This policy applies to the following:

	Standard Opt-in		PDPD		Marketplace		Medical Benefit	✓	Medicare Part B
	Standard Opt-out		ACSF		MMT		Medical Benefit: Biosimilars First		Medicare Part B: Biosimilars First
	VF		Balanced		Medical Benefit: Managed Medicaid		Medical Benefit: Add-on		Medicare Part B: Add-on

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POLICY Document for RITUXAN, RUXIENCE, TRUXIMA

The overall objective of this policy is to support the appropriate and cost effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall clinically appropriate use. This document provides specific information to each section of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA

RITUXIMAB PRODUCTS

PREFERRED PRODUCTS: RITUXAN, RITUXAN HYCELA, RUXIENCE

POLICY

This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the rituximab products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members who are new to treatment with a targeted product for the first time.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Rituximab products

	Product(s)
Preferred	• **Rituxan (rituximab)** • **Rituxan Hycela (rituximab and hyaluronidase human)** • **Ruxience (rituximab-PVVR)**
Targeted	• **Truxima (rituximab-abbs)**

II. EXCEPTION CRITERIA

This policy applies to the following:

	Standard Opt-in		**PDPD**		**Marketplace**		**Medical Benefit**	✓	**Medicare Part B**
	Standard Opt-out		**ACSF**		**MMT**		**Medical Benefit: Biosimilars First**		**Medicare Part B: Biosimilars First**
	VF		**Balanced**		**Medical Benefit: Managed Medicaid**		**Medical Benefit: Add-on**		**Medicare Part B: Add-on**

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Coverage for the targeted product is provided when the member meets one of the following criteria:

A. Member has received treatment with the targeted product in the past 365 days.
B. The member has had a documented intolerable adverse event to all of the preferred products. The adverse event must not be an expected adverse event attributed to the active ingredient as described in the prescribing information (i.e., known adverse reaction for both the brand and biosimilar medication).

Section 2: Clinical Criteria

STANDARD MEDICARE PART B MANAGEMENT

RITUXAN (rituximab)

RUXIENCE (rituximab-pvvr)

TRUXIMA (rituximab-abbs)

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, Ruxience, and Truxima are indicated for:

1. Non-Hodgkin's Lymphoma (NHL) in adult patients with:
   a. Relapsed or refractory, low-grade or follicular, CD20-positive, B-cell NHL as a single agent

This policy applies to the following:

	Standard Opt-in		**PDPD**		**Marketplace**		**Medical Benefit**	✓	**Medicare Part B**
	Standard Opt-out		**ACSF**		**MMT**		**Medical Benefit: Biosimilars First**		**Medicare Part B: Biosimilars First**
	VF		**Balanced**		**Medical Benefit: Managed Medicaid**		**Medical Benefit: Add-on**		**Medicare Part B: Add-on**

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b. 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
c. 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
d. 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. 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.
3. Granulomatosis with Polyangiitis (Wegener's Granulomatosis) and Microscopic Polyangiitis in combination with glucocorticoids.

Rituxan and Truxima are also indicated for:

Rheumatoid Arthritis (RA)

Rituxan or Truxima, in combination with methotrexate, is indicated for the treatment of adult patients with moderately- to severely- active rheumatoid arthritis who have had an 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[3]
   ii. Burkitt lymphoma
   iii. Castleman's disease
   iv. Diffuse large B-cell lymphoma
   v. High-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma)
   vi. High-grade B-cell lymphoma, not otherwise specified
   vii. Histological transformation from follicular lymphoma to diffuse large B-cell lymphoma
   viii. Histological transformation from nodal marginal zone lymphoma to diffuse large B-cell lymphoma
   ix. Follicular lymphoma
   x. Mantle cell lymphoma
   xi. Marginal zone lymphoma (nodal, splenic, gastric/non-gastric MALT)
   xii. Post-transplant lymphoproliferative disorder (PTLD)
   xiii. B-cell lymphoblastic lymphoma
2. Malignant ascites, in advanced low-grade non-Hogkin lymphoma
3. B-cell acute lymphoblastic leukemia (ALL)
4. CLL/small lymphocytic lymphoma (SLL)

This policy applies to the following:

	Standard Opt-in		**PDPD**		**Marketplace**		**Medical Benefit**	✓	**Medicare Part B**
	Standard Opt-out		**ACSF**		**MMT**		**Medical Benefit: Biosimilars First**		**Medicare Part B: Biosimilars First**
	VF		**Balanced**		**Medical Benefit: Managed Medicaid**		**Medical Benefit: Add-on**		**Medicare Part B: Add-on**

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5. Hairy cell leukemia
6. Hodgkin's lymphoma, lymphocyte-predominant
7. Hodgkin's lymphoma, CD20-positive, relapsed or progressive
8. Primary cutaneous B-cell lymphoma
9. Central nervous system (CNS) cancers
   i. Leptomeningeal metastases from lymphomas
   ii. Primary CNS lymphoma
10. Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma
11. Rheumatoid arthritis, moderate or high disease activity despite disease-modifying anti-rheumatic drug (DMARD) monotherapy
12. Autoimmune hemolytic anemia
13. Immune or idiopathic thrombocytopenic purpura (ITP), as initial therapy
14. Immune or idiopathic thrombocytopenic purpura (ITP), relapsed/refractory to standard therapy (e.g., corticosteroids, immune globulin)
15. Thrombotic thrombocytopenic purpura
16. Relapsing-remitting multiple sclerosis
17. Primary progressive multiple sclerosis
18. Myasthenia gravis, refractory to standard therapy (e.g., corticosteroids, immunosuppressants)
19. Systemic lupus erythematosus, refractory to standard therapy (e.g., corticosteroids, immunosuppressants)
20. Sjögren's syndrome
21. Chronic graft-versus-host disease (GVHD)
22. Prevention of Epstein-Barr virus (EBV)-related PTLD in hematopoietic stem cell transplant in (HSCT) recipients
23. Evans syndrome
24. Nephrotic syndrome, refractory to standard therapy (e.g., corticosteroids, immunosuppressants)
25. Acquired factor VIII deficiency (acquired hemophilia A)
26. Idiopathic inflammatory myopathy, refractory
27. Immune checkpoint inhibitor-related toxicities

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

1. Rheumatoid arthritis

Authorization of 24 months may be granted for the treatment of rheumatoid arthritis when any of the following criteria are met.

This policy applies to the following:

	Standard Opt-in		**PDPD**		**Marketplace**		**Medical Benefit**	✓	**Medicare Part B**
	Standard Opt-out		**ACSF**		**MMT**		**Medical Benefit: Biosimilars First**		**Medicare Part B: Biosimilars First**
	VF		**Balanced**		**Medical Benefit: Managed Medicaid**		**Medical Benefit: Add-on**		**Medicare Part B: Add-on**

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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 there is a clinical reason to avoid treatment with methotrexate (e.g., renal or hepatic impairment).

2. 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 the 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 with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma)
vi. High-grade B-cell lymphoma, not otherwise specified
vii. Histological transformation from follicular lymphoma to diffuse large B-cell lymphoma
viii. Histological transformation from nodal marginal zone lymphoma to diffuse large B-cell lymphoma
ix. Follicular lymphoma
x. Mantle cell lymphoma
xi. Marginal zone lymphoma (nodal, splenic, gastric MALT, nongastric MALT)
xii. Post-transplant lymphoproliferative disorder
xiii. 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-Hogkin 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

This policy applies to the following:

	Standard Opt-in		**PDPD**		**Marketplace**		**Medical Benefit**	✓	**Medicare Part B**
	Standard Opt-out		**ACSF**		**MMT**		**Medical Benefit: Biosimilars First**		**Medicare Part B: Biosimilars First**
	VF		**Balanced**		**Medical Benefit: Managed Medicaid**		**Medical Benefit: Add-on**		**Medicare Part B: Add-on**

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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 the 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 the treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma.

3. 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)

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

5. Myasthenia gravis
Authorization of 12 months may be granted for the 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.

6. Systemic lupus erythematosus

This policy applies to the following:

	Standard Opt-in		PDPD		Marketplace		Medical Benefit	✓	Medicare Part B
	Standard Opt-out		ACSF		MMT		Medical Benefit: Biosimilars First		Medicare Part B: Biosimilars First
	VF		Balanced		Medical Benefit: Managed Medicaid		Medical Benefit: Add-on		Medicare Part B: Add-on

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Authorization of 12 months may be granted for the 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.

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

8. **Sjögren's syndrome**
   Authorization of 12 months may be granted for the treatment of Sjögren's syndrome.

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

10. **Idiopathic inflammatory myopathy**
    Authorization of 12 months may be granted for the treatment of refractory idiopathic inflammatory myopathy.

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

12. **Other indications**
    Authorization of 12 months may be granted for the treatment of any of the following indications:
    1. Chronic GVHD
    2. Prevention of EBV-related PTLD in HSCT recipients
    3. Pemphigus vulgaris

III. CONTINUATION OF THERAPY

This policy applies to the following:

	Standard Opt-in		**PDPD**		**Marketplace**		**Medical Benefit**	✓	**Medicare Part B**
	Standard Opt-out		**ACSF**		**MMT**		**Medical Benefit: Biosimilars First**		**Medicare Part B: Biosimilars First**
	VF		**Balanced**		**Medical Benefit: Managed Medicaid**		**Medical Benefit: Add-on**		**Medicare Part B: Add-on**

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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, or Truxima.
   2. Rituxan, Ruxience, or Truxima is being used to treat an indication enumerated in Section II.
   3. The member is receiving benefit from therapy.

B. Authorization for 24 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, or Truxima.
   2. Rituxan, Ruxience, or Truxima is being used to treat an indication enumerated in Section II.
   3. The member is receiving benefit from therapy.

UNIVERSAL CRITERIA

POLICY for RITUXAN HYCELA

The Specialty Universal Med B Criteria ensure appropriate utilization of Specialty medications and confirm that selection elements established in the FDA-approved product labeling and relevant compendia are followed. The criteria may be applied in situations where specific criteria are pending development.

Authorization of 12 months may be granted for a requested medication when clinically appropriate

REFERENCES:

SECTION 1

1. Rituxan [package insert]. South San Francisco, CA: Genentech, Inc.; August 2020.
2. Rituxan Hycela [package insert]. South San Francisco, CA: Genentech, Inc.; May 2020.
3. Ruxience [package insert]. New York, NY: Pfizer; May 2020.
4. Truxima [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc; May 2020.

SECTION 2

1. Rituxan [package insert]. South San Francisco, CA: Genentech, Inc.; March 2020.
2. Truxima [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc; December 2019.
3. The NCCN Drugs & Biologics Compendium® © 2020 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 22, 2020.
4. IBM Micromedex [Internet database]. Ann Arbor, MI: Truven Health Analytics. Updated periodically. Accessed November 17, 2019.

This policy applies to the following:

	Standard Opt-in		**PDPD**		**Marketplace**		**Medical Benefit**	✓	**Medicare Part B**
	Standard Opt-out		**ACSF**		**MMT**		**Medical Benefit: Biosimilars First**		**Medicare Part B: Biosimilars First**
	VF		**Balanced**		**Medical Benefit: Managed Medicaid**		**Medical Benefit: Add-on**		**Medicare Part B: Add-on**

Reference #
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5. Lexicomp Online®, Lexi-Drugs® Drug Information, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; http://online.lexi.com [available with subscription]. Accessed April 23, 2020.
6. Lexicomp Online®, AHFS® Drug Information, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc.; http://online.lexi.com [available with subscription]. Accessed April 23, 2020.
7. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care Res.* 2016;68(1):1-25.
8. The NCCN Clinical Practice Guidelines in Oncology® Acute Lymphoblastic Leukemia (Version 1.2020). © 2020 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 22, 2020.
9. Clinical Consult: CVS Caremark Clinical Programs Review. Focus on Hematology-Oncology Clinical Programs. July 2019.
10. Ruxience [package insert]. NY, NY: Pfizer Biosimilars; July 2019.