DRUG DETERMINATION POLICY

Title: DDP-17 Rituximab (Rituxan and biosimilars)

Effective Date: 4/26/23

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs that require prior approval.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Rituximab (originator: Rituxan/Hycela, biosimilars: Ruxience,Truxima, Riabni) is an immunosuppressant specialty drug indicated for a number of diagnoses and is associated with significant toxicity. These criteria were developed and implemented to ensure appropriate use for the intended diagnoses and mitigation of toxicity, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. General Considerations for use.

A. Appropriate Medication Use [must meet all listed below]:

1. Diagnosis: meets standard diagnostic criteria that designates signs, symptoms, and test results to support specific diagnosis

2. Food and Drug Administration (FDA) approval Status [must meet one listed below]:

a. FDA approved: product, indication, and/or dosage regimen.

b. Non-FDA approved use: Compendium support (Lexicomp®) for use of a drug for a non-FDA approve indication or dosage regimen.

3. Place in therapy: sequence of therapy supported by national or internationally accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

B. Approval.

1. Initial: six months.

2. Re-approval: decreased or sustained reduction in disease activity.

a. Rheumatoid arthritis: one year

b. All other indications: six months

II. Non-Oncology Indications [must meet one listed below]:

A. Rheumatoid Arthritis [must meet all listed below]:

1. Diagnosis and severity: moderate to severe rheumatoid arthritis.

2. Other therapies: contraindicated, failed, or significant adverse effects with two anti-tumor necrosis factor inhibitors.

3. Dosage regimen: Rituxan, Ruxience, and Truxima only [must meet both listed below]:

a. Rituximab intravenous: 1,000mg on days one and fifteen of a six-month cycle.

b. Combination with methotrexate (if contraindicated use leflunomide or other standard disease modifying antirheumatic drugs).

B. Polyangiitis [must meet all listed below]:

1. Age: at least two years.

2. Diagnosis and severity [must meet one listed below]:

a. Granulomatosis with Polyangiitis (Wegener Granulomatosis).

b. Microscopic polyangiitis

3. Dosage regimen:

a. Combination with methylprednisolone or prednisone.

b. Induction: rituximab 375mg per m2 one time per week for four doses with methylprednisolone intravenous for one to three days, and then oral prednisone one time per day.

c. Maintenance:

- Adult: rituximab intravenous 500mg week zero and two, then 500mg every 6 months.

- Pediatric: rituximab 250mg per m^2 week zero and two, then 250mg per m^2 every six months

C. Pemphigus Vulgaris.

1. Diagnosis and severity [must meet both listed below below]:

   a. Treatment of moderate to severe pemphigus vulgaris in adults.

   b. Refractory disease.

2. Other therapies: contraindication, inadequate response after four months, or significant adverse effects to one in each category listed below:

   a. Steroids: initial treatment, then taper or increase as needed.

   b. Disease modifying rheumatoid agents: azathioprine, mycophenolate, dapsone.

3. Dosage regimen: Rituxan intravenous only.

   a. Initial: 1000mg at weeks zero and two.

   b. Maintenance: 500mg at months twelve and then every six months thereafter or based on clinical evaluation.

   c. Relapse: 1000mg for one dose, no sooner than 16 weeks following previous dose.

   d. Concurrent therapy:

      - Combination with tapering glucocorticoids and with relapse consider resuming or increasing steroid dose.

      - Pre-medicate with methylprednisolone intravenous 30 minutes prior to each rituximab dose.

III. Oncology.

A. Non-Hodgkin's Lymphoma (NHL): CD20 positive [must meet one listed below]:

1. Diffuse large B-cell NHL - untreated [must meet both listed below]:

   a. Combination regimen with CHOP regimen or other anthracycline-based regimen.

   b. Dosage regimen.

      - Rituximab intravenous: 375mg per m2 on day one of each cycle for at least eight infusions.

      - Rituxan Hycela subcutaneous (r-hyaluronidase SQ): 1,400mg/23,400units day one cycles two through eight (use rituximab IV cycle one).

2. Follicular B-Cell NHL - untreated or partial or complete response [must meet all listed below]:

   a. Combination regimen with first line chemotherapy.

   b. Induction dosage regimen - untreated.

- Rituximab intravenous 375mg per m2 day one of each cycle for up to eight infusions.

- Rituxan Hycela subcutaneous (r-hyaluronidase SQ): 1,400mg/23,400units day one cycles two through eight (use rituximab intravenous cycle one).

c. Maintenance monotherapy dosage regimen - partial or complete response:

- Rituximab intravenous 375mg per m2 every eight weeks for twelve doses.

- Rituxan Hycela subcutaneous (r-hyaluronidase SQ): 1,400mg/23,400units every eight weeks for twelve doses.

3. Low grade B-cell NHL: non-progressing or stable [must meet all listed below]:

a. Second line treatment after six to eight cycles of first line CVP regimen.

b. Dosage regimen:

- Rituximab intravenous 75mg per m2 one time weekly times four every six months for up to 16 doses.

- Rituxan Hycela subcutaneous (r-hyaluronidase SQ): 1,400mg/23,400units one time per week for three weeks or up to 16 doses (use rituximab intravenous one time weekly for four doses).

4. Low-grade or follicular B-Cell NHL - relapsing or refractory.

a. Dosage regimen:

- Rituximab intravenous 375mg per m2 one time per week up to eight doses.

- Rituxan Hycela subcutaneous (r-hyaluronidase SQ): 1,400mg/23,400units one time per week for three weeks (use rituximab intravenous week one).

b. Retreatment following disease progression:

- Rituximab 375mg per m2 every three months for two years.

B. Chronic Lymphocytic Leukemia - CD20 positive [must meet both listed below]:

1. Combination regimen with fludarabine and cyclophosphamide.

2. Dosage regimen:

a. Rituximab 375mg per m2 one-day prior to chemotherapy in cycle one of 28-day cycle, then 500mg per m2 on day one of cycles two through six.

b. Rituxan Hycela subcutaneous (r-hyaluronidase SQ): 1,600mg/26,800units on day one of 28-day cycle in cycles two through six (use rituximab intravenous week one).

4.0 Coding:

APPLICABLE CODING

HCPCS Code	Brand	Generic	HCPCS Billing (1u)	Prior Approval Required
J9312	Rituxan	rituximab	10mg	Y
J9311	Rituxan Hycela	rituximab r-hyaluronidase	10mg	Y
Q5119	Ruxience	Rituximab-pvvr	10mg	Y
Q5115	Truxima	Rituximab-abbs	10mg	Y
Q5123	Riabni	Rituximab-arrx	10mg	Y

5.0 References, Citations & Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Rituxan, Rituxan Hycela accessed March, 2022.
2. Package insert rituximab Genetech/Biogen https://www.gene.com/download/pdf/rituxan_prescribing.pdf accessed April 2020.

6.0 Appendices:

See page 6.

7.0 Revision History:

Original Effective Date: 12/14/2005

Next Review Date: 05/01/2024

Revision Date	Reason for Revision
4/19	Moving to new format; presented and approved by P&T Committee
3/20	Annual review; added indication Pemphigus Vulgaris, added drugs Ruxience, Truxima, replaced abbreviations RA – clarified combo with MTX, PA – added pediatric indication
2/21	Annual review; replaced abbreviations, added Riabni, added appropriate use section; approved at 4/28/21 P&T
9/21	Changed code for Riabni
2/22	Annual review
2/23	Annual review; added general considerations for use section with defined approval and re-approval time frames and moved appropriate use section, updated Riabni billing units, fixed formatting/numbering scheme

A/ppendix I: Monitoring & Patient Safety – Adverse Reactions and Monitoring

Drug	Adverse Reactions	Monitoring	REMS
Rituxan Rituxan Hycela Rituximab/ Hyaluronic-dase	• Cardiovascular (CV): peripheral edema (8-16%), hypertension (6-12%) • Central Nervous System (CNS): fever (5-53%), fatigue (13-39%), chills (3-33%), headache (17-19%), insomnia (≤4%), pain (12%) • Dermatology: rash (8-23%), pruritus (5-17%), angioedema (11%) • Gastrointestinal (GI): nausea (8-23%), diarrhea (10-17%), abdominal. pain (2-14%), weight gain (11%) • Hematology: lymphopenia (48%), anemia (8-35%), leukopenia (14%), neutropenia (14%), thrombocytopenia (12%) • Hepatic: increased ALT (liver function test) • Neurology/Musculoskeletal: neuropathy (≤30%), weakness (2-26%) muscle spasm (≤17%), arthralgia (6-13%) • Respiratory: cough (13%), rhinitis (3-12%), epistaxis (≤11%) • Pregnancy Category: C	• CV: CV monitoring • Labs: CBC with different , platelets. (onc - weekly to monthly, RA (2-4 mons); peripheral CD20 • GI: abdominal pain • Neurological: PML • Renal: function, fluid balance • Vital signs • Other: infusion reactions	None Needed