Primary Cutaneous B-Cell Lymphoma

**DIAGNOSIS**

**ESSENTIAL:**
- Review of all slides with at least one paraffin block representative of the tumor should be done by a pathologist with expertise in the diagnosis of primary cutaneous B-cell lymphoma. Rebiopsy if consult material is nondiagnostic.
- Histopathology review of adequate biopsy (punch, incisional, excisional).
- Adequate immunophenotyping to establish diagnosis
  - Recommended panel for paraffin section immunohistochemistry: CD20, CD79a, CD3, CD5, CD10, BCL2, BCL6, Ki-67, kappa/lambda, MUM1

**USEFUL IN CERTAIN CIRCUMSTANCES:**
- Peripheral blood flow cytometry
- Additional immunohistochemical studies to establish lymphoma subtype
  - Paraffin panel: cyclin D1
  - Molecular genetic analysis to detect: antigen receptor gene rearrangements; IgH gene rearrangement by PCR
  - Cytogenetics or FISH: t(14;18)

**WORKUP**

**ESSENTIAL:**
- Complete history and physical examination—including complete skin exam
- CBC, differential, comprehensive metabolic panel
- LDH
- Hepatitis B testing if rituximab considered
- Chest/abdominal/pelvic CT
- Bone marrow biopsy, if PC-DLBCL, Leg type
- Pregnancy testing in women of child-bearing age (if chemotherapy planned)

**USEFUL IN SELECTED CASES:**
- PET-CT scan
- Bone marrow biopsy
  - Consider if PCFCL
  - Optional if PCMZL
- SPEP/quantitative immunoglobulins for PCMZL

**CUTB-1**

For non-cutaneous, see Nongastric MALT Lymphoma (NGMLT-1).

See Use of Immunophenotyping in Differential Diagnosis of Mature B-cell and T/NK-cell Neoplasms (NHODG-A).

Rule out drug-induced lymphoma.

Hepatitis B testing is indicated because of the risk of reactivation with immunotherapy + chemotherapy. Tests include hepatitis B surface antigen and core antibody for a patient with no risk factors. For patients with risk factors or previous history of hepatitis B, add e-antigen. If positive, check viral load and consult with gastroenterologist.

Note: All recommendations are category 2A unless otherwise indicated. Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.
PRIMARY CUTANEOUS MARGINAL ZONE OR FOLLICLE CENTER B-CELL LYMPHOMA

STAGE

INITIAL THERAPY

Solitary/regional, T1-2 (Ann Arbor Stage IE)

| Locoregional RT or Excision or Observation (selected cases) or Topicals (selected cases) | CR/PR | Persistent or progressive disease |
| Regional | CR/PR | Generalized disease (extracutaneous disease) |
| Generalized disease (skin only), T3 | Observation or Rituximab or Topicals or Locoregional RT for palliation of symptoms or Palliative chemotherapy such as chlorambucil or CVP ± rituximab | CR/PR | Persistent or progressive disease |

SECONDARY THERAPY

| Observation or Excision or Topicals or Injected steroids or Locoregional RT | Relapsed disease, See CUTB-3 |

| Generalized disease (extracutaneous disease) | Manage as per FOLL-2 |
| Generalized disease (skin only) |

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^Unless clinically indicated, additional imaging studies during the course of treatment are not needed.

^See TNM Classification of Cutaneous Lymphoma other than MF/SS (CUTB-A).

^Observation may be appropriate if local therapy is contraindicated or undesirable.

^Topicals may include steroids, imiquimod, nitrogen mustard, bexarotene.

^When RT or surgical treatment is either not feasible or desired.

^See Treatment References (CUTB-B).

^In rare circumstances for very extensive disease, other combination chemotherapy regimens listed in FOLL-B are used.

See Rituximab and Viral Reactivation (NHODG-D)
PRIMAR CUTANEOUS MARGINAL ZONE OR FOLLICLE CENTER B-CELL LYMPHOMA

RELAPSED DISEASE

STAGE

ADDITIONAL THERAPY

Observation or Excision or Topicals or Injected steroids or Locoregional RT

CR/PR

Refractory

Generalized disease (extracutaneous disease)

Manage as per FOLL-2

Regional

Persistent or progressive disease

Generalized disease (skin only)

Manage as per FOLL-2

Solitary/regional, T1-2 (Ann Arbor Stage IE)

Relapsed disease

Generalized disease (skin only), T3

Extracutaneous disease

CR/PR

Refractory

Persistent or progressive disease

See Rituximab and Viral Reactivation (NHODG-D)

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Primary Cutaneous B-Cell Lymphoma

**PRIMARY CUTANEOUS DIFFUSE LARGE B-CELL LYMPHOMA, LEG TYPE**

**STAGE f**

<table>
<thead>
<tr>
<th>Solitary regional, T1-2 (Ann Arbor Stage IE)</th>
<th>INITIAL THERAPY</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-CHOP&lt;sup&gt;m&lt;/sup&gt; + locoregional RT or Locoregional RT&lt;sup&gt;n&lt;/sup&gt; or Clinical trial</td>
<td>CR/PR</td>
</tr>
</tbody>
</table>

**SECONDARY THERAPY**

- Persistent or progressive disease:
  - Regional
  - Manage as per BCEL-5
  - Locoregional RT

- Generalized disease:
  - Manage as per BCEL-5

- Extracutaneous disease:
  - Manage as per BCEL-2

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<sup>f</sup>See TNM Classification of Cutaneous Lymphoma other than MF/SS (CUTB-A).

<sup>m</sup>For alternate regimens, see BCEL-C.

<sup>n</sup>For patients not able to tolerate chemotherapy.

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TNM CLASSIFICATION OF CUTANEOUS LYMPHOMA OTHER THAN MF/SS<sup>a,b</sup>

<table>
<thead>
<tr>
<th>T</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Solitary skin involvement</td>
</tr>
<tr>
<td>T1a</td>
<td>A solitary lesion &lt; 5 cm diameter</td>
</tr>
<tr>
<td>T1b</td>
<td>A solitary &gt; 5 cm diameter</td>
</tr>
<tr>
<td>T2</td>
<td>Regional skin involvement: multiple lesions limited to 1 body region or 2 contiguous body regions&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>T2a</td>
<td>All-disease-encompassing in a &lt; 15-cm-diameter circular area</td>
</tr>
<tr>
<td>T2b</td>
<td>All-disease-encompassing in a &gt; 15- and &lt; 30-cm-diameter circular area</td>
</tr>
<tr>
<td>T2c</td>
<td>All-disease-encompassing in a &gt; 30-cm-diameter circular area</td>
</tr>
<tr>
<td>T3</td>
<td>Generalized skin involvement</td>
</tr>
<tr>
<td>T3a</td>
<td>Multiple lesions involving 2 noncontiguous body regions&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>T3b</td>
<td>Multiple lesions involving ≥ 3 body regions&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>N</th>
<th>Definition</th>
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</thead>
<tbody>
<tr>
<td>N0</td>
<td>No clinical or pathologic lymph node involvement</td>
</tr>
<tr>
<td>N1</td>
<td>Involvement of 1 peripheral lymph node region&lt;sup&gt;c&lt;/sup&gt; that drains an area of current or prior skin involvement</td>
</tr>
<tr>
<td>N2</td>
<td>Involvement of 2 or more peripheral lymph node regions&lt;sup&gt;c&lt;/sup&gt; or involvement of any lymph node region that does not drain an area of current or prior skin involvement</td>
</tr>
<tr>
<td>N3</td>
<td>Involvement of central lymph nodes</td>
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<thead>
<tr>
<th>M</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
<td>No evidence of extracutaneous non-lymph node disease</td>
</tr>
<tr>
<td>M1</td>
<td>Extracutaneous non-lymph node disease present</td>
</tr>
</tbody>
</table>

<sup>a</sup>This work was originally published in Blood. Kim YH, Willemze R, Pimpinell Ni, et al, for the ISCL and the EORTC. TNM classification system for primary cutaneous lymphomas other than mycosis fungoides and Sézary syndrome: A proposal of the International Society for Cutaneous Lymphomas (ISCL) and the Cutaneous Lymphoma Task Force of the European Organization of Research and Treatment of Cancer (EORTC) Blood 2007;110:479-484. © the American Society of Hematology.

<sup>b</sup>For definition of body regions, see Body Regions for the Designation of T (skin involvement) Category (CUTB-A 2 of 2).

<sup>c</sup>Definition of lymph node regions is consistent with the Ann Arbor system: Peripheral sites: antecubital, cervical, supraclavicular, axillary, inguinal-femoral, and popliteal. Central sites: mediastinal, pulmonary hilar, paraaortic, iliac.

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BODY REGIONS FOR THE DESIGNATION OF T (SKIN INVOLVEMENT) CATEGORY


\(^b\)Left and right extremities are assessed as separate body regions. The designation of these body regions are based on regional lymph node drainage patterns.


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TREATMENT REFERENCES

Rituximab

Chlorambucil