

Rituxan Hycela® (rituximab and hyaluronidase human) (Subcutaneous)



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I. Length of Authorization ¹

Coverage will be provided for 6 months and may be renewed unless otherwise specified.

- Maintenance therapy for mantle cell lymphoma may be renewed until disease progression or intolerable toxicity.
- Maintenance therapy for all other indications may be renewed for up to a maximum of 2 years.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Rituxan Hycela 1,400 mg/23,400 Units per 11.7 mL single-dose vial:
4 vials per 28 day supply
- Rituxan Hycela 1,600 mg/26,800 Units per 13.4 mL single-dose vial:
1 vial per 28 day supply

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

| |
|--|
| Follicular Lymphoma (FL): Relapsed-Refractory <ul style="list-style-type: none"> • 1,400 mg/23,400 U (140 billable units) weekly up to 7 doses Previously Untreated <ul style="list-style-type: none"> • 1,400 mg/23,400 U (140 billable units) every 21 days x 7 doses • 1,400 mg/23,400 U (140 billable units) every 8 weeks x 12 doses (maintenance) Non-progressing after first line CVP chemotherapy <ul style="list-style-type: none"> • 1,400 mg/23,400 U (140 billable units) weekly x 3 doses at 6 month intervals (up to a maximum of 15 doses). |
| Diffuse Large B-Cell Lymphoma (DLBCL): <ul style="list-style-type: none"> • 1,400 mg/23,400 U (140 billable units) every 14 or 21 days x 7 doses |
| Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL): <ul style="list-style-type: none"> • 1,600 mg/26,800 U (160 billable units) every 28 days x 5 doses |
| Other indications: <ul style="list-style-type: none"> • 1,400 mg/23,400 U (140 billable units) weekly for 3-7 doses in a 6-month period; OR • 1,400 mg/23,400 U (140 billable units) every 8 weeks (maintenance treatment) |

III. Initial Approval Criteria ^{1,2,6}

Coverage is provided in the following conditions:

- Patient age is at least 18 years of age; **AND**

Universal Criteria

- Patient does not have a severe, active infection; **AND**
- Patient has been screened for the presence of hepatitis B virus (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 is CD20 antigen expression positive; **AND**
- Patient has received at least one full dose of a rituximab product by intravenous infusion prior to initiating therapy; **AND**
- Rituxan Hycela will not be used with intravenous chemotherapy agents; **AND**

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

B-Cell Lymphomas* † ‡

- Follicular Lymphoma (FL) † Φ
- Diffuse Large B-Cell Lymphoma (DLBCL) † Φ
- High Grade B-Cell Lymphomas ‡
- Castleman's Disease ‡
- Gastric & Non-gastric MALT Lymphoma ‡
- Mantle Cell Lymphoma ‡
- Nodal & Splenic Marginal Zone Lymphoma ‡
- Histologic transformation of Nodal Marginal Zone Lymphoma to Diffuse Large B-Cell Lymphoma ‡
- Post-transplant lymphoproliferative disorder (PTLD) ‡

Hairy Cell Leukemia ‡

Primary Cutaneous B-Cell Lymphoma ‡

**Note: Patient must meet relevant initial criteria and receive at least ONE dose of the intravenous formulation of rituximab prior to initiating therapy with the subcutaneous formulation. This substitution CANNOT be made for intravenous rituximab when used in combination with ibritumomab tiuxetan.*

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA-labeled indication(s); ‡ Compendia recommended indication(s); Φ Orphan Drug

IV. Renewal Criteria ¹

Coverage can be renewed based upon the following 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 section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: severe hypersensitivity or other administration reactions (i.e. local cutaneous reactions), tumor lysis syndrome (TLS), severe mucocutaneous reactions, progressive multifocal leukoencephalopathy (PML), hepatitis B virus reactivation, serious bacterial, fungal, or viral infections, cardiac adverse reactions, renal toxicity, bowel obstruction or perforation, etc.; **AND**
- 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 Sections I, II, and V

V. Dosage/Administration ¹

| Indication | Dose |
|---------------------------------------|---|
| Follicular Lymphoma (FL) | <p>1,400 mg/23,400 Units subcutaneously, at a fixed dose, irrespective of patient's BSA, according to the following schedules:</p> <p><u>Relapsed or Refractory</u></p> <ul style="list-style-type: none"> • Administer once weekly for 3 or 7 weeks following a full dose of a rituximab IV product at week 1 (i.e., 4 or 8 weeks in total) <p><u>Retreatment for Relapsed or Refractory</u></p> <ul style="list-style-type: none"> • Administer once weekly for 3 weeks following a full dose of a rituximab IV product at week 1 (i.e., 4 weeks in total) <p><u>Previously Untreated</u></p> <ul style="list-style-type: none"> • Administer on Day 1 of Cycles 2–8 of chemotherapy (every 21 days), for up to 7 cycles following a full dose of a rituximab IV product on day 1 of cycle 1 (i.e., up to 8 cycles in total). In patients with complete or partial response, initiate maintenance treatment 8 weeks following completion of initial therapy as a single agent every 8 weeks for 12 doses. <p><u>Non-progressing after first line CVP chemotherapy</u></p> <ul style="list-style-type: none"> • Following completion of 6–8 cycles of CVP chemotherapy and a full dose of a rituximab IV product at week 1, administer once weekly for 3 weeks (i.e., 4 weeks in total) at 6 month intervals to a maximum of 16 doses. |
| Diffuse Large B-Cell Lymphoma (DLBCL) | <p>1,400 mg/23,400 Units subcutaneously, at a fixed dose, irrespective of patient's BSA.</p> <ul style="list-style-type: none"> – Administer on Day 1 of Cycles 2–8 of chemotherapy for up to 7 cycles (i.e., up to 6-8 cycles in total). Cycle length is either 14 or 21 days. |
| CLL/SLL | <p>1,600 mg/26,800 Units subcutaneously, at a fixed dose, irrespective of patient's BSA.</p> <ul style="list-style-type: none"> – Administer on Day 1 of Cycles 2–6 (every 28 days) for a total of 5 cycles (i.e., 6 cycles in total). Cycle length is 28 days. |
| All other indications | <p>1,400 mg/23,400 Units subcutaneously, at a fixed dose, irrespective of patient's BSA.</p> <ul style="list-style-type: none"> • Administer up to once weekly for 3-7 doses in a 6-month period: OR • Administer once every 8 weeks (maintenance treatment) |

Note: Patient must receive at least ONE dose of the intravenous formulation of rituximab prior to initiating therapy with the subcutaneous formulation. (This substitution CANNOT be made for intravenous rituximab when used in combination with ibritumomab tiuxetan). Must be administered by a healthcare provider.

VI. Billing Code/Availability Information

HCPCS Code:

- J9311 – Injection, rituximab 10 mg and hyaluronidase: 1 billable unit = 10 mg

NDC:

- Rituxan Hycela 1,400 mg rituximab/23,400 Units hyaluronidase human single-dose vial: 50242-0108-xx
- Rituxan Hycela 1,600 mg rituximab/26,800 Units hyaluronidase human single-dose vial : 50242-0109-xx

VII. References (STANDARD)

1. Rituxan Hycela [package insert]. South San Francisco, CA; Genentech, Inc; May 2020. Accessed September 2020.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) rituximab and hyaluronidase human. 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 September 2020.
3. Davies A, Merli F, Mihaljević B, et al. Efficacy and safety of subcutaneous rituximab versus intravenous rituximab for first-line treatment of follicular lymphoma (SABRINA): a randomised, open-label, phase 3 trial. *Lancet Haematol.* 2017 Jun;4(6):e272-e282. doi: 10.1016/S2352-3026(17)30078-9. Epub 2017 May 2.
4. Lugtenburg P, Avivi I, Berenschot H, et al. Efficacy and safety of subcutaneous and intravenous rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone in first-line diffuse large B-cell lymphoma: the randomized MabEase study. *Haematologica.* 2017 Nov;102(11):1913-1922. doi: 10.3324/haematol.2017.173583. Epub 2017 Sep 21.
5. Assouline S, Buccheri V, Delmer A, et al. Pharmacokinetics, safety, and efficacy of subcutaneous versus intravenous rituximab plus chemotherapy as treatment for chronic lymphocytic leukaemia (SAWYER): a phase 1b, open-label, randomised controlled non-inferiority trial. *Lancet Haematol.* 2016 Mar;3(3):e128-38. doi:10.1016/S2352-3026(16)00004-1.
6. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 4.2020. 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 September 2020.

7. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) B-Cell Lymphoma. Version 4.2020. 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 September 2020.
8. National Government Services, Inc. Local Coverage Article: Billing and Coding: Rituximab, biosimilars and Rituximab and hyaluronidase human (Rituxan Hycela™) (A52452). Centers for Medicare & Medicaid Services, Inc. Updated on 07/24/2020 with effective date of 08/01/2020. Accessed August 2020.
9. Palmetto GBA. Local Coverage Article: Billing and Coding: Rituximab (A56380). Centers for Medicare & Medicaid Services, Inc. Updated on 01/29/2020 with effective date of 02/06/2020. Accessed August 2020.

VIII. References (ENHANCED)

- 1e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Primary Cutaneous Lymphomas. Version 2.2020. 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 September 2020.
- 2e. Magellan Health, Magellan Rx Management. Rituxan Hycela Clinical Literature Review Analysis. Last updated September 2020. Accessed September 2020.

Appendix 1 – Covered Diagnosis Codes

| ICD-10 | ICD-10 Description |
|--------|--|
| C82.00 | Follicular lymphoma grade I, unspecified site |
| C82.01 | Follicular lymphoma grade I, lymph nodes of head, face and neck |
| C82.02 | Follicular lymphoma, grade I, intrathoracic lymph nodes |
| C82.03 | Follicular lymphoma grade I, intra-abdominal lymph nodes |
| C82.04 | Follicular lymphoma grade I, lymph nodes of axilla and upper limb |
| C82.05 | Follicular lymphoma grade I, lymph nodes of inguinal regional and lower limb |
| C82.06 | Follicular lymphoma grade I, intrapelvic lymph nodes |
| C82.07 | Follicular lymphoma grade I, spleen |
| C82.08 | Follicular lymphoma grade I, lymph nodes of multiple sites |
| C82.09 | Follicular lymphoma grade I, extranodal and solid organ sites |
| C82.10 | Follicular lymphoma grade II, unspecified site |

| | |
|--------|---|
| C82.11 | Follicular lymphoma grade II, lymph nodes of head, face and neck |
| C82.12 | Follicular lymphoma, grade II, intrathoracic lymph nodes |
| C82.13 | Follicular lymphoma grade II, intra-abdominal lymph nodes |
| C82.14 | Follicular lymphoma grade II, lymph nodes of axilla and upper limb |
| C82.15 | Follicular lymphoma grade II, lymph nodes of inguinal region and lower limb |
| C82.16 | Follicular lymphoma grade II, intrapelvic lymph nodes |
| C82.17 | Follicular lymphoma grade II, spleen |
| C82.18 | Follicular lymphoma grade II, lymph nodes of multiple sites |
| C82.19 | Follicular lymphoma grade II, extranodal and solid organ sites |
| C82.20 | Follicular lymphoma grade III, unspecified, unspecified site |
| C82.21 | Follicular lymphoma grade III, unspecified, lymph nodes of head, face and neck |
| C82.22 | Follicular lymphoma, grade III, unspecified, intrathoracic lymph nodes |
| C82.23 | Follicular lymphoma grade III, unspecified, intra-abdominal lymph nodes |
| C82.24 | Follicular lymphoma grade III, unspecified, lymph nodes of axilla and upper limb |
| C82.25 | Follicular lymphoma grade III, unspecified, lymph nodes of inguinal region and lower limb |
| C82.26 | Follicular lymphoma grade III, unspecified, intrapelvic lymph nodes |
| C82.27 | Follicular lymphoma grade III, unspecified, spleen |
| C82.28 | Follicular lymphoma grade III, unspecified, lymph nodes of multiple sites |
| C82.29 | Follicular lymphoma grade III, unspecified, extranodal and solid organ sites |
| C82.30 | Follicular lymphoma grade IIIa, unspecified site |
| C82.31 | Follicular lymphoma grade IIIa, lymph nodes of head, face and neck |
| C82.32 | Follicular lymphoma, grade IIIa, intrathoracic lymph nodes |
| C82.33 | Follicular lymphoma grade IIIa, intra-abdominal lymph nodes |
| C82.34 | Follicular lymphoma grade IIIa, lymph nodes of axilla and upper limb |
| C82.35 | Follicular lymphoma grade IIIa, lymph nodes of inguinal region and lower limb |
| C82.36 | Follicular lymphoma grade IIIa, intrapelvic lymph nodes |
| C82.37 | Follicular lymphoma grade IIIa, spleen |
| C82.38 | Follicular lymphoma grade IIIa, lymph nodes of multiple sites |
| C82.39 | Follicular lymphoma grade IIIa, extranodal and solid organ sites |
| C82.40 | Follicular lymphoma grade IIIb, unspecified site |
| C82.41 | Follicular lymphoma grade IIIb, lymph nodes of head, face and neck |
| C82.42 | Follicular lymphoma, grade IIIb, intrathoracic lymph nodes |
| C82.43 | Follicular lymphoma grade IIIb, intra-abdominal lymph nodes |
| C82.44 | Follicular lymphoma grade IIIb, lymph nodes of axilla and upper limb |
| C82.45 | Follicular lymphoma grade IIIb, lymph nodes of inguinal region and lower limb |
| C82.46 | Follicular lymphoma grade IIIb, intrapelvic lymph nodes |
| C82.47 | Follicular lymphoma grade IIIb, spleen |
| C82.48 | Follicular lymphoma grade IIIb, lymph nodes of multiple sites |
| C82.49 | Follicular lymphoma grade IIIb, extranodal and solid organ sites |
| C82.50 | Diffuse follicle center lymphoma, unspecified site |

| | |
|--------|---|
| C82.51 | Diffuse follicle center lymphoma, lymph nodes of head, face and neck |
| C82.52 | Diffuse follicle center lymphoma, intrathoracic lymph nodes |
| C82.53 | Diffuse follicle center lymphoma, intra-abdominal lymph nodes |
| C82.54 | Diffuse follicle center lymphoma, lymph nodes of axilla and upper limb |
| C82.55 | Diffuse follicle center lymphoma, lymph nodes of inguinal region and lower limb |
| C82.56 | Diffuse follicle center lymphoma, intrapelvic lymph nodes |
| C82.57 | Diffuse follicle center lymphoma, spleen |
| C82.58 | Diffuse follicle center lymphoma, lymph nodes of multiple sites |
| C82.59 | Diffuse follicle center lymphoma, extranodal and solid organ sites |
| C82.60 | Cutaneous follicle center lymphoma, unspecified site |
| C82.61 | Cutaneous follicle center lymphoma, lymph nodes of head, face and neck |
| C82.62 | Cutaneous follicle center lymphoma, intrathoracic lymph nodes |
| C82.63 | Cutaneous follicle center lymphoma, intra-abdominal lymph nodes |
| C82.64 | Cutaneous follicle center lymphoma, lymph nodes of axilla and upper limb |
| C82.65 | Cutaneous follicle center lymphoma, lymph nodes of inguinal region and lower limb |
| C82.66 | Cutaneous follicle center lymphoma, intrapelvic lymph nodes |
| C82.67 | Cutaneous follicle center lymphoma, spleen |
| C82.68 | Cutaneous follicle center lymphoma, lymph nodes of multiple sites |
| C82.69 | Cutaneous follicle center lymphoma, extranodal and solid organ sites |
| C82.80 | Other types of follicular lymphoma, unspecified site |
| C82.81 | Other types of follicular lymphoma, lymph nodes of head, face and neck |
| C82.82 | Other types of follicular lymphoma, intrathoracic lymph nodes |
| C82.83 | Other types of follicular lymphoma, intra-abdominal lymph nodes |
| C82.84 | Other types of follicular lymphoma, lymph nodes of axilla and upper limb |
| C82.85 | Other types of follicular lymphoma, lymph nodes of inguinal region and lower limb |
| C82.86 | Other types of follicular lymphoma, intrapelvic lymph nodes |
| C82.87 | Other types of follicular lymphoma, spleen |
| C82.88 | Other types of follicular lymphoma, lymph nodes of multiple sites |
| C82.89 | Other types of follicular lymphoma, extranodal and solid organ sites |
| C82.90 | Follicular lymphoma, unspecified, unspecified site |
| C82.91 | Follicular lymphoma, unspecified, lymph nodes of head, face and neck |
| C82.92 | Follicular lymphoma, unspecified, intrathoracic lymph nodes |
| C82.93 | Follicular lymphoma, unspecified, intra-abdominal lymph nodes |
| C82.94 | Follicular lymphoma, unspecified, lymph nodes of axilla and upper limb |
| C82.95 | Follicular lymphoma, unspecified lymph nodes of inguinal region and lower limb |
| C82.96 | Follicular lymphoma, unspecified, intrapelvic lymph nodes |
| C82.97 | Follicular lymphoma, unspecified, spleen |
| C82.98 | Follicular lymphoma, unspecified, lymph nodes of multiple sites |
| C82.99 | Follicular lymphoma, unspecified, extranodal and solid organ sites |
| C83.00 | Small cell B-cell lymphoma, unspecified site |

| | |
|--------|--|
| C83.01 | Small cell B-cell lymphoma, lymph nodes of head, face and neck |
| C83.02 | Small cell B-cell lymphoma, intrathoracic lymph nodes |
| C83.03 | Small cell B-cell lymphoma, intra-abdominal lymph nodes |
| C83.04 | Small cell B-cell lymphoma, lymph nodes of axilla and upper limb |
| C83.05 | Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb |
| C83.06 | Small cell B-cell lymphoma, intrapelvic lymph nodes |
| C83.07 | Small cell B-cell lymphoma, spleen |
| C83.08 | Small cell B-cell lymphoma, lymph nodes of multiple sites |
| C83.09 | Small cell B-cell lymphoma, extranodal and solid organ sites |
| C83.10 | Mantle cell lymphoma, unspecified site |
| C83.11 | Mantle cell lymphoma, lymph nodes of head, face and neck |
| C83.12 | Mantle cell lymphoma, intrathoracic lymph nodes |
| C83.13 | Mantle cell lymphoma, intra-abdominal lymph nodes |
| C83.14 | Mantle cell lymphoma, lymph nodes of axilla and upper limb |
| C83.15 | Mantle cell lymphoma, lymph nodes of inguinal region and lower limb |
| C83.16 | Mantle cell lymphoma, intrapelvic lymph nodes |
| C83.17 | Mantle cell lymphoma, spleen |
| C83.18 | Mantle cell lymphoma, lymph nodes of multiple sites |
| C83.19 | Mantle cell lymphoma, extranodal and solid organ sites |
| C83.30 | Diffuse large B-cell lymphoma unspecified site |
| C83.31 | Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck |
| C83.32 | Diffuse large B-cell lymphoma intrathoracic lymph nodes |
| C83.33 | Diffuse large B-cell lymphoma intra-abdominal lymph nodes |
| C83.34 | Diffuse large B-cell lymphoma lymph nodes of axilla and upper limb |
| C83.35 | Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb |
| C83.36 | Diffuse large B-cell lymphoma intrapelvic lymph nodes |
| C83.37 | Diffuse large B-cell lymphoma, spleen |
| C83.38 | Diffuse large B-cell lymphoma lymph nodes of multiple sites |
| C83.39 | Diffuse large B-cell lymphoma extranodal and solid organ sites |
| C83.80 | Other non-follicular lymphoma, unspecified site |
| C83.81 | Other non-follicular lymphoma, lymph nodes of head, face and neck |
| C83.82 | Other non-follicular lymphoma, intrathoracic lymph nodes |
| C83.83 | Other non-follicular lymphoma, intra-abdominal lymph nodes |
| C83.84 | Other non-follicular lymphoma, lymph nodes of axilla and upper limb |
| C83.85 | Other non-follicular lymphoma, lymph nodes of inguinal region and lower limb |
| C83.86 | Other non-follicular lymphoma, intrapelvic lymph nodes |
| C83.87 | Other non-follicular lymphoma, spleen |
| C83.88 | Other non-follicular lymphoma, lymph nodes of multiple sites |
| C83.89 | Other non-follicular lymphoma, extranodal and solid organ sites |
| C85.20 | Mediastinal (thymic) large B-cell lymphoma, unspecified site |

| | |
|--------|---|
| C85.21 | Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face and neck |
| C85.22 | Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes |
| C85.23 | Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes |
| C85.24 | Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb |
| C85.25 | Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb |
| C85.26 | Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes |
| C85.27 | Mediastinal (thymic) large B-cell lymphoma, spleen |
| C85.28 | Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites |
| C85.29 | Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites |
| C85.80 | Other specified types of non-Hodgkin lymphoma, unspecified site |
| C85.81 | Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face and neck |
| C85.82 | Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes |
| C85.83 | Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes |
| C85.84 | Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb |
| C85.85 | Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region of lower limb |
| C85.86 | Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes |
| C85.87 | Other specified types of non-Hodgkin lymphoma, spleen |
| C85.88 | Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites |
| C85.89 | Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites |
| C88.4 | Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT-lymphoma) |
| C91.10 | Chronic lymphocytic leukemia of B-cell type not having achieved remission |
| C91.12 | Chronic lymphocytic leukemia of B-cell type in relapse |
| C91.40 | Hairy cell leukemia not having achieved remission |
| C91.42 | Hairy cell leukemia, in relapse |
| D36.0 | Benign neoplasm of lymph nodes |
| D47.Z1 | Post-transplant lymphoproliferative disorder (PTLD) |
| D47.Z2 | Other neoplasms of uncertain behavior of lymphoid, hematopoietic and related tissue – Castleman |
| R59.0 | Localized enlarged lymph nodes |
| R59.1 | Generalized enlarged lymph nodes |
| R59.9 | Enlarged lymph nodes, unspecified |

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at:

<http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA):

| | |
|---|---|
| Jurisdiction(s): 6, K | NCD/LCD/LCA Document (s): A52452 |
| https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A52452&bc=gAAAAAAAAAAAAAA== | |

| | |
|---|---|
| Jurisdiction(s): J, M | NCD/LCD/LCA Document (s): A56380 |
| https://www.cms.gov/medicare-coverage-database/search/article-date-search.aspx?DocID=A56380&bc=gAAAAAAAAAAAAAA | |

| Medicare Part B Administrative Contractor (MAC) Jurisdictions | | |
|--|---|---|
| Jurisdiction | Applicable State/US Territory | Contractor |
| E (1) | CA, HI, NV, AS, GU, CNMI | Noridian Healthcare Solutions, LLC |
| F (2 & 3) | AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ | Noridian Healthcare Solutions, LLC |
| 5 | KS, NE, IA, MO | Wisconsin Physicians Service Insurance Corp (WPS) |
| 6 | MN, WI, IL | National Government Services, Inc. (NGS) |
| H (4 & 7) | LA, AR, MS, TX, OK, CO, NM | Novitas Solutions, Inc. |
| 8 | MI, IN | Wisconsin Physicians Service Insurance Corp (WPS) |
| N (9) | FL, PR, VI | First Coast Service Options, Inc. |
| J (10) | TN, GA, AL | Palmetto GBA, LLC |
| M (11) | NC, SC, WV, VA (excluding below) | Palmetto GBA, LLC |
| L (12) | DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA) | Novitas Solutions, Inc. |
| K (13 & 14) | NY, CT, MA, RI, VT, ME, NH | National Government Services, Inc. (NGS) |
| 15 | KY, OH | CGS Administrators, LLC |

Appendix 3 – CLINICAL LITERATURE REVIEW

OS = overall survival; PFS = progression-free survival; ORR = objective response rate; CR = complete response; PR = partial response; DoR = duration of response; TTP = time to progression; FFS = failure-free survival; EFS = event-free survival; PFR = progression free rate; IV = intravenous; SC = subcutaneous; PK = pharmacokinetic

Chronic lymphocytic leukemia/Small lymphocytic lymphoma (CLL/SLL)

| First line therapy | | | | | | | |
|--------------------|---------------|--------------|--|-------------------|-------------------|-----------------|---|
| Regimen | NCCN Category | FDA Approved | Trial Design | Comparator | Primary End-Point | Line of Therapy | Conclusion |
| Rituximab SC + FC | 2A | Yes | Phase 1b (SAWYER) , open-label, randomized, controlled non-inferiority | Rituximab IV + FC | PK profile | First-line | <ul style="list-style-type: none"> When combined with fludarabine and cyclophosphamide, subcutaneous rituximab 1600 mg achieved trough serum concentrations that were pharmacokinetically non-inferior to those achieved with intravenous rituximab 500 mg/m², with a similar safety and efficacy profile between the two groups. |

Non-Hodgkin’s lymphomas (NHL)

| Follicular Lymphoma (FL) | | | | | | | |
|-----------------------------|---------------|--------------|--|-----------------------------|-------------------|-----------------|---|
| Regimen | NCCN Category | FDA Approved | Trial Design | Comparator | Primary End-Point | Line of Therapy | Conclusion |
| Rituximab SC + chemotherapy | 2A | Yes | Phase 3 (SABRINA) , randomized, open-label | Rituximab IV + chemotherapy | ORR | First line | <ul style="list-style-type: none"> Intravenous and subcutaneous rituximab had similar efficacy and safety profiles, and no new safety concerns were noted. Subcutaneous administration does not compromise the anti-lymphoma activity of rituximab when given with chemotherapy. |

Diffuse Large B-Cell Lymphoma (DLBCL)

| Regimen | NCCN Category | FDA Approved | Trial Design | Comparator | Primary End-Point | Line of Therapy | Conclusion |
|---------------------|---------------|--------------|---|---------------------|-------------------|-----------------|---|
| Rituximab SC + CHOP | 2A | Yes | Phase 3 (MabEase) , multi-center, randomized, open-label | Rituximab IV + CHOP | CR | First line | <ul style="list-style-type: none"> Overall, subcutaneous and intravenous rituximab had similar efficacy and safety, with improved patient satisfaction and time savings. |