## Clinical Trials
The NCCN recommends cancer patient participation in clinical trials as the gold standard for treatment. Cancer therapy selection, dosing, administration, and the management of related adverse events can be a complex process that should be handled by an experienced healthcare team. Clinicians must choose and verify treatment options based on the individual patient; drug dose modifications and supportive care interventions should be administered accordingly. The cancer treatment regimens below may include both U.S. Food and Drug Administration-approved and unapproved indications/regimens. These regimens are only provided to supplement the latest treatment strategies.

These Guidelines are a work in progress that may be refined as often as new significant data becomes available. The NCCN Guidelines® are a consensus statement of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN Guidelines® is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use, or application and disclaims any responsibility for their application or use in any way.

### Primary Cutaneous Marginal Zone Lymphoma or Follicular Center Lymphoma Initial Therapy

**Note:** All recommendations are Category 2A unless otherwise indicated.

#### Solitary/Regional T1-2*

<table>
<thead>
<tr>
<th>REGIMEN</th>
<th>DOSING</th>
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<tbody>
<tr>
<td><strong>Topicals</strong></td>
<td><strong>Topical nitrogen mustard</strong>&lt;br&gt;Day 1–15: Topical clobetasol propionate 0.05% cream once daily.&lt;br&gt;OR Day 1–15: Mechlorethamine 0.02% aqueous solution once daily.</td>
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<td></td>
<td><strong>Topical bexarotene</strong>&lt;br&gt;Topical bexarotene gel applied BID until lesions disappear, then use on a needed basis (use with intralesional triamcinolone and interferon alfa).</td>
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<td></td>
<td><strong>Topical imiquimod</strong>&lt;br&gt;Imiquimod 5% cream daily until an inflammatory response develops, then apply to all areas 2–4 times weekly until all inflammation had subsided fully. Then, maintain treatment for another 2 months. Treat for a total of 8 months.</td>
</tr>
<tr>
<td><strong>Intralesional steroids</strong>&lt;br&gt;Triamcinolone 20mg/mL injected into lesions once monthly until lesions are gone or no further improvement is noted (use with interferon alfa and topical bexarotene gel).&lt;br&gt;OR Interferon alfa 5 million units SC/IM every 4 weeks for 5 months.</td>
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</tbody>
</table>

#### Generalized Disease (Skin Only), T31

| Rituximab | Rituximab 375mg/m² IV once weekly for 4–8 weeks. OR Rituximab 3mL of stem solution (10mg/mL) injection into the stigmatizing nodules 3 times a week every 28 days for 6 months. |
| **Topicals** | **Topical nitrogen mustard**<br>Day 1–15: Topical clobetasol propionate 0.05% cream once daily.<br>OR Day 1–15: Mechlorethamine 0.02% aqueous solution once daily. |
| | **Topical bexarotene**<br>Topical bexarotene gel applied BID until lesions disappear, then use on an a needed basis (use with intralesional triamcinolone and interferon alfa). |
| | **Topical imiquimod**<br>Imiquimod 5% cream daily until an inflammatory response develops, then apply to all areas 2–4 times weekly until all inflammation subsides fully. Then, maintain treatment for another 2 months. Treat for a total of 8 months. |
| **Intralesional steroids**<br>Triamcinolone 20mg/mL injected into lesions once monthly until lesions are gone or no further improvement is noted (use with interferon alfa and topical bexarotene gel).<br>OR Interferon alfa 5 million units SC/IM every 4 weeks for 5 months. |

#### Palliative chemotherapy

| Chlorambucil + rituximab | Chlorambucil 4–10mg IV daily over a median period of 16 weeks (range 8–23 weeks) Rituximab 375mg/m² IV once weekly for 8 weeks. OR CVP + rituximab Day 1: Cyclophosphamide 750mg/m² IV Day 1: Vincristine 1.4mg/m² (max 2mg) IV Days 1–5: Prednisone 40mg/m² PO daily Day 1: Rituximab 275mg/m² IV. Repeat every 21 days for a max of 8 cycles. |
## Extracutaneous Disease

Manage as per Follicular Lymphoma (Grade 1–2) Stage I, II.

### Primary Cutaneous Marginal Zone Lymphoma or Follicular Center Lymphoma Relapsed Disease

<table>
<thead>
<tr>
<th>Solitary/Regional T1-2*</th>
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<tr>
<td><strong>REGIMEN</strong></td>
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<td><strong>Topical imiquimod</strong></td>
</tr>
<tr>
<td><strong>Intralesional steroids</strong></td>
</tr>
</tbody>
</table>

### Generalized Disease (Skin Only), T3†

**Rituximab**

- **Rituximab 375mg/m² IV once weekly for 4–8 weeks.**
- **Rituximab 3mL of stem solution (10mg/mL) injection into the stigmatizing nodules 3 times a week every 28 days for 6 months.**

**Topicals**

- **Topical nitrogen mustard**
- **Topical bexarotene**
- **Topical imiquimod**

### Intralesional steroids

- **Triamcinolone 20mg/mL injected into lesions once monthly until lesions are gone or no further improvement is noted (use with interferon-alfa and topical bexarotene gel).**
- **Interferon-alfa 5 million units SC/IM every 4 weeks for 5 months.**

### Palliative chemotherapy

**Chlorambucil + rituximab**

- **Chlorambucil 4–10mg IV daily over a median period of 16 weeks (range 8–23 weeks)**
- **Rituximab 375mg/m² IV once weekly for 8 weeks.**

**CVP + rituximab**

- **Cyclophosphamide 750mg/m² IV**
- **Vincristine 1.4mg/m² (max 2mg) IV**
- **Prednisone 40mg/m² PO daily**
- **Rituximab 275mg/m² IV. Repeat every 21 days for a max of 8 cycles.**

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**Extracutaneous Disease**

Manage as per Follicular Lymphoma (Grade 1–2) Stage I, II.
### Primary Cutaneous Diffuse Large B-Cell Lymphoma, Leg Type

#### REGIMEN | DOsing
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**RCHOP + local RT**<sup>11</sup> | **Day 0:** Rituximab 375mg/m<sup>2</sup> IV  
**Day 1:** Cyclophosphamide 750mg/m<sup>2</sup> IV  
**Day 1:** Doxorubicin 50mg/m<sup>2</sup> IV  
**Day 1:** Vincristine 1.4mg/m<sup>2</sup> (max 2mg) IV  
**Days 1-5:** Prednisone 100mg/m<sup>2</sup> PO daily. Repeat every 3 weeks for 6–8 cycles (6 cycles if complete response is achieved after 4 cycles, all others received 8 cycles). Long-term interferon-alfa maintenance initiated at a dose of 3 x 5 million U/week and reduced according to observed adverse effects. Interferon-alfa maintenance therapy was given until lymphoma progression or the development of intolerable adverse effects.

#### Generalized Disease (Skin Only), T3<sup>‡</sup>

**RCHOP + clinical trial**<sup>11</sup> | **Day 0:** Rituximab 375mg/m<sup>2</sup> IV  
**Day 1:** Cyclophosphamide 750mg/m<sup>2</sup> IV  
**Day 1:** Doxorubicin 50mg/m<sup>2</sup> IV  
**Day 1:** Vincristine 1.4mg/m<sup>2</sup> (max 2mg) IV  
**Days 1-5:** Prednisone 100mg/m<sup>2</sup> PO daily. Repeat every 3 weeks for 6–8 cycles (6 cycles if complete response is achieved after 4 cycles, all others received 8 cycles).

### Extracutaneous Disease
Manage as per Diffuse Large B-Cell Lymphoma induction therapy.

* Treatment consists of local radiotherapy (preferred), or excision, or observation  
† Treatment consists of local radiotherapy for palliation of symptoms or observation  
‡ Treatment consists of local radiotherapy or clinical trial  
¶ Treatment consists of clinical trial

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### References

(Revised 9/2014)

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