Ibritumomab tiuxetan (Zevalin) is a CD20-directed radiotherapeutic antibody administered as part of the ibritumomab tiuxetan therapeutic regimen indicated for the treatment of relapsed or refractory, low-grade or follicular B-cell non-Hodgkin’s lymphoma (NHL) and for previously untreated follicular NHL in patients who have achieved a partial or complete response to first-line chemotherapy.

Ibritumomab tiuxetan is the immunoconjugate resulting from a stable thiourea covalent bond between the monoclonal antibody ibritumomab and the linker-chelator tiuxetan \([N\text{-}[2\text{-bis (carboxymethyl) amino}]-3\text{-}(p\text{o}so\text{thiocyanatophenyl})-\text{propyl}]\text{-}[N\text{-}[2\text{-bis (carboxymethyl) amino}]-2\text{-}(methyl)-\text{ethyl}]\text{ glycine. This linker-chelator provides a high affinity, conformationally restricted chelation site for Yttrium-90.}

II. Criteria/Guidelines

A. Ibritumomab tiuxetan is covered (subject to Administrative Guidelines) when recommended by an oncologist in the treatment of:

1. Relapsed or refractory low-grade NHL
2. Follicular lymphoma:
   a. Relapsed or refractory follicular NHL
   b. For previously untreated follicular NHL in patients who achieve a partial or complete response to first-line chemotherapy
   c. As first-line radioimmunotherapy alone in elderly or infirm patients with the indications for treatment in the setting of comorbidities where tolerability of combination chemotherapy is a concern
   d. Following induction chemotherapy
   e. Chemoimmunotherapy as first-line consolidation therapy
f. As second-line radioimmunotherapy for refractory or progressive disease in patients with the indications for treatment.

3. Gastric and Nongastric MALT lymphoma
   a. As first-line radioimmunotherapy alone in elderly or infirm patients with the indications for treatment in the setting of comorbidities where tolerability of combination chemotherapy is a concern
   b. Following induction chemotherapy
   c. Chemoimmunotherapy as first-line consolidation therapy stage IIIE-IV disease; or
   d. As second-line radioimmunotherapy for recurrent or progressive disease in patients with the indications for treatment.

4. Primary cutaneous B-cell lymphoma
   a. Radioimmunotherapy alone, including in elderly or infirm patients with the indications for treatment in the setting of comorbidities where tolerability of combination chemotherapy is a concern
   b. Following induction chemotherapy
   c. Chemoimmunotherapy as first-line consolidation therapy for refractory generalized cutaneous marginal zone follicle center lymphoma
   d. As second-line radioimmunotherapy for refractory generalized cutaneous disease or relapsed generalized extracutaneous disease in patients with the indications for treatment.

5. Splenic marginal zone lymphoma- For progressive disease following initial treatment for splenomegaly in patients with the indications for the treatment as:
   a. As first-line radioimmunotherapy alone in elderly or infirm patients with the indications for treatment in the setting of comorbidities where tolerability of combination chemotherapy is a concern
   b. Following induction chemotherapy
   c. Chemoimmunotherapy as first-line consolidation therapy
   d. Second-line radioimmunotherapy

B. For the indications listed above, the following criteria must be met:

1. Lymphoma involvement of the bone is less than 25 percent
2. Platelet count is greater than or equal to 100,000 cells/cubic millimeter
3. Neutrophil count is greater than or equal to 1,500 cells/cubic millimeter
4. Prior external beam radiation therapy not to exceed 25 percent of the bone marrow
5. No prior history of myeloablative therapy/autologous bone marrow transplant

C. Relapsed is defined as the reappearance of disease in the region of prior disease (recurrence) and/or in new regions (extensions) after initial therapy and attainment of complete response. Refractory is defined as no longer responding to therapy.

D. For all indications, HMSA follows NCCN level 1 or 2A and/or DrugDex level I or IIA recommendations
III. Administrative Guidelines

A. Precertification is required. To precertify, complete HMSA's Drug Review Request and mail or fax the form as indicated. Include the following documentation.

1. Clinical notes including any previous treatments.
2. Oncology notes
3. Pathology reports
4. Imaging studies

B. Applicable codes:

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>79403</td>
<td>Radiopharmaceutical therapy, radiolabeled monoclonal antibody by intravenous infusion</td>
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</table>

<table>
<thead>
<tr>
<th>HCPCS</th>
<th>Description</th>
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<tbody>
<tr>
<td>A9543</td>
<td>Yttrium Y-90 ibritumomab tiuxetan, therapeutic, per treatment dose, up to 40 mCi</td>
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</tbody>
</table>

IV. Important Reminder

The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii's Patients' Bill of Rights and Responsibilities Act (Hawaii Revised Statutes § 432E-1.4), generally accepted standards of medical practice, and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA's determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

V. References