Rituximab and hyaluronidase (Rituxan Hycela®)

Prior Authorization Drug Coverage Policy

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Lines of Business: Commercial
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This Drug Coverage Policy provides parameters for the coverage of Rituximab and hyaluronidase (Rituxan Hycela®)**.** Consideration of medically necessary indications are based upon U.S. Food and Drug Administration (FDA) indications, recommended uses within the Centers of Medicare & Medicaid Services (CMS) five recognized compendia, including the National Comprehensive Cancer Network (NCCN) Drugs & Biologics Compendium (Category 1 or 2A recommendations), and peer-reviewed scientific literature eligible for coverage according to the CMS, Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 titled, "Off-Label Use of Anti-Cancer Drugs and Biologics." This policy evaluates whether the drug therapy is proven to be effective based on published evidence-based medicine.

Drug Description[1]

Rituximab is a monoclonal antibody that targets the CD20 (cluster of differentiation) antigen expressed on the surface of pre-B and mature B-lymphocytes. Upon binding to CD20, rituximab mediates B-cell lysis. Possible mechanisms of cell lysis include complement dependent cytotoxicity (CDC) and antibody dependent cell mediated cytotoxicity (ADCC). Hyaluronan is a polysaccharide found in the extracellular matrix of the subcutaneous tissue. It is depolymerized by the naturally occurring enzyme hyaluronidase. Unlike the stable structural components of the interstitial matrix, hyaluronan has a half-life of approximately 0.5 days. Hyaluronidase human increases permeability of the subcutaneous tissue by temporarily depolymerizing hyaluronan.

FDA Indications[1]

Rituximab and hyaluronidase (Rituxan Hycela®) is FDA indicated for the following:

- Follicular Lymphoma
    - Relapsed or refractory, follicular lymphoma as a single agent
    - Previously untreated follicular lymphoma in combination with first line chemotherapy and, in patients achieving a complete or partial response to rituximab in combination with chemotherapy, as single agent maintenance therapy
    - Non-progressing (including stable disease), follicular lymphoma as a single agent after first-line cyclophosphamide, vincristine, and prednisone (CVP) chemotherapy

- Diffuse Large B-cell Lymphoma
    - Previously untreated diffuse large B-cell lymphoma in combination with cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) or other anthracycline-based chemotherapy regimens
- Chronic Lymphocytic Leukemia (CLL)
    - Previously untreated and previously treated CLL in combination with fludarabine and cyclophosphamide (FC)

NCCN Compendium Supported Indications

- B-Cell Lymphomas/Non-Hodgkin's lymphomas (NHL)
- Hairy Cell Leukemia
- Primary Cutaneous Lymphomas
- Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

Coverage Determinations[1,2]

Rituximab and hyaluronidase (Rituxan Hycela®) will require prior authorization. This agent is considered medically necessary for the following oncology indications if all criteria below are met:

Follicular Lymphoma

- The member has a diagnosis of follicular lymphoma **AND**
- One of the following applies:
    - Previously untreated disease and will be using Rituxan Hycela® in combination with first line chemotherapy and, in patients achieving a complete or partial response to Rituxan Hycela® in combination with chemotherapy, as single-agent maintenance therapy **OR**
    - Non-progressing (including stable disease) disease, as a single agent after first line cyclophosphamide, vincristine, and prednisone chemotherapy **OR**
    - Relapsed or refractory disease, as a single agent

Recommended dosage: Rituximab and hyaluronidase (Rituxan Hycela®) 1,400 mg/23,400 units subcutaneously according to recommended treatment schedule

Diffuse Large B-cell Lymphoma

- The member has a diagnosis of diffuse large B-cell lymphoma **AND**
- The member has previously untreated disease and will be using Rituxan Hycela® in combination with cyclophosphamide, doxorubicin, vincristine, and prednisone or with another anthracycline-based chemotherapy regimen

Recommended dosage: Rituximab and hyaluronidase (Rituxan Hycela®) 1,400 mg/23,400 units SC according to recommended treatment schedule

Chronic Lymphocytic Leukemia

- The member must have a diagnosis of chronic lymphocytic leukemia **AND**

- The member will be using Rituxan Hycela® as monotherapy or in combination with fludarabine and cyclophosphamide

Recommended dosage: Rituximab and hyaluronidase (Rituxan Hycela®) 1,600 mg/26,800 units subcutaneously **OR** Rituximab and hyaluronidase (Rituxan Hycela®) 1,400 mg/23,400 units subcutaneously according to recommended treatment schedule

B-Cell Lymphomas/Non-Hodgkin's lymphomas (NHL), including, but not limited to:

- Castleman's Disease
  - May be substituted for rituximab as a single agent or in combination with other systemic therapies after patients have received the first full dose of rituximab by intravenous infusion
- Gastric MALT Lymphoma
  - May be substituted for rituximab as a single agent or in combination with other systemic therapies (except ibritumomab tiuxetan) after patients have received the first full dose of rituximab by intravenous infusion
- High-Grade B-Cell Lymphomas
  - May be substituted for rituximab as a single agent or in combination with other systemic therapies after patients have received the first full dose of rituximab by intravenous infusion
- Histologic Transformation of Nodal Marginal Zone Lymphoma to Diffuse Large B-Cell Lymphoma
  - May be substituted for rituximab as a single agent or in combination with other systemic therapies (except for ibritumomab tiuxetan) after patients have received the first full dose of rituximab by intravenous infusion
- Mantle Cell Lymphoma
  - May be substituted for rituximab as a single agent or in combination with other systemic therapies after patients have received the first full dose of rituximab by intravenous infusion
- Nodal Marginal Zone Lymphoma
  - May be substituted for rituximab as a single agent or in combination with other systemic therapies (except ibritumomab tiuxetan) after patients have received the first full dose of rituximab by intravenous infusion
- Nongastric MALT Lymphoma (Noncutaneous)
  - May be substituted for rituximab as a single agent or in combination with other systemic therapies (except ibritumomab tiuxetan) after patients have received the first full dose of rituximab by intravenous infusion
- Post-Transplant Lymphoproliferative Disorders
  - May be substituted for rituximab as a single agent or in combination with other systemic therapies after patients have received the first full dose of rituximab by intravenous infusion
- Splenic Marginal Zone Lymphoma
  - May be substituted for rituximab as a single agent or in combination with other systemic therapies (except ibritumomab tiuxetan) after patients have received the first full dose of rituximab by intravenous infusion

Recommended dosage: Rituximab and hyaluronidase (Rituxan Hycela®) 1,400 mg/23,400 units subcutaneously

Hairy Cell Leukemia

- May be substituted for rituximab as a single agent or in combination with other systemic therapies in patients who have received at least one full dose of a rituximab product by intravenous route

Recommended dosage: Rituximab and hyaluronidase (Rituxan Hycela®) 1,400 mg/23,400 units subcutaneously according to recommended treatment schedule

Primary Cutaneous B-Cell Lymphomas

- May be substituted for rituximab after patients have received the first full dose of rituximab by intravenous infusion as therapy for primary cutaneous marginal zone or follicle center lymphoma with
    - solitary/regional, T1-2 disease that is refractory to initial therapy
    - generalized disease (skin only), T3

Recommended dosage: Rituximab and hyaluronidase (Rituxan Hycela®) 1,400 mg/23,400 units subcutaneously according to recommended treatment schedule

Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma

- May be substituted for rituximab as a single agent or in combination with other systemic therapies after patients have received the first full dose of rituximab by intravenous infusion

Recommended dosage: Rituximab and hyaluronidase (Rituxan Hycela®) 1,400 mg/23,400 units subcutaneously according to recommended treatment schedule

All indications:

- Rituximab and hyaluronidase (Rituxan Hycela®) will be approved through clinical review for up to a 12-month duration

Coverage Limitations

Treatment with Rituximab and hyaluronidase (Rituxan Hycela®) is not considered medically necessary for members with the following concomitant conditions:

- The member will be using Rituximab and hyaluronidase (Rituxan Hycela®) for the treatment of a non-malignant condition (e.g. rheumatoid arthritis).

- Initiate treatment with Rituximab and hyaluronidase (Rituxan Hycela®) only after patients have received at least one full dose of a rituximab product by intravenous infusion without severe adverse reactions.
- Indications not supported by NCCN category 2A or higher recommendations may not be considered medically necessary

Contraindications/Warnings/Precautions[1]

- Warnings/precautions:
    - Severe mucocutaneous reactions (boxed warning)
    - Hepatitis B reactivation (boxed warning)
    - Progressive multifocal leukoencephalopathy (boxed warning)
    - Hypersensitivity and other administration reactions
    - Tumor lysis syndrome
    - Infections
    - Cardiac adverse reactions
    - Renal toxicity
    - Bowel obstruction and perforation
    - Immunizations: live virus vaccines prior to or during treatment not recommended
    - Embryo-fetal toxicity

For specific recommendations on contraindications, warnings and precautions, patient monitoring, and on dose adjustments and discontinuation, please refer to the current prescribing information.

Billing

- Description: Injection, rituximab 10 mg and hyaluronidase
    - J9311

Disclaimer

Drug Coverage Policies are developed as needed, regularly reviewed, updated at least annually, and are subject to change. Other policies and coverage determination guidelines may apply. Federal and state regulatory requirements and member specific benefit plan documents, if applicable, must be reviewed prior to this Drug Coverage Policy. This Drug Coverage Policy is for informational purposes only and does not constitute medical advice or dictate how providers should practice medicine. This policy should not be reproduced, stored in a retrieval system, or altered from its original form without written permission from Oncology Analytics, Inc.

References

1. Rituxan Hycela [package insert]. Genentech, Inc., South San Francisco, CA. Available at: https://www.gene.com/download/pdf/rituxan_hycela_prescribing.pdf

2. Rituximab and hyaluronidase human. NCCN Drugs & Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium/content/
3. Davies A, Merli F, Mihalijevic B, et al. Efficacy and safety of subcutaneous rituximab versus intravenous rituximab for first-line treatment of follicular lymphoma (SABRINA): a randomized, open-label, phase 3 trial. Lancet Haematol. 2017;4(6:e272-e282.
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.
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;3:e128–38.