NCCN Guidelines Version 1.2013  
Primary Cutaneous B-Cell Lymphomas

**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 non-diagnostic.
- Histopathology review of adequate biopsy (punch, incisional, excisional).
- Adequate immunophenotyping to establish diagnosis.
  - IHC panel: CD20, CD79a, CD3, CD5, CD10, BCL2, BCL6, kappa/lambda, IRF4/MUM1

**USEFUL IN CERTAIN CIRCUMSTANCES:**
- Additional immunohistochemical studies to establish lymphoma subtype
  - IHC panel: Ki-67, CD43, CD21, CD23
  - Paraffin panel: Cyclin D1
  - Assessment of IgM and IgD expression (to further help in distinguishing DLBCL, leg type from follicle center lymphoma)
- Molecular analysis to detect: antigen receptor gene rearrangements; IG gene rearrangement by PCR
- Cytogenetics or FISH: t(14;18)
- If adequate biopsy material available, flow cytometry can be useful in determining B-cell clonality.

**NOTE:** A germinal (or follicle) center phenotype and large cells in a skin lesion is not equivalent to DLBCL but is consistent with primary cutaneous germinal/follicle center lymphoma.

**WORKUP**

**ESSENTIAL:**
- History and physical exam, 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
- Peripheral blood flow cytometry, if CBC demonstrates lymphocytosis
- SPEP/quantitative immunoglobulins for PCMZL

**PCMZL:** Primary Cutaneous Marginal Zone Lymphoma
**PCFCL:** Primary Cutaneous Follicle Center Lymphoma
**PC-DLBCL, Leg type:** Primary Cutaneous Diffuse Large B-cell Lymphoma, Leg type

**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.

dRule out drug-induced cutaneous lymphoid hyperplasia.

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

bSee Use of Immunophenotyping and Genetic Testing in Differential Diagnosis of Mature B-Cell and NK/T-Cell Neoplasms (NHODG-A).

cTypical immunophenotype: PC-DLBCL: CD20+ BCL2+ CD10- BCL6+/- IRF4/MUM1+/- ; PCFCL: CD20+ BCL2- CD10-/+ BCL6+ IRF4/MUM1+ ; PCMZL: CD20+ BCL2+/ CD10- BCL6- IRF4/MUM1+/- cytoplasmic kappa+ or lambda+ in about 40%.
**NCCN Guidelines Version 1.2013**

**Primary Cutaneous B-Cell Lymphomas**

**Primary Cutaneous Marginal Zone Lymphoma or Follicle Center Lymphoma**

**Stage**

- **Solitary/regional, T1-2 (Ann Arbor Stage IE)**
  - Local RT (preferred) or Excision
  - In selected cases: Observation or Topicals or Intralesional steroids
  - CR/PR
  - Persistent or progressive disease

- **Generalized disease (skin only), T3**
  - Observation or Rituximab or Topicals or Local RT for palliation of symptoms or Intralesional steroids or Palliative chemotherapy such as chlorambucil ± rituximab or CVP ± rituximab
  - CR/PR
  - Persistent or progressive disease

- **Extracutaneous disease**
  - Manage as per FOLL-2

**Secondary Therapy**

- CR/PR Relapsed disease

- Persistent or progressive disease
  - Generalized disease (extracutaneous disease)
  - Generalized disease (skin only)
  - Manage as per FOLL-2
  - Relapsed disease, See CUTB-3

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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).*

*See Treatment References (CUTB-B).*

*When RT or surgical treatment is neither feasible nor desired.*

*There are case reports showing efficacy of topicals, which include steroids, imiquimod, nitrogen mustard, and bexarotene.*

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

**See monoclonal antibody and viral reactivation (NHODG-B)**
Primary Cutaneous Marginal Zone Lymphoma or Follicle Center Lymphoma

Relapsed Disease

Stage 9

Additional Therapy

Observation or Excision or Topicals or Local RT

CR/PR

Persistent or progressive disease

Generalized disease (extracutaneous disease)

Manage as per FOLL-2

Regional

Generalized disease (skin only)

Observation or Excision or Topicals or Intralesional steroids or Local RT

CR/PR

Persistent or progressive disease

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

Observation or Excision or Topicals or Local RT for palliation of symptoms or Intralesional steroids or Palliative chemotherapy such as chlorambucil ± rituximab or CVP ± rituximab

CR/PR

Refractory

Manages per FOLL-2

Generalized disease (skin only), T3

Refractory

Persistent or progressive disease

Extracutaneous disease

Relapsed disease

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

**STAGE**

**INITIAL THERAPY**

| Solitary regional, T1-2 (Ann Arbor Stage IE) | RCHOPᵐ + local RT or Local RTⁿ or Clinical trial |
| Generalized disease (skin only), T3 | RCHOPᵐ ± local RT or Clinical trial |
| Extracutaneous disease | Manage as per BCEL-3 |

<table>
<thead>
<tr>
<th>CR</th>
<th>Observe</th>
<th>Relapse</th>
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</thead>
<tbody>
<tr>
<td>PR</td>
<td></td>
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**SECONDARY THERAPY**

| RCHOP (if not previously received) or Manage as per BCEL-6 or Local RT to previously unirradiated tumor |
| Manage as per BCEL-6 or Local RT for palliation or Radioimmunotherapy |

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

ᵐFor patients who cannot tolerate anthracyclines, see BCEL-C for regimens for patients with poor left ventricular function.

ⁿFor patients not able to tolerate chemotherapy.

Consider prophylaxis for tumor lysis syndrome (See NHODG-B)

See monoclonal antibody and viral reactivation (NHODG-B)

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### TNM CLASSIFICATION OF CUTANEOUS LYMPHOMA OTHER THAN MF/SS\(^a,b\)

<table>
<thead>
<tr>
<th>T</th>
<th>Solitary skin involvement</th>
<th>Regional skin involvement: multiple lesions limited to 1 body region or 2 contiguous body regions(^b)</th>
<th>Generalized skin involvement</th>
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<tbody>
<tr>
<td>T1</td>
<td>T1a: a solitary lesion &lt;5 cm diameter</td>
<td>T2a: all-disease-encompassing in a &lt;15-cm-diameter circular area</td>
<td>T3a: multiple lesions involving 2 noncontiguous body regions(^b)</td>
</tr>
<tr>
<td></td>
<td>T1b: a solitary &gt;5 cm diameter</td>
<td>T2b: all-disease-encompassing in a &gt;15- and &lt;30-cm-diameter circular area</td>
<td>T3b: multiple lesions involving ≥3 body regions(^b)</td>
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<tr>
<td>T2</td>
<td>T2c: all-disease-encompassing in a &gt;30-cm-diameter circular area</td>
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</table>

<table>
<thead>
<tr>
<th>N</th>
<th>No clinical or pathologic lymph node involvement</th>
<th>Involvement of 1 peripheral lymph node region(^c) that drains an area of current or prior skin involvement</th>
<th>Involvement of 2 or more peripheral lymph node regions(^c) or involvement of any lymph node region that does not drain an area of current or prior skin involvement</th>
<th>Involvement of central lymph nodes</th>
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<tbody>
<tr>
<td>N0</td>
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<tr>
<td>N1</td>
<td>Involvement of 1 peripheral lymph node region(^c) that drains an area of current or prior skin involvement</td>
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<tr>
<td>N2</td>
<td>Involvement of 2 or more peripheral lymph node regions(^c) or involvement of any lymph node region that does not drain an area of current or prior skin involvement</td>
<td></td>
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<tr>
<td>N3</td>
<td>Involvement of central lymph nodes</td>
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</table>

<table>
<thead>
<tr>
<th>M</th>
<th>No evidence of extracutaneous non–lymph node disease</th>
<th>Extracutaneous non-lymph node disease present</th>
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</thead>
<tbody>
<tr>
<td>M0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M1</td>
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</table>

\(^a\)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.

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

\(^c\)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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**Discussion**


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

**Definition of body regions:**
- **Head and neck:** inferior border—superior border of clavicles, T1 spinous process.
- **Chest:** superior border—superior border of clavicles; inferior border—inferior margin of rib cage; lateral borders—mid-axillary lines, glenohumeral joints (inclusive of axillae).
- **Abdomen/genital:** superior border—inferior margin of rib cage; inferior border—inguinal folds, anterior perineum; lateral borders—mid-axillary lines.

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Rituximab

Topicals
Topical/intralesional corticosteroids

Topical nitrogen mustard

Topical bexarotene

Topical imiquimod

Chemotherapy

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