma
2. Malignant ascites, in advanced low-grade non-Hodgkin lymphoma
3. B-cell acute lymphoblastic leukemia (ALL)
4. CLL/small lymphocytic lymphoma (SLL)
5. Hairy cell leukemia
6. Rosai-Dorfman disease
7. Hodgkin's lymphoma, lymphocyte-predominant
8. Hodgkin's lymphoma, CD20-positive, relapsed or progressive
9. Primary cutaneous B-cell lymphoma
10. Central nervous system (CNS) cancers
    i. Leptomeningeal metastases from lymphomas
    ii. Primary CNS lymphoma
11. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma
12. Rheumatoid arthritis, moderate or high disease activity despite disease-modifying anti-rheumatic drug (DMARD) monotherapy
13. Autoimmune hemolytic anemia
14. Immune or idiopathic thrombocytopenic purpura (ITP), as initial therapy
15. Immune or idiopathic thrombocytopenic purpura (ITP), relapsed/refractory to standard therapy (e.g., corticosteroids, immune globulin)
16. Thrombotic thrombocytopenic purpura
17. Relapsing-remitting multiple sclerosis
18. Primary progressive multiple sclerosis
19. Myasthenia gravis, refractory to standard therapy (e.g., corticosteroids, immunosuppressants)
20. Systemic lupus erythematosus, refractory to standard therapy (e.g., corticosteroids, immunosuppressants)
21. Sjögren's syndrome
22. Chronic graft-versus-host disease (GVHD)
23. Prevention of Epstein-Barr virus (EBV)-related PTLD in hematopoietic stem cell transplant in (HSCT) recipients
24. Evans syndrome
25. Nephrotic syndrome, refractory to standard therapy (e.g., corticosteroids, immunosuppressants)
26. Acquired factor VIII deficiency (acquired hemophilia A)
27. Idiopathic inflammatory myopathy, refractory
28. Immune checkpoint inhibitor-related toxicities
29. Allogeneic transplant conditioning

30. Lung disease with systemic sclerosis
31. Thyroid eye disease (moderate to severe)

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. CRITERIA FOR INITIAL APPROVAL

A. Rheumatoid arthritis

Authorization of 12 months may be granted for treatment of rheumatoid arthritis when any of the following criteria are met.

1. The member has previously received treatment with a biologic or targeted synthetic DMARD (e.g., TNF inhibitor, Xeljanz) for the treatment of rheumatoid arthritis.
2. The member has had an inadequate response to methotrexate or leflunomide or there is a clinical reason to avoid treatment with methotrexate or leflunomide (e.g., renal or hepatic impairment).

B. Oncologic indications

Oncologic disorders must be CD20-positive as confirmed by testing or analysis to identify the CD20 protein on the surface of the B-cell.

1. B-cell lymphoma

Authorization of 12 months may be granted for treatment of any of the following indications:

i. AIDS-related B-cell lymphoma
ii. Burkitt lymphoma
iii. Castleman's disease
iv. Diffuse large B-cell lymphoma
v. High grade B-cell lymphoma (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
vi. Histological transformation of indolent lymphomas to diffuse large B-cell lymphoma
vii. Follicular lymphoma
viii. Mantle cell lymphoma
ix. Marginal zone lymphoma (nodal, splenic, gastric MALT, nongastric MALT)
x. Post-transplant lymphoproliferative disorder
xi. Pediatric aggressive mature B-cell lymphomas
xii. B-cell lymphoblastic lymphoma

2. Malignant ascites

Authorization of 12 months may be granted for treatment of malignant ascites in patients with advanced low-grade non-Hodgkin lymphoma.

3. B-cell acute lymphoblastic leukemia (ALL)

Authorization of 12 months may be granted for treatment of B-cell ALL.

4. Chronic lymphocytic leukemia/small lymphocytic lymphoma

Authorization of 12 months may be granted for treatment of CLL/SLL.

5. Hairy cell leukemia

Authorization of 12 months may be granted for treatment of hairy cell leukemia.

6. **Hodgkin's lymphoma**
   Authorization of 12 months may be granted for treatment of any of the following indications:
   i. Lymphocyte-predominant Hodgkin's lymphoma
   ii. CD20-positive relapsed or progressive Hodgkin's lymphoma

7. **Primary cutaneous B-cell lymphoma**
   Authorization of 12 months may be granted for treatment of primary cutaneous B-cell lymphoma.

8. **Central nervous system (CNS) cancers**
   Authorization of 12 months may be granted for treatment of any of the following indications:
   i. Leptomeningeal metastases from lymphomas
   ii. Primary CNS lymphoma

9. **Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma**
   Authorization of 12 months may be granted for treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma.

10. **Rosai-Dorfman disease**
    Authorization of 12 months may be granted for the treatment of Rosai-Dorfman disease.

C. Hematologic indications
Authorization of 12 months may be granted for treatment of any of the following indications:
1. Autoimmune hemolytic anemia
2. Immune or idiopathic thrombocytopenic purpura
3. Thrombotic thrombocytopenic purpura
4. Evans syndrome
5. Acquired factor VIII deficiency (acquired hemophilia A)

D. Multiple sclerosis
Authorization of 12 months may be granted for treatment of relapsing-remitting multiple sclerosis and primary progressive multiple sclerosis.

E. Myasthenia gravis
Authorization of 12 months may be granted for treatment of myasthenia gravis that is refractory to standard therapy (e.g., corticosteroids, immunosuppressants) or if there is a clinical reason to avoid standard therapy.

F. Systemic lupus erythematosus
Authorization of 12 months may be granted for treatment of systemic lupus erythematosus that is refractory to standard therapy (e.g., corticosteroids, immunosuppressants) or if there is a clinical reason to avoid standard therapy.

G. Granulomatosis with polyangiitis (Wegener's granulomatosis) and microscopic polyangiitis
Authorization of 12 months may be granted for treatment of granulomatosis with polyangiitis and microscopic polyangiitis.

H. Sjögren's syndrome
Authorization of 12 months may be granted for treatment of Sjögren's syndrome.

I. Nephrotic syndrome
Authorization of 12 months may be granted for treatment of nephrotic syndrome (e.g., minimal change disease) that is refractory to standard therapy (e.g., corticosteroids, immunosuppressants) or if there is a clinical reason to avoid standard therapy.

J. Idiopathic inflammatory myopathy
Authorization of 12 months may be granted for treatment of refractory idiopathic inflammatory myopathy.

K. Immune checkpoint inhibitor-related toxicities
Authorization of 3 months may be granted for treatment of immune checkpoint inhibitor-related toxicities.

L. Lung disease with systemic sclerosis
Authorization of 12 months may be granted for the treatment of lung disease with systemic sclerosis that is refractory to standard therapy (e.g., cyclophosphamide, mycophenolate) or if there is a clinical reason to avoid standard therapy.

M. Thyroid eye disease (moderate to severe)
Authorization of 12 months may be granted for the treatment of moderate to severe thyroid eye disease (excluding patients with risk for dysthyroid optic neuropathy) that is refractory to standard therapy (e.g., IV glucocorticoids) or if there is a clinical reason to avoid standard therapy.

N. Other indications
Authorization of 12 months may be granted for treatment of any of the following indications:
1. Chronic GVHD
2. Prevention of EBV-related PTLD in HSCT recipients
3. Pemphigus vulgaris
4. As part of a non-myeloablative conditioning regimen for allogeneic transplant

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

A. Authorization for 3 months may be granted for the diagnosis of immune checkpoint inhibitor-related toxicities when all of the following criteria are met:
   1. The member is currently receiving therapy with Rituxan, Ruxience, Truxima, or Riabni.
   2. Rituxan, Ruxience, Truxima, or Riabni is being used to treat an indication enumerated in Section II.
   3. The member is receiving benefit from therapy.

B. Authorization for 12 months may be granted for all diagnoses (except immune checkpoint inhibitor-related toxicities) when all of the following criteria are met:
   1. The member is currently receiving therapy with Rituxan, Ruxience, Truxima, or Riabni.
   2. Rituxan, Ruxience, Truxima, or Riabni is being used to treat an indication enumerated in Section II.
   3. The member is receiving benefit from therapy.

IV. REFERENCES

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