**Prior Authorization DRUG Guidelines**

**Bexarr (tositumomab)**

Effective Date: 10/22/13  
Date Developed: 9/3/13 by Albert Reeves MD  
Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19, 2/18/20

**Pharmacologic Category:** Antineoplastic Agent, Monoclonal Antibody; Radiopharmaceutical

**Preauthorization Criteria:** Treatment of relapsed or refractory CD20 positive, low-grade, follicular, or transformed non-Hodgkin's lymphoma (NHL), with progression during or after rituximab treatment

**Dosage:** **Non-Hodgkin's lymphoma (NHL), relapsed or refractory:** I.V.: Dosing consists of four components administered in 2 steps. Refer to manufacturer’s labeling for additional details. Indicated for a single treatment course. Thyroid protective agents (SSKI, Lugol's solution or potassium iodide) should be administered beginning at least 24 hours prior to step 1 (Refer to Additional Information or Pharmacotherapy Pearls). Premedicate with acetaminophen 650 mg and diphenhydramine 50 mg orally 30 minutes prior to step 1 and step 2.

**Step 1: Dosimetric step (Day 0):**

Tositumomab 450 mg administered over 60 minutes

Iodine I 131 tositumomab (containing I-131 5 mCi and tositumomab 35 mg) administered over 20 minutes

**Note:** Whole body dosimetry and biodistribution should be determined on Day 0; days 2, 3, or 4; and day 6 or 7 prior to administration of Step 2. If biodistribution is not acceptable, do not administer the therapeutic step. On day 6 or 7, calculate the patient specific activity of iodine I 131 tositumomab to deliver 75 cGy total body dose (TBD) or 65 cGy TBD (in mCi).

**Step 2: Therapeutic step (one dose administered 7-14 days after step 1):**

Tositumomab 450 mg administered over 60 minutes

*Iodine I 131 tositumomab:*

Platelets ≥150,000/mm³: Iodine I 131 calculated to deliver 75 cGy total body irradiation and tositumomab 35 mg over 20 minutes

Platelets ≥100,000/mm³ and <150,000/mm³: Iodine I 131 calculated to deliver 65 cGy total body irradiation and tositumomab 35 mg over 20 minutes
Administration: I.V.: Refer to manufacturer’s labeling for additional details.

Tositumomab: Infuse over 60 minutes

Iodine I 131 tositumomab: Infuse over 20 minutes

Administer via an I.V. tubing set with an in-line 0.22 micron filter; do not change primary infusion set
or filter at any time during the dosimetric or therapeutic step; changing the filter may result in up
to a 7% loss of the iodine I 131 tositumomab dose (use the same infusion set and filter for
tositumomab and iodine I 131 tositumomab). Flush with NS after iodine I 131 tositumomab
infusion.

Prior to infusion, patients should be premedicated (with acetaminophen and an antihistamine) and a
thyroid-protective agent should be started. Reduce the rate of tositumomab or iodine 131
tositumomab infusion by 50% for mild-to-moderate infusion-related toxicities; interrupt for
severe infusion reaction (once severe infusion reaction has resolved, infusion may be restarted
at half the previous rate). Discontinue for serious allergic reaction.

Major adverse reactions and Black Box Warnings:

>10%:

Central nervous system: Fever (37%), pain (19%), chills (18%), headache (16%)
Dermatologic: Rash (17%; grades 3/4: <1%)
Endocrine & metabolic: Hypothyroidism (7% to 19%)
Gastrointestinal: Nausea (36%), abdominal pain (15%), vomiting (15%), anorexia (14%),
diarrhea (12%)
Hematologic: Myelosuppression (grades 3/4: 71%; nadir: 4-7 weeks; duration: ~30 days),
neutropenia (grades 3/4: 63%; median duration: 31 days; grade 4: 25%),
thrombocytopenia (grades 3/4: 53%; median duration: 32 days; grade 4: 21%),
lymphocytopenia (recovery: ~12 weeks after treatment), anemia (grades 3/4: 29%; median
duration: 23 days; grade 4: 5%), secondary leukemia/myelodysplastic syndrome (overall:
3% to 10%; 2-year follow-up: 2% to 5%; 5-year follow-up: 6% to 15%),
hemorrhage (12%)
Neuromuscular & skeletal: Weakness (46%), myalgia (13%)
Respiratory: Cough (21%), pharyngitis (12%), dyspnea (11%)
Miscellaneous: Infusion-related reactions (29%, occurred within 14 days of infusion, included
bronchospasm, chills, dyspnea, fever, hypotension, nausea, rigors, diaphoresis); infection
(21% to 45%, serious: 9%); g HAMA-positive seroconversion (10% to 11%)
1% to 10%:

Cardiovascular: Hypotension (7%), peripheral edema (9%), chest pain (7%), vasodilation (5%)  
Central nervous system: Dizziness (5%), somnolence (5%)  
Dermatologic: Pruritus (10%)  
Gastrointestinal: Constipation (6%), dyspepsia (6%), weight loss (6%)  
Local: Injection site hypersensitivity  
Neuromuscular & skeletal: Arthralgia (10%), back pain (8%), neck pain (6%)  
Respiratory: Rhinitis (10%), pneumonia (6%)  
Miscellaneous: Diaphoresis (8%), hypersensitivity/allergic reaction (6%), secondary malignancies (nonhematologic: 5%)  

<1% (Limited to important or life-threatening): Anaphylactic reaction, angioedema, bacteremia, bronchitis, dehydration, flu-like syndrome, herpes virus infection, laryngismus, pleural effusion, septicemia, serum sickness, skin infections

**Contraindications**

There are no contraindications listed in the manufacturer’s labeling.

Bone marrow suppression: [U.S. Boxed Warning]: Severe and prolonged cytopenias, including neutropenia and thrombocytopenia are common; do not administer in patients with >25% lymphoma marrow involvement, platelet count <100,000/mm$^3$ or neutrophil count <1500/mm$^3$. Hematologic toxicity is reported to be the most common adverse effect with 27% patients requiring supportive care; cytopenias may be prolonged and severe.

- Hypersensitivity/anaphylactoid reactions: [U.S. Boxed Warning]: Serious hypersensitivity reactions (including anaphylaxis) have been reported; permanently discontinue for severe reaction; medications for the treatment of reactions should be readily available in the event of severe reactions. Signs and symptoms of severe allergic reactions include fever, rigors/chills, sweating, hypotension, dyspnea, bronchospasm, or nausea; may occur during or within 48 hours of infusion. Premedicate with acetaminophen and diphenhydramine prior to both the dosimetric and therapeutic doses.

**Special handling:**

- Radioactive isotopes: [U.S. Boxed Warning]: Treatment involves radioactive isotopes and should only be administered by or under supervision of physicians enrolled in the Bexxar® therapeutic regimen certification program; appropriate precautions for
Handling and administration must be followed. Patients must be instructed in measures to minimize exposure of others.

References:


Revision History:
Date Approved by P&T Committee: 10/22/13
Date Reviewed/No Updates: 1/28/14 by C. Sanders MD
Date Approved by P&T Committee: 1/28/14
Date Reviewed/No Updates: 1/13/15 by C. Sanders, MD
Date Approved by P&T Committee: 1/27/15
Date Approved by P&T Committee: 1/26/16
Date Reviewed/No Updates: 1/14/17 by C. Sanders, MD
Date Approved by P&T Committee: 1/24/17
Date Reviewed/No Updates: 1/23/18 by C. Sanders, MD
Date Approved by P&T Committee: 1/23/18
Date Reviewed/No Updates: 1/22/19 by C. Sanders, MD; R. Sterling, MD
Date Approved by P&T Committee: 1/22/19
Date Reviewed/No Updates: 2/18/20 by H. Taekman, MD; R. Sterling, MD
Date Approved by P&T Committee: 2/18/20
<table>
<thead>
<tr>
<th>Revision Date</th>
<th>Content Revised (Yes/No)</th>
<th>Contributors</th>
<th>Review/Revision Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/24/17</td>
<td>No</td>
<td>Catherine Sanders, MD; Robert Sterling, MD</td>
<td>Annual review</td>
</tr>
<tr>
<td>1/23/18</td>
<td>No</td>
<td>Catherine Sanders, MD; Robert Sterling, MD</td>
<td>Annual review</td>
</tr>
<tr>
<td>1/22/19</td>
<td>No</td>
<td>Catherine Sanders, MD; Robert Sterling, MD</td>
<td>Annual review</td>
</tr>
<tr>
<td>2/18/20</td>
<td>No</td>
<td>Howard Taekman, MD; Robert Sterling, MD</td>
<td>Annual review</td>
</tr>
</tbody>
</table>