Approved Revision: Do Not Implement Until 6/2/21

Rituximab Products (Rituxan®, Rituximab-abbs [Truxima®], Rituximab-arrx [Riabni™] and Rituximab-pvvr [Ruxience®])

NDC CODE(S)

50242-0051-XX RITUXAN 10MG/ML Solution (GENENTECH)
50242-0053-XX RITUXAN 10MG/ML Solution (GENENTECH)
63459-0103-XX TRUXIMA 10MG/ML Solution (TEVA PHARMACEUTICALS USA)
63459-0104-XX TRUXIMA 10MG/ML Solution (TEVA PHARMACEUTICALS USA)
00069-0238-XX RUXIENCE 10MG/ML Solution (PFIZER U.S.)
00069-0249-XX RUXIENCE 10MG/ML Solution (PFIZER U.S.)
55513-0224-XX RIABNI 10MG/ML Solution (AMGEN)
55513-0326-XX RIABNI 10MG/ML Solution (AMGEN)

DESCRIPTION

Rituximab is a genetically engineered monoclonal antibody which binds specifically to the human CD20 antigen. The CD20 antigen is expressed on greater than 90% of B-cell non-Hodgkin's lymphomas and is found on the abnormal B-cells of chronic lymphocytic leukemia (CLL). Additionally, B-cells expressing the CD20 antigen are believed to play a role in the pathogenesis of rheumatoid arthritis.

In binding with the CD-20 antigen on B lymphocytes, rituximab likely recruits immune effector functions to mediate B-cell lysis, possibly through complement-dependent cytotoxicity (CDC) or antibody-dependent cell mediated cytotoxicity (AIDCC). Rituximab has also been shown to induce apoptosis in the DHL-4 human B-cell lymphoma line.

Rituximab biosimilar products are approved by the FDA only as biosimilar products, not as interchangeable products, although their response has so far been shown to be the same as that of the innovator product, rituximab: Upon binding to CD20, rituximab products lead to B-cell lysis) and antibody dependent cell mediated cytotoxicity (ADCC) as with Rituximab. Available products include Rituximab-abbs (Truxima®), Rituximab-arrx (Riabni™) and Rituximab-pvvr (Ruxience®).

POLICY

- Rituximab products for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met: **(See Medical Appropriateness below.)**
  - Acute lymphoblastic leukemia (ALL)
  - Autoimmune Hemolytic Anemia (AIHA)
  - Central nervous system cancers
  - Chronic graft-versus-host disease
  - Chronic lymphocytic leukemia (CLL) / Small lymphocytic lymphoma (SLL)
  - Granulomatosis with polyangiitis (GPA) / microscopic polyangiitis (MPA) (Wegener's granulomatosis [WG])
  - Hodgkin's Lymphoma (Classic)
  - Idiopathic/immune thrombocytopenic purpura (ITP)
  - Idiopathic inflammatory myopathy (e.g., myositis, dermatomyositis, polymyositis)
  - Management of Immunotherapy-Related Toxicities
  - Neuromyelitis optica / neuromyelitis optica spectrum disease (NMO/NMOSD)
  - Non-Hodgkin's lymphomas (NHL), including, but not limited to:
    - AIDS-related B-Cell Lymphoma
    - Burkitt Lymphoma
    - Castleman's Disease
    - Diffuse Large B-Cell Lymphoma

    - Follicular Lymphoma
    - Gastric & Non-gastric Malt Lymphoma
    - Hairy Cell Leukemia
    - High Grade B-Cell Lymphoma
    - Histologic transformation of Marginal Zone Lymphoma to Diffuse Large B-Cell Lymphoma
    - Low-grade
    - Lymphoma following solid organ transplant or allogeneic hematopoietic stem cell transplantation
    - Mantle Cell Lymphoma
    - Marginal Zone Lymphoma
    - Nodal & Splenic Marginal Zone Lymphoma
    - Post-transplant lymphoproliferative disorder (PTLD)
    - Primary Cutaneous B-Cell Lymphomas
  - Pediatric Aggressive Mature B-Cell Lymphomas
  - Pemphigus vulgaris
  - Rheumatoid arthritis (RA)
  - Thrombotic Thrombocytopenic Purpura (TTP)
  - Waldenström's macroglobulinemia / lymphoplasmacytic lymphoma
- Rituximab products for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

- Patient is at least 18 years of age (unless otherwise specified); **AND**
- Patient is currently on and will be continuing treatment with rituximab (Rituxan®); **OR**
- Patient has a contraindication, inadequate response or intolerable side effects with a prior trial of one of the following:
  - Rituximab-abbs (Truxima®); **OR**
  - Rituximab-pvvr (Ruxience®)

NOTE: *New to therapy or patients switching from Rituxan® require use of one of the preferred biosimilars before a non-preferred product except as outlined above*.

Universal Criteria

- Patient does not have a severe, active infection; **AND**
- Patient has been screened for the presence of hepatitis B (HBV) infection (i.e., HBsAg and anti-HBc) prior to initiating therapy and patients with evidence of current or prior HBV infection will be monitored for HBV reactivation during treatment; **AND**
- Patient has not received a live vaccine within 28 days prior to starting treatment and live vaccines will not be administered concurrently while on treatment; **AND**

Oncology Indications

- Patient CD20 antigen expression is positive; **AND**

Acute Lymphoblastic Leukemia (ALL)

- Induction/Consolidation Treatment
  - Patient has Philadelphia chromosome-negative (Ph-) disease; **AND**
    - Patient is at least 15 years of age; **AND**

        - Used in combination with an anthracycline, cyclophosphamide, and vincristine-based regimen
- Relapsed/Refractory Treatment
    - Patient has Philadelphia chromosome-negative (Ph-) disease OR tyrosine kinase inhibitor (TKI) refractory Philadelphia chromosome-positive (Ph+) disease; **AND**
        - Used in combination with MOpAD regimen (methotrexate, vincristine, pegaspargase, dexamethasone)

Central Nervous System (CNS) Cancer

- Patient has leptomeningeal metastases from lymphomas; **AND**
    - Rituximab will be administered intrathecally; **OR**
- Patient has primary CNS lymphoma; **AND**
    - Patient will receive as a component of induction therapy in combination with a methotrexate-containing regimen, temozolomide, lenalidomide, or as a single agent; **OR**
    - Patient will receive in combination with a methotrexate-containing regimen as a component of consolidation therapy with a complete response (CR) or a complete response unconfirmed (CRu) to induction therapy; **OR**
    - Patient has relapsed or refractory disease and will receive rituximab as a single agent, or in combination with temozolomide, lenalidomide, or high-dose methotrexate

Hodgkin Lymphoma

- Patient has nodular lymphocyte-predominant disease

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)

- Used in combination with fludarabine and cyclophosphamide (FC); **OR**
- Patient has disease that is <u>without</u> del(17p)/TP53 mutation; **AND**
    - Used as first-line therapy in combination with one of the following:
        - Bendamustine *(patients ≥ 65 years, or younger patients with or without significant comorbidities)*
        - Fludarabine *(patient is without del(11q) and is <65 years without significant comorbidities)*; **OR**
    - Used for relapsed or refractory disease in combination with one of the following:
        - Alemtuzumab
        - Bendamustine *(patients < 65 years without significant comorbidities)*
        - Chlorambucil *(patients ≥ 65 years, or younger patients with significant comorbidities)*
        - High-dose methylprednisolone
        - Idelalisib
        - Lenalidomide
        - Venetoclax
        - PCR (pentostatin, cyclophosphamide, and rituximab); **OR**
- Patient has disease with del(17p)/TP53 mutation; **AND**
    - Used as first-line therapy in combination with one of the following:
        - Alemtuzumab
        - High-dose methylprednisolone; **OR**
    - Used for relapsed or refractory disease in combination with one of the following:
        - Alemtuzumab
        - High-dose methylprednisolone
        - Idelalisib
        - Lenalidomide
        - Venetoclax; **OR**

- Used as first line therapy for histologic (Richter's) transformation to diffuse large B-cell lymphoma in combination with cyclophosphamide, doxorubicin, and vincristine based regimens or as a component of OFAR (oxaliplatin, fludarabine, cytarabine, and rituximab)

Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma

Non-Hodgkin's Lymphomas (NHL) including, but not limited to, the following:

- AIDS-Related B-Cell Lymphoma
  - Disease is related to Burkitt Lymphoma or diffuse large B-cell lymphoma *(including HHV8-positive DLBCL, not otherwise specified, or primary effusion lymphoma)*
- Burkitt Lymphoma
  - Used in combination with chemotherapy
- Castleman's Disease
  - Patient has multicentric disease; **OR**
  - Patient has unicentric disease; **AND**
    - Used as second-line therapy for relapsed or refractory disease; **OR**
    - Used for patients with symptoms after resection or unresectable disease
- Diffuse Large B-Cell Lymphoma
- Low-grade or Follicular Lymphoma
- Gastric & Non-Gastric MALT Lymphoma
- High Grade B-Cell Lymphoma
- Mantle Cell Lymphoma
- Nodal & Splenic Marginal Zone Lymphoma
- Histologic transformation of Follicular or Nodal Marginal Zone Lymphoma to Diffuse Large B-Cell Lymphoma
- Post-transplant lymphoproliferative disorder (PTLD) (B-cell type)
  - Patient has had solid organ transplant or allogeneic hematopoietic stem cell transplantation
- Pediatric Aggressive Mature B-Cell Lymphomas
  - Used in combination with chemotherapy
- Primary Cutaneous B-Cell Lymphomas

Hairy Cell Leukemia

- Used in combination with cladribine as initial therapy; OR
- Used for relapsed or refractory disease or in patients with a less than complete response (CR) to initial therapy

Management of Immunotherapy-Related Toxicities

- Patient has been receiving therapy with an immune checkpoint inhibitor (e.g., cemiplimab, nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab, ipilimumab, etc.); **AND**
  - Patient has non-viral encephalitis related to their immunotherapy; **AND**
    - Patient is autoimmune-encephalopathy-antibody positive; **OR**
    - Patient is refractory to methylprednisolone with or without IV immunoglobulin (IVIG); **OR**
  - Patient has bullous dermatitis related to their immunotherapy; **AND**
    - Used as additional therapy for moderate (G2), severe (G3) or life-threatening (G4) disease; **OR**
  - Patient has severe (G3-4) myasthenia gravis related to their immunotherapy that is refractory to plasmapheresis or IV immunoglobulin (IVIG)

<u>Non-Oncology Indications</u>

- Patient is not on concurrent treatment with another TNF-inhibitor, biologic response modifier or other non-biologic agent (i.e., apremilast tofacitinib, baricitinib, upadacitinib); **AND**

Rheumatoid Arthritis (RA)

- Documented moderate to severe disease; **AND**
- Used in combination with methotrexate unless the patient has a contraindication or intolerance; **AND**
- Patient tried and failed at least a 3 month trial with ONE oral disease modifying antirheumatic drug (DMARD) (e.g., methotrexate, azathioprine, auranofin, hydroxychloroquine, penicillamine, sulfasalazine, leflunomide, etc.); **AND**
- Previous failure with one or more preferred TNF antagonists at least one of which should be a self-injectable; **AND**
- Physician has assessed baseline disease severity utilizing an objective measure/tool; **AND**
- Patient has not had treatment with rituximab in the previous 4 months

Pemphigus Vulgaris

- Patient has a diagnosis of pemphigus vulgaris as determined by the following:
  - One or more of the following clinical features:
    - Appearance of lesions, erosions and/or blisters
    - Nikolsky sign (induction of blistering via mechanical pressure at the edge of a blister or on normal skin)
    - Characteristic scarring and lesion distribution; **AND**
  - Histopathologic confirmation by skin/mucous membrane biopsy; **AND**
  - Presence of autoantibodies as detected by indirect immunofluorescence or enzyme-linked immunosorbent assay (ELISA); **AND**
- Patient has moderate to severe disease as assessed utilizing an objective measure/tool (i.e., PDAI, PSS, ABSIS); **AND**
- Patient is on combination glucocorticoid therapy; **AND**
- Other causes of blistering or erosive skin and mucous membrane diseases have been ruled out

Granulomatosis with Polyangiitis (GPA) (Wegener's granulomatosis) and Microscopic Polyangiitis (MPA)

- Patient is at least 2 years of age; **AND**
- Used in combination with glucocorticoids (e.g., prednisone, methylprednisolone, etc.)

Thrombocytopenic Purpura

- Patient has previously failed or has a contraindication or intolerance to therapy with corticosteroids; **AND**
- Patient is at increased risk for bleeding as indicated by platelet count (within the previous 28 days) less than 30 × 109/L (30,000/mm³); **AND**
- Patient diagnosis includes one of the following:
  - Primary thrombocytopenia
  - Idiopathic (Immune) thrombocytopenia purpura (ITP)
  - Evan's syndrome
  - Congenital and hereditary thrombocytopenic purpura
  - Thrombotic thrombocytopenic purpura in patients with ADAMTS13-deficiency

Chronic Graft-Versus-Host Disease (cGVHD)

- Patient is post-allogeneic stem cell transplant (generally 3 or more months); **AND**

- Used as additional therapy in combination with corticosteroids; **AND**
- Patient has failed one or more previous lines of systemic therapy for the treatment of cGVHD (e.g., corticosteroids or immunosuppressants such as cyclosporine); **AND**
- Patient must try and have an inadequate response, contraindication, or intolerance to at least a three (3) month trial of ibrutinib

Autoimmune Hemolytic Anemia (AIHA)

- Patient has warm-reactive disease refractory to or dependent on glucocorticoids; **OR**
- Patient has cold agglutinin disease with symptomatic anemia, transfusion-dependence, and/or disabling circulatory symptoms

Neuromyelitis Optica Spectrum Disorder (NMOSD)

- Patient has a confirmed diagnosis based on the following:
  - Patient was found to be seropositive for aquaporin-4 (AQP4) IgG antibodies; **AND**
    - Patient has at least one core clinical characteristic*; **AND**
    - Alternative diagnoses have been excluded (e.g., multiple sclerosis, sarcoidosis, cancer, chronic infection, etc.); **OR**
  - Patient was found to be seronegative for AQP-4 IgG antibodies OR has unknown AQP-4-IgG status; **AND**
    - Patient has at least two core clinical characteristics occurring as a result of one or more clinical attacks*; **AND**
    - Patient experienced ALL of the following:
      - At least 1 core clinical characteristic must be optic neuritis, acute myelitis with LETM***, or area postrema syndrome; **AND**
      - Dissemination in space (≥2 different core clinical characteristics); **AND**
      - Fulfillment of additional MRI requirements, as applicable**; **AND**
    - Alternative diagnoses have been excluded (e.g., multiple sclerosis, sarcoidosis, cancer, chronic infection, etc.); **AND**
- Used as a single agent or in combination with immunosuppressive therapy (e.g. azathioprine, methotrexate, mycophenolate, etc.)

***Core Clinical Characteristics of NMOSD**
▪ Optic neuritis ▪ Acute myelitis ▪ Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting ▪ Acute brainstem syndrome ▪ Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions ▪ Symptomatic cerebral syndrome with NMOSD-typical brain lesions
****Additional MRI requirements - NMOSD without AQP4-IgG and NMOSD unknown AQP4-IgG status**
Acute optic neuritis: requires brain MRI showing (a) normal findings or only nonspecific white matter lesions, OR (b) optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium-enhancing lesion extending over >1/2 optic nerve length or involving optic chiasm **Acute myelitis**: requires associated intramedullary MRI lesion extending over ≥3 contiguous segments (LETM***) OR ≥3 contiguous segments of focal spinal cord atrophy in patients with history compatible with acute myelitis **Area postrema syndrome**: requires associated dorsal medulla/area postrema lesions **Acute brainstem syndrome**: requires associated peri-ependymal brainstem lesions
****LETM = longitudinally extensive transverse myelitis lesions*

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc., identified in Initial Approval Criteria; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe infusion-related reactions, tumor lysis syndrome (TLS), severe mucocutaneous reactions, progressive multifocal leukoencephalopathy (PML), hepatitis B virus reactivation, serious bacterial, fungal, or viral infections, cardiac arrhythmias, renal toxicity, bowel obstruction or perforation, etc.; **AND**

Oncology Indications

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Patient has not exceeded dosing or duration limits as defined in Length of Authorization, Dosing Limits and Dosage/Administration table

Non-Oncology Indications

Rheumatoid arthritis (RA)

- Disease response as indicated by improvement in signs and symptoms compared to baseline such as the number of tender and swollen joint counts, reduction of C-reactive protein, improvement of patient global assessment, and/or an improvement on a disease activity scoring tool [e.g. an improvement on a composite scoring index such as Disease Activity Score-28 (DAS28) of 1.2 points or more or a ≥20% improvement on the American College of Rheumatology-20 (ACR20) criteria]; **AND**
- Dose escalation (up to the maximum dose and frequency specified below) may occur upon clinical review on a case by case basis provided that the patient has:
  - Shown an initial response to therapy; **AND**
  - Received a minimum of one maintenance dose at the dose and interval specified below; **AND**
  - Responded to therapy with subsequent loss of response

Thrombocytopenic purpura

- Disease response as indicated by the achievement and maintenance of a platelet count of at least 50×10^9/L as necessary to reduce the risk for bleeding

Thrombotic thrombocytopenic purpura (TTP)

- Disease response as indicated by an increase in ADAMTS13 activity with a reduction in thrombotic risk

Granulomatosis with Polyangiitis (GPA) (Wegener's granulomatosis) and Microscopic polyangiitis (MPA)

- Disease response as indicated by disease control and improvement in signs and symptoms of condition compared to baseline; **AND**
- A decreased frequency in the occurrence of major relapses (defined by the reappearance of clinical and/or laboratory signs of vasculitis activity that could lead to organ failure or damage, or could be life threatening)

Pemphigus vulgaris

- Patient is currently receiving tapering doses of corticosteroids or has discontinued use of corticosteroids; **AND**
  - Disease response as indicated by complete epithelialization of lesions and improvement in signs and symptoms of condition compared to baseline; **OR**
  - Patient has not experienced continued development of new lesions, continued extension of old lesions, or failure of established lesions to begin to heal despite therapy; **OR**
    - For Relapses ONLY: Patient has had active disease control; **AND**
    - Patient has the appearance of 3 or more new lesions a month that do not heal spontaneously within 1 week, or by the extension of established lesions

Chronic graft-versus-host disease (cGVHD)

- May not be renewed

Autoimmune hemolytic anemia (AIHA)

- Disease response as indicated by improvement in anemia signs and symptoms (e.g., dyspnea, fatigue, etc.) as well as: improvement in laboratory values (Hb/Hct), reduced transfusion needs, and/or reduced glucocorticoid use

NMOSD

- Disease response as indicated by stabilization/improvement in any of the following: neurologic symptoms as evidenced by a decrease in acute relapses, stability reduced hospitalizations, reduction/discontinuation in plasma exchange treatments, and/or reduction/discontinuation of corticosteroids without relapse

DOSAGE/ADMINISTRATION

INDICATION	DOSE	
CLL/SLL	Initial Therapy	375 mg/m² intravenously (IV) weekly for 8 doses; **OR** 375 mg/m² IV cycle 1, then 500 mg/m² every 28 days cycles 2-6 (6 total doses)
	Renewal Therapy	375 mg/m² IV once weekly for 4 doses per 6 month period; **OR** 375 mg/ m² IV every 8 weeks
NHL, PTLD, Waldenström's, Castleman's, or HL	Initial Therapy	375 mg/m2 IV once weekly for 4 - 8 doses in a 6 month period
	Renewal Therapy	375 mg/m² IV once weekly for 4 doses per 6 month period; **OR** 375 mg/ m² IV every 8 weeks
Pediatric Aggressive B-cell Lymphoma		**Induction*** 375 mg/m2 IV once to twice during the first week of the induction cycle (typically 21-day cycle) **Consolidation*** 375 mg/m2 IV once weekly on day-1 of the consolidation cycle (typically 21-day cycle) **Relapsed/Refractory** RCYVE – 375mg/m2 IV on day-1 of each 21-day cycle RICE – 375 mg/m2 IV on days 1 and 3 of courses 1 and 2, and on day 1 only of course 3 if needed. **Note: dosing and dosing schedules are highly variable and dependent on regimen used, please refer to NCCN for different protocols.*
CNS Lymphoma		**Intravenous administration**

	Initial Therapy: 375 mg/m2 IV once weekly for 4 - 8 doses in a 6 month period Renewal Therapy: 375 mg/m² IV once weekly for 4 doses per 6 month period; **OR** 375 mg/m² IV every 8 weeks **Intrathecal/Intraventricular administration** 10-40 mg weekly to every 3 weeks
ALL	375 mg/m² IV once weekly for 4 - 8 doses in a 6 month period
Hairy Cell Leukemia	375 mg/m² IV once weekly for 4 - 8 doses
RA	1,000 mg IV on days 1 and 15, repeated every 24 weeks. May repeat up to every 16 weeks in patients requiring more frequent dosing based on clinical evaluation.
Pemphigus Vulgaris	Initiation ▫ Administer 1,000 mg IV on days 1 and 15 in combination with tapering doses of glucocorticoids Maintenance ▫ Administer 500 mg IV at month 12 and repeat every 6 months thereafter or based on clinical evaluation Relapse ▫ Administer 1,000 mg IV upon relapse, resumption of glucocorticoids may be considered **Subsequent infusions (maintenance and relapse) should be no sooner than 16 weeks after the previous infusion.*
Thrombocytopenia, AIHA	375 mg/m² IV weekly for 4 doses in a 6 month period
Immunotherapy Toxicity Treatment	Bullous dermatitis 1,000 mg IV every 2 weeks for 2 doses, then 500 mg IV at months 12 and 18 as needed Myasthenia gravis/Encephalitis 375 mg/m² IV weekly for 4 doses; **OR** 500 mg/m² IV every 2 weeks for 2 doses
GPA (WG), MPA	Induction (Pediatric and Adult) ▫ 375 mg/m² IV weekly for 4 doses Maintenance* ▫ Pediatric: • 250 mg/m² IV on days 1 and 15, then 250 mg/m² IV every 6 months thereafter based on clinical evaluation ▫ Adult: • 500 mg IV on days 1 and 15, then 500 mg IV every 6 months thereafter based on clinical evaluation. **Initial MAINTENANCE infusions should be no sooner than 16 weeks and no later than 24 weeks after the previous infusion if Rituxan was used for initial induction therapy.* **Initial MAINTENANCE infusions should be initiated within 4 weeks following disease control when initial induction occurred with other standard of care immunosuppressants.*
cGVHD	375 mg/m² IV weekly for 4 doses, then 375 mg/m² IV monthly for 4 months **-OR-**

	375 mg/m² IV weekly for 4 doses (*Note: A second course of 4 weekly doses may be administered 8 weeks after initial therapy for patients with lack of or incomplete response.)* **-OR-** 375 mg/m² IV weekly for 4 - 8 doses
NMOSD	1,000 mg IV once on days 1 and 15, repeat every 6 months **-OR-** 375 mg/m2 once weekly for 4 weeks, repeat every 6 months

LENGTH OF AUTHORIZATION

Coverage will be provided for 6 months (12 months initially for pemphigus vulgaris) and may be renewed unless otherwise specified:

- Maintenance therapy for oncology indications (excluding ALL, Hairy Cell Leukemia, and Mantle cell lymphoma) may be renewed for up to a maximum of 2 years.
  - Mantle cell lymphoma may be renewed until disease progression or intolerable toxicity.
  - Acute lymphoblastic leukemia (ALL) and Hairy Cell Leukemia may not be renewed.
- Management of Immunotherapy-Related Toxicities:
  - Myasthenia gravis/encephalitis may not be renewed.
  - Bullous dermatitis may be renewed for a maximum of 18 months (4 total doses).
- Relapse therapy for pemphigus vulgaris must be at least 16 weeks past a prior infusion.
- Chronic Graft-Versus-Host Disease (cGVHD) may not be renewed.

DOSAGE LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

Oncology Indications:

Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Leukemia (SLL):
• Initial therapy:
  ○ Loading dose: 100 billable units x 1 dose
  ○ Subsequent doses - 130 billable units every 28 days x 5 doses per 6 months
• Renewal therapy - 100 billable units per dose every 8 weeks x 4 doses per 6 months

Immunotherapy Toxicity • 100 billable units per dose weekly x 4 doses in a 6 months period
All other oncology indications: • Initial therapy: 100 billable units per dose weekly x 8 doses per 6 months • Renewal therapy: 100 billable units per dose every 8 weeks x 4 doses per 6 months
Non Oncology Indications:
Rheumatoid Arthritis (RA): • 100 billable units per dose every 14 days x 2 doses in a 16 week period
Pemphigus Vulgaris: • Initiation: 100 billable units every 14 days x 2 doses in a 12 month period • Maintenance: 50 billable units every 16 weeks
GPA(WG)/MPA • Induction: 100 billable units per dose weekly x 4 doses in a 4 month period • Initial Maintenance: 100 billable units x 2 doses in a 6 month period • Subsequent Maintenance**:** 50 billable units every 6 months
cGVHD

• 100 billable units per dose weekly x 4 doses, then 100 units monthly x 4 months; **OR** • 100 billable units per dose weekly x 4 - 8 doses
Neuromyelitis Optica Spectrum Disorders (NMOSD) • 100 billable units per dose every 14 days x 2 doses in a 24 week period; **OR** • 100 billable units per dose weekly x 4 doses in a 6 month period
All other non-oncology indications • 100 billable units per dose weekly x 4 doses in a 6 month period

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

1. Rituxan [package insert]. South San Francisco, CA; Genentech, Inc; August 2020. Accessed November 2020.
2. Truxima [package insert]. Incheon, Korea; Celltrion, Inc; May 2020. Accessed November 2020.
3. Ruxience [package insert]. New York, NY; Pfizer, Inc; May 2020. Accessed November 2020.
4. Riabni [package insert]. Thousand Oaks, CA; Amgen, Inc; December 2020. Accessed December 2020.
5. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) rituximab. National Comprehensive Cancer Network, 2020. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed November 2020.
6. Arnold DM, Dentali F, Crowther MA, et al. Systematic review: efficacy and safety of rituximab for adults with idiopathic thrombocytopenic purpura. Ann Intern Med 2007; 146:25-33.
7. Zaja F, Baccarani M, Mazza P, et al: Dexamethasone plus rituximab yields higher sustained response rates than dexamethasone monotherapy in adults with primary immune thrombocytopenia. Blood 2010; 115(14):2755-2762.

8. Stasi R, Pagano A, Stipa E, et al: Rituximab chimeric anti-CD10 monoclonal antibody treatment for adults with chronic idiopathic thrombocytopenic purpura. Blood 2001; 98(4):952-957.
9. Neunert C, Lim W, Crowther M, Cohen A, Solberg L Jr, Crowther MA. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. Blood. 117(16):4190-4207.
10. Joly P, Mouquet H, Roujeau JC, et al. A single cycle of rituximab for the treatment of severe pemphigus. N Engl J Med 2007; 357:545-52.
11. Ahmed AR, Spigelman Z, Cavacini LA et al. Treatment of pemphigus vulgaris with rituximab and intravenous immune globulin. N Engl J Med 2006; 355:1772-9.
12. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care Res (Hoboken). 2015 Nov 6. doi: 10.1002/acr.22783.
13. Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017 Mar 6. pii: annrheumdis-2016- 210715.
14. González-Barca E, Domingo-Domenech E, Capote FJ, et al. Prospective phase II trial of extended treatment with rituximab in patients with B-cell post-transplant lymphoproliferative disease. Haematologica. 2007 Nov; 2(11):1489-94.
15. Chamberlain MC, Johnston SK, Van Horn A, et al. Recurrent lymphomatous meningitis treated with intra-CSF rituximab and liposomal ara-C. J Neurooncol. 2009 Feb;91(3):271-7.
16. Scully M, Cohen H, Cavenagh J, et al. Remission in acute refractory and relapsing thrombotic thrombocytopenic purpura following rituximab is associated with a reduction in IgG antibodies to ADAMTS-13. Br J Haematol 2007;136:451-461.
17. Fakhouri F, Vernant JP, Veyradier A, et al. Efficiency of curative and prophylactic treatment with rituximab in ADAMTS13-deficient thrombotic thrombocytopenic purpura: a study of 11 cases. Blood. 2005;106:1932-37.
18. Elliott MA, Heit JA, Rajiv K, et al. Rituximab for refractory and or relapsing thrombotic thrombocytopenic purpura related to immune-mediated severe ADAMTS13-deficiency: a report of four cases and a systematic review of the literature. Eur J Haematol 2009. Epub ahead of print, doi:10.1111/j.1600-0609.2009.01292.
19. Scully M, McDonald V, Cavenagh J, et al. A phase 2 study of the safety and efficacy of rituximab with plasma exchange in acute acquired thrombotic thrombocytopenic purpura. Blood. 2011;118(7):1746-1753.
20. Tun NM, Villani GM. Efficacy of rituximab in acute refractory or chronic relapsing non-familial idiopathic thrombotic thrombocytopenic purpura: a systematic review with pooled data analysis. J Thromb Thrombolysis. 2012;34(3):347-359.
21. Froissart A, Buffet M, Veyradier A, et al: Efficacy and safety of first-line rituximab in severe, acquired thrombotic thrombocytopenic purpura with a suboptimal response to plasma exchange. Experience of the French Thrombotic Microangiopathies Reference Center. Crit Care Med 2012; 40(1):104-111.
22. van Dorp S, Resemann H, te Boome L, et al. The immunological phenotype of rituximab-sensitive chronic graft-versus-host disease: a phase II study. Haematologica 2011;96(9):1380-1384.
23. Kim SJ, Lee JW, Jung CW, et al. Weekly rituximab followed by monthly rituximab treatment for steroid-refractory chronic graft-versus-host disease: results from a prospective, multicenter, phase II study. Haematologica 2010;95(11):1935-1942.
24. Cutler C, Miklos D, Kim HT, et al, “Rituximab for Steroid-Refractory Chronic Graft-Versus-Host Disease,” Blood, 2006, 108(2):756-62.
25. Wolff D, Schleuning M, von Harsdorf S, et al. Consensus Conference on Clinical Practice in Chronic GVHD: Second-Line Treatment of Chronic Graft-versus-Host Disease. Biol Blood Marrow Transplant. 2011 Jan;17(1):1-17. doi: 10.1016/j.bbmt.2010.05.011.
26. Frame JN, Fichtner R, McDevitt PW. Rituximab for the treatment of autoimmune hemolytic anemia (AIHA) in adults: an analysis of literature reports in 92 patients. Blood 2004;104:Abstract 3721.
27. Birgens H, Frederiksen H, Hasselbalch HC, et al: A phase III randomized trial comparing glucocorticoid monotherapy versus glucocorticoid and rituximab in patients with autoimmune haemolytic anaemia. Br J Haematol 2013; 163(3):393-399.
28. Schollkopf C, Kjeldsen L, Bjerrum OW, et al: Rituximab in chronic cold agglutinin disease: a prospective study of 20 patients. Leuk Lymphoma 2006; 47(N2):253-260.

29. Berentsen S, Ulvestad E, Gjertsen BT, et al: Rituximab for primary chronic cold agglutinin disease: a prospective study of 37 courses of therapy in 27 patients. Blood 2004; 103(8):2925-2928.
30. Reynaud Q, Durieu I, Dutertre M, et al. Efficacy and safety of rituximab in autoimmune hemolytic anemia: A meta-analysis of 21 studies. Autoimmun Rev. 2015;14(4):304-313.
31. Barcellini W, Zaja F, Zaninoni A, et al, "Low-dose Rituximab in Adult Patients With Idiopathic Autoimmune Hemolytic Anemia: Clinical Efficacy and Biologic Studies," Blood, 2012, 119(16):3691-7.
32. Roumier M, Loustau V, Guillaud C, et al. Characteristics and outcome of warm autoimmune hemolytic anemia in adults: New insights based on a single-center experience with 60 patients. Am J Hematol. 2014;89(9):E150-E155.
33. Gobert D, Bussel JB, Cunningham-Rundles C, et al. Efficacy and safety of rituximab in common variable immunodeficiency-associated immune cytopenias: a retrospective multicentre study on 33 patients. Br J Haematol. 2011;155(4):498-508.
34. YW Shin, ST Lee, KI Park, et al. Treatment strategies for autoimmune encephalitis. Ther Adv Neurol Disord. 2017 Aug 16;11:1756285617722347. doi: 10.1177/1756285617722347. eCollection 2018. Review.
35. Murrell DF, Dick S, Ahmed AR, et al. Consensus statement on definitions of disease, end points, and therapeutic response for pemphigus. J Am Acad Dermatol. 2008 June; 58(6): 1043–1046. doi:10.1016/j.jaad.2008.01.012. Avail at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2829665/pdf/nihms82304.pdf
36. Grover, S. Scoring Systems in Pemphigus. Indian J Dermatol. 2011 Mar-Apr; 56(2): 145–149. doi: 10.4103/0019-5154.80403
37. Daniel BS, Hertl M, Weth VP, et al. Severity score indexes for blistering diseases. Clin Dermatol. 2012 Jan-Feb; 30(1): 108–113. doi: 10.1016/j.clindermatol.2011.03.017
38. Joly P, Litrowski N. Pemphigus group (vulgaris, vegetans, foliaceus, herpetiformis, brasiliensis). Clin Dermatol 2011; 29:432.
39. Lambert MP, Gernsheimer TB. Clinical updates in adult immune thrombocytopenia. Blood. 2017. 129:2829-2835. doi:10.1182/blood-2017-03-754119
40. Schulz H, Pels H, Schmidt-Wolf I, et al. Intraventricular treatment of relapsed central nervous system lymphoma with the anti-CD20 antibody rituximab. Haematologica January 2004 89: 753-754.
41. Fahrenbruch R, Kintzel P, Bott AM, et al. Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association. J Oncol Pract. 2018 Mar;14(3):e130-e136.
42. Hematology/Oncology Pharmacy Association (2019). Intravenous Cancer Drug Waste Issue Brief. Retrieved from http://www.hoparx.org/images/hopa/advocacy/Issue-Briefs/Drug_Waste_2019.pdf
43. Bach PB, Conti RM, Muller RJ, et al. Overspending driven by oversized single dosevials of cancer drugs. BMJ. 2016 Feb 29;352:i788.
44. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas 4.2020. National Comprehensive Cancer Network, 2020. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed November 2020.
45. Imbruvica [package insert]. Horsham, PA; Janssen Biotech, Inc. August 2020. Accessed November 2020.
46. Keystone E, Burmester GR, Furie R, et al. Improvement in patient-reported outcomes in a rituximab trial in patients with severe rheumatoid arthritis refractory to antitumor necrosis factor therapy. Arthritis Rheum. 2008 Jun 15;59(6):785-93. doi: 10.1002/art.23715.
47. Mease PJ, Cohen S, Gaylis NB, et al. Efficacy and Safety of Retreatment in Patients with Rheumatoid Arthritis with Previous Inadequate Response to Tumor Necrosis Factor Inhibitors: Results from the SUNRISE Trial. The Journal of Rheumatology May 2010, 37 (5) 917-927; DOI: https://doi.org/10.3899/jrheum.090442
48. Tak PP, Rigby W, Rubbert-Roth A, et al. Sustained inhibition of progressive joint damage with rituximab plus methotrexate in early active rheumatoid arthritis: 2-year results from the randomised controlled trial IMAGE. Ann Rheum Dis. 2012 Mar;71(3):351-7. doi: 10.1136/annrheumdis-2011-200170. Epub 2011 Oct 19.

49. Emery P, Deodhar A, Rigby WF, et al. Efficacy and safety of different doses and retreatment of rituximab: a randomised, placebo-controlled trial in patients who are biological naive with active rheumatoid arthritis and an inadequate response to methotrexate (Study Evaluating Rituximab's Efficacy in MTX iNadequate rEsponders (SERENE)). Ann Rheum Dis. 2010 Sep;69(9):1629-35. doi: 10.1136/ard.2009.119933. Epub 2010 May 20. Erratum in: Ann Rheum Dis. 2011 Aug;70(8):1519.
50. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Pediatric Aggressive Mature B-Cell Lymphomas 2.2020. National Comprehensive Cancer Network, 2020. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed November 2020.
51. Lee KH, Lee J, Bae JS, et al. Analytical similarity assessment of rituximab biosimilar CT-P10 to reference medicinal product. MAbs. 2018;10(3):380-396
52. Ogura M, Sancho JM, Cho S-G, et al. Efficacy, pharmacokinetics, and safety of the biosimilar CT-P10 in comparison with rituximab in patients with previously untreated low-tumour- burden follicular lymphoma: a randomised, double-blind, parallel-group phase 3 trial. Lancet Haematol. 2018;5:e543-e553.
53. Gulácsi L, Brodszky V, Baji P, et al. The rituximab biosimilar CT-P10 in rheumatology and cancer: a budget impact analysis in 28 European countries. Adv Ther. 2017; 34: 1128-1144.
54. Yoo DH, Suh CH, Shim SC, et al. A multicentre randomised controlled trial to compare the pharmacokinetics, efficacy and safety of CT-P10 and innovator rituximab in patients with rheumatoid arthritis. Ann Rheum Dis. 2017; 76: 566-570.
55. Suh C, Berrocal Kasay A, Chalouhi El-Khouri E, et al. Pharmacokinetics and safety of three formulations of rituximab (CT-P10, US-sourced innovator rituximab and EU-sourced innovator rituximab) in patients with rheumatoid arthritis: results from phase 3 randomized controlled trial over 24 weeks. Arthritis Rheumatol. 2016; 68: 1634.
56. Kim WS, Buske C, Ogura M, et al. Efficacy, pharmacokinetics, and safety of the biosimilar CT-P10 compared with rituximab in patients with previously untreated advanced-stage follicular lymphoma: a randomised, double-blind, parallel-group, noninferiority phase 3 trial. Lancet Haematol. 2017; 4: e362-e373.
57. Cohen S, Emery P, Greenwald M, et al. A phase I pharmacokinetics trial comparing PF-05280586 (a potential biosimilar) and rituximab in patients with active rheumatoid arthritis. Br J Clin Pharmacol. 2016 Jul;82(1):129-38.
58. Williams JH, Hutmacher MM, Zierhut ML, et al. Comparative assessment of clinical response in patients with rheumatoid arthritis between PF-05280586, a proposed rituximab biosimilar, and rituximab. Br J Clin Pharmacol. 2016 Dec;82(6):1568-1579.
59. Sharman JP, Liberati AM, Ishizawa K, et al. A Randomized, Double-Blind, Efficacy and Safety Study of PF-05280586 (a Rituximab Biosimilar) Compared with Rituximab Reference Product (MabThera®) in Subjects with Previously Untreated CD20-Positive, Low-Tumor-Burden Follicular Lymphoma (LTB-FL). BioDrugs. 2019 Dec 9. doi: 10.1007/s40259-019-00398-7.
60. Cohen SB, Burgos-Vargas R, Emery P, et al. Comparative assessment of clinical response in patients with rheumatoid arthritis between PF-05280586, a proposed rituximab biosimilar, and rituximab. Br J Clin Pharmacol. 2016 Dec;82(6):1568-1579.
61. Dedee F, Murrel MA, Bmbch MD, et al. Diagnosis and management of pemphigus: Recommendations of an international panel of experts. JAAD: Mar2020;82;3;575-585. DOI:https://doi.org/10.1016/j.jaad.2018.02.021.
62. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Management of Immunotherapy-Related Toxicities 1.2020. National Comprehensive Cancer Network, 2020. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed November 2020.
63. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia [published correction appears in Blood Adv. 2020 Jan 28;4(2):252]. Blood Adv. 2019;3(23):3829-3866. Doi:10.1182/bloodadvances.2019000966.

64. McLaughlin P, Grillo-López AJ, Link BK, et al. Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: half of patients respond to a four-dose treatment program. J Clin Oncol. 1998 Aug;16(8):2825-33.
65. Piro LD, White CA, Grillo-López AJ, et al. Extended Rituximab (anti-CD20 monoclonal antibody) therapy for relapsed or refractory low-grade or follicular non-Hodgkin's lymphoma. Ann Oncol. 1999;10(6):655-661. doi:10.1023/a:1008389119525.
66. Davis TA, Grillo-López AJ, White CA, et al. Rituximab anti-CD20 monoclonal antibody therapy in non-Hodgkin's lymphoma: safety and efficacy of re-treatment. J Clin Oncol. 2000;18(17):3135-3143. doi:10.1200/JCO.2000.18.17.3135.
67. Marcus R, Imrie K, Belch A, et al. CVP chemotherapy plus rituximab compared with CVP as first-line treatment for advanced follicular lymphoma. Blood. 2005;105(4):1417-1423. doi:10.1182/blood-2004-08-3175.
68. Salles G, Seymour JF, Offner F, et al. Rituximab maintenance for 2 years in patients with high tumour burden follicular lymphoma responding to rituximab plus chemotherapy (PRIMA): a phase 3, randomised controlled trial [published correction appears in Lancet. 2011 Apr 2;377.
69. Hochster H, Weller E, Gascoyne RD, et al. Maintenance rituximab after cyclophosphamide, vincristine, and prednisone prolongs progression-free survival in advanced indolent lymphoma: results of the randomized phase III ECOG1496 Study. J Clin Oncol. 2009;27(10):1607-1614. doi:10.1200/JCO.2008.17.1561.
70. Habermann TM, Weller EA, Morrison VA, et al. Rituximab-CHOP versus CHOP alone or with maintenance rituximab in older patients with diffuse large B-cell lymphoma. J Clin Oncol. 2006;24(19):3121-3127. doi:10.1200/JCO.2005.05.1003,
71. Coiffier B, Thieblemont C, Van Den Neste E, et al. Long-term outcome of patients in the LNH-98.5 trial, the first randomized study comparing rituximab-CHOP to standard CHOP chemotherapy in DLBCL patients: a study by the Groupe d'Etudes des Lymphomes de l'Adulte. Blood. 2010;116(12):2040-2045. doi:10.1182/blood-2010-03-276246.
72. Pfreundschuh M, Kuhnt E, Trümper L, et al. CHOP-like chemotherapy with or without rituximab in young patients with good-prognosis diffuse large-B-cell lymphoma: 6-year results of an open-label randomised study of the MabThera International Trial (MInT) Group. Lancet Oncol. 2011;12(11):1013-1022. doi:10.1016/S1470-2045(11)70235-2.
73. Dakhil S, Hermann R, Schreeder MT, et al. Phase III safety study of rituximab administered as a 90-minute infusion in patients with previously untreated diffuse large B-cell and follicular lymphoma. Leuk Lymphoma. 2014;55(10):2335-2340. doi:10.3109/10428194.2013.877135.
74. Fischer K, Bahlo J, Fink AM, et al. Long-term remissions after FCR chemoimmunotherapy in previously untreated patients with CLL: updated results of the CLL8 trial. Blood. 2016;127(2):208-215. doi:10.1182/blood-2015-06-651125.
75. Robak T, Dmoszynska A, Solal-Céligny P, et al. Rituximab plus fludarabine and cyclophosphamide prolongs progression-free survival compared with fludarabine and cyclophosphamide alone in previously treated chronic lymphocytic leukemia. J Clin Oncol. 2010 Apr 1;28(10):1756-65.
76. Stone JH, Merkel PA, Spiera R, et al. Rituximab versus cyclophosphamide for ANCA-associated vasculitis. N Engl J Med. 2010;363(3):221-232. doi:10.1056/NEJMoa0909905.
77. Guillevin L, Pagnoux C, Karras A, et al. Rituximab versus azathioprine for maintenance in ANCA-associated vasculitis. N Engl J Med. 2014;371(19):1771-1780. doi:10.1056/NEJMoa1404231.
78. Niles JL, Merkel PA, Mertz L, et al. Long-Term Safety of Rituximab in Granulomatosis with Polyangiitis or Microscopic Polyangiitis: Results of the Four-Year Study of Rituximab in ANCA-Associated Vasculitis Registry [abstract]. Arthritis Rheumatol. 2018; 70 (suppl 10).
79. Brogan P, Cleary G, Hersh AO, et al. Pediatric Open-Label Clinical Study of Rituximab for the Treatment of Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA) [abstract]. Arthritis Rheumatol. 2018; 70 (suppl 10).
80. Joly P, Maho-Vaillant M, Prost-Squarcioni C, et al. First-line rituximab combined with short-term prednisone versus prednisone alone for the treatment of pemphigus (Ritux 3): a prospective, multicentre, parallel-group, open-label randomised trial. Lancet. 2017;389(10083):2031-2040. doi:10.1016/S0140-6736(17)30070-3.

81. Thomas DA, O'Brien S, Faderl S, et al. Chemoimmunotherapy with a modified hyper-CVAD and rituximab regimen improves outcome in de novo Philadelphia chromosome-negative precursor B-lineage acute lymphoblastic leukemia. J Clin Oncol. 2010;28(24):3880-3889. doi:10.1200/JCO.2009.26.9456.
82. Kadia TM, Kantarjian HM, Thomas DA, et al. Phase II study of methotrexate, vincristine, pegylated-asparaginase, and dexamethasone (MOpAD) in patients with relapsed/refractory acute lymphoblastic leukemia. Am J Hematol. 2015;90(2):120-124. doi:10.1002/ajh.23886.
83. Goldman S, Smith L, Anderson JR, et al. Rituximab and FAB/LMB 96 chemotherapy in children with Stage III/IV B-cell non-Hodgkin lymphoma: a Children's Oncology Group report. Leukemia. 2013;27(5):1174-1177. doi:10.1038/leu.2012.255.
84. Griffin TC, Weitzman S, Weinstein H, et al. A study of rituximab and ifosfamide, carboplatin, and etoposide chemotherapy in children with recurrent/refractory B-cell (CD20+) non-Hodgkin lymphoma and mature B-cell acute lymphoblastic leukemia: a report from the Children's Oncology Group. Pediatr Blood Cancer. 2009;52(2):177-181. doi:10.1002/pbc.21753.
85. Choquet S, Leblond V, Herbrecht R, et al. Efficacy and safety of rituximab in B-cell post-transplantation lymphoproliferative disorders: results of a prospective multicenter phase 2 study. Blood. 2006;107(8):3053-3057. doi:10.1182/blood-2005-01-0377.
86. Trappe R, Oertel S, Leblond V, et al. Sequential treatment with rituximab followed by CHOP chemotherapy in adult B-cell post-transplant lymphoproliferative disorder (PTLD): the prospective international multicentre phase 2 PTLD-1 trial. Lancet Oncol. 2012;13(2):196-206.
87. Ghobrial IM, Hong F, Padmanabhan S, et al. Phase II trial of weekly bortezomib in combination with rituximab in relapsed or relapsed and refractory Waldenström macroglobulinemia. J Clin Oncol. 2010;28(8):1422-1428. doi:10.1200/JCO.2009.25.3237.
88. Advani RH, Horning SJ, Hoppe RT, et al. Mature results of a phase II study of rituximab therapy for nodular lymphocyte-predominant Hodgkin lymphoma. J Clin Oncol. 2014;32(9):912-918. doi:10.1200/JCO.2013.53.2069.
89. Godeau B, Porcher R, Fain O, et al. Rituximab efficacy and safety in adult splenectomy candidates with chronic immune thrombocytopenic purpura: results of a prospective multicenter phase 2 study. Blood. 2008;112(4):999-1004. doi:10.1182/blood-2008-01-131029.
90. Wingerchuk DM, Banwell B, Bennett JL, et al. International consensus diagnostic criteria for neuromyelitis optica spectrum disorders. Neurology. 2015 Jul;85(2):177-89. Epub 2015 Jun 19.
91. Trebst C, Jarius S, Berthele A, et al. Update on the diagnosis and treatment of neuromyelitis optica: recommendations of the Neuromyelitis Optica Study Group (NEMOS). J Neurol 2014; 261:1.
92. Nikoo Z, Badihian S, Shaygannejad V, et al. Comparison of the efficacy of azathioprine and rituximab in neuromyelitis optica spectrum disorder: a randomized clinical trial. J Neurol. 2017;264(9):2003. Epub 2017 Aug 22.
93. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Lymphoblastic Leukemia 2.2020. National Comprehensive Cancer Network, 2020. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Guidelines, go online to NCCN.org. Accessed November 2020.
94. Thomas DA, O'Brien S, Bueso-Ramos C, et al. Rituximab in relapsed or refractory hairy cell leukemia. Blood. 2003 Dec 1;102(12):3906-11. doi: 10.1182/blood-2003-02-0630.
95. Nieva J, Bethel K, Saven A. Phase 2 study of rituximab in the treatment of cladribine-failed patients with hairy cell leukemia. Blood. 2003 Aug 1;102(3):810-3.
96. Chihara D, Kantarjian H, O'Brien S, et al. Long-term durable remission by cladribine followed by rituximab in patients with hairy cell leukaemia: update of a phase II trial. Br J Haematol. 2016 Sep;174(5):760-6.
97. Else M, Dearden CE, Matutes E, et al. Rituximab with pentostatin or cladribine: an effective combination treatment for hairy cell leukemia after disease recurrence. Leuk Lymphoma. 2011 Jun;52 Suppl 2:75-8. doi: 10.3109/10428194.2011.568650.

98. Zenhäusern R, Simcock M, Gratwohl A, et al; Swiss Group for Clinical Cancer Research (SAKK). Rituximab in patients with hairy cell leukemia relapsing after treatment with 2-chlorodeoxyadenosine (SAKK 31/98). Haematologica. 2008 Sep;93(9):1426-8.
99. Birgens H, Frederiksen H, Hasselbalch HC, et al. A phase III randomized trial comparing glucocorticoid monotherapy versus glucocorticoid and rituximab in patients with autoimmune haemolytic anaemia. Br J Haematol. 2013 Nov;163(3):393-9. doi: 10.1111/bjh.12541.
100. Niederwieser, D., Hamm, C., Cobb, P. et al. Efficacy and Safety of ABP 798: Results from the JASMINE Trial in Patients with Follicular Lymphoma in Comparison with Rituximab Reference Product. Targ Oncol 15, 599–611 (2020). https://doi.org/10.1007/s11523-020-00748-4.
101. Burmester, G., Drescher, E., Hrycaj, P. et al. Efficacy and safety results from a randomized double-blind study omparing proposed biosimilar ABP 798 with rituximab reference product in subjects with moderate-to-severe rheumatoid arthritis. Clin Rheumatol 39, 3341–3352 (2020). https://doi.org/10.1007/s10067-020-05305-y.
102. Lexi-Comp Online. (2020). AHFS DI. Rituximab. Retrieved November 2, 2020 from Lexi-Comp Online with AHFS.
103. MICROMEDEX Healthcare Series. Drugdex Drug Evaluations. (2021, January). Rituximab. Retrieved January 25, 2021 from MICROMEDEX Healthcare Series.

EFFECTIVE DATE 6/2/2021

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