*National Imaging Associates, Inc.	
Clinical Guideline: **NON-HODGKIN'S LYMPHOMA**	**Original Date: June 2013**
Radiation Oncology	**Last Revised Date: May 2023**
Guideline Number: NIA_CG_133	**Implementation Date: January 2024**

GENERAL INFORMATION

- *It is an expectation that all patients receive care/services from a licensed clinician. All appropriate supporting documentation, including recent pertinent office visit notes, laboratory data, and results of any special testing must be provided. If applicable: All prior relevant imaging results and the reason that alternative imaging cannot be performed must be included in the documentation submitted.*
- *Where a specific clinical indication is not directly addressed in this guideline, medical necessity determination will be made based on widely accepted standard of care criteria. These criteria are supported by evidence-based or peer-reviewed sources such as medical literature, societal guidelines and state/national recommendations.*

INDICATIONS FOR RADIATION THERAPY AND TREATMENT OPTIONS:

Three-dimensional conformal radiation therapy (3D-CRT) or two-dimensional (2D) radiation therapy (2D) is the appropriate technique for treatment of Non-Hodgkin's Lymphomas. The following include radiation dose guidelines for the following lymphomas:

- Definitive Radiation:
    - Follicular lymphoma (24-30 Gy, or 36 Gy if bulky) up to 24 fractions[1-3]
        - Mantle cell lymphoma (24-36 Gy) up to 24 fractions[1-3]
        - MALT lymphoma – Marginal Zone (24-30 Gy) up to 20 fractions[1-3]
            - Gastric: 24-30 Gy up to 20 fractions
            - Orbital and Salivary Gland: 4Gy in 2 fractions for selected patients (e.g., elderly, patients with Sjogren syndrome, otherwise 24 Gy up to 16 fractions
        - Diffuse large B cell lymphoma (30-55 Gy) up to 37 fractions[1,3]
            - Consolidation after chemotherapy:
                - CR (Deauville 1-3): 30-36 Gy up to 20 fractions
                - PR (Deauville 4): 36-50 Gy up to 28 fractions
                - Refractory Disease (Deauville 4-5): 40-55 Gy up to 31 fractions
            - Primary treatment (without chemoimmunotherapy): 40-55 Gy up to 30 fractions

        - In combination with hematopoietic cell transplantation: 20-36 Gy up to 24 fractions depending on sites of disease and prior RT exposure
        - Prophylactic testicular irradiation: 25-30 Gy up to 20 fractions
    - Primary cutaneous anaplastic large cell lymphoma[4]:
        - Consolidation after chemotherapy CR: 30-36 Gy up to 24 fractions
        - Complementary after PR: 30-50 Gy up to 28 fractions
        - Primary treatment for refractory or non-candidates for chemotherapy: 40-55 Gy up to 31 fractions
        - In combination with hematopoietic cell transplantation: 20-36 Gy up to 24 fractions depending on sites of disease and prior RT exposure
        - Hypofractionation for older patients and unfavorable prognosis: 12 Gy in 6 fractions, 8 Gy in 2 fractions both cautiously depending on the volume of the disease
    - NK/T Lymphoma[4]
        - Primary treatment: 50-55 Gy up to 31 fractions
        - Combined modality: 45-56 Gy up to 32 fractions
        - Combined modality (non-asparaginase-based):
            - Sequential 45-50.4 Gy up to 28 fractions
            - Sandwich: 56 Gy up to 32 fractions
            - Concurrent
                - 50 Gy up to 28 fractions in combination with DeVIC
                - 50-54 Gy up to 30 fractions in combination with Cisplatin followed by VIPD
    - Localized chronic lymphocytic leukemia (CLL) and Small Lymphocytic Lymphoma (SLL): 24-30 Gy up to 17 fractions[5]
- Palliative dose (up to 10 fractions) for symptom control
    - FL/MZL/MCL/SLL: 4 Gy in 1-2 fractions maybe repeated as needed, doses up to 30 Gy in 10 fractions may be appropriate in select circumstances (e.g., tumors ≥ 6cm, SUV ≥ 10)
    - DLBCL/HGBL/PMBL/Gray zone lymphoma with Burkitt lymphoma: 20-30 Gy up to 10 fractions
    - NK/T lymphoma: 20-36 Gy up to 18 fractions
    - AIDS-related B-cell lymphomas and PTLD: based on underlying histologic subtype and treatment intent

Unless otherwise indicated, standard radiation fractionation consists of 1.5 Gy to 2.0 Gy per day. [1-3]

Total Skin Electron Beam Therapy (TSEBT)

A variety of techniques, using electron beam, may be utilized to cover the entire cutaneous surface.

- Dosage Guidelines:

- 8-36 Gy, 1- 2 Gy per fraction, 4-5 days per week, up to 36 fractions. "Shadowed" areas may need to be supplemented with individual electron fields. Individual tumors may be boost with doses of 4-12 Gy

TREATMENT OPTIONS (WILL BE REVIEWED ON A CASE-BY-CASE BASIS)

Intensity modulated radiation therapy (IMRT)[6]

IMRT is not indicated as a standard treatment option and should not be used routinely for the delivery of radiation therapy for non-Hodgkin's lymphoma. IMRT is strictly defined by the utilization of inverse planning modulation techniques. IMRT may be appropriate for limited circumstances in which radiation therapy is indicated and 3D conformal radiation therapy (3D-CRT) techniques cannot adequately deliver the radiation prescription without exceeding normal tissue radiation tolerance, the delivery is anticipated to contribute to potential late toxicity, or tumor volume dose heterogeneity is such that unacceptable hot or cold spots are created.

Clinical rationale and documentation for performing IMRT rather than 2D or 3D-CRT treatment planning and delivery will need to:

- Demonstrate how 3D-CRT isodose planning cannot produce a satisfactory treatment plan (as stated above) via the use of patient-specific dose volume histograms and isodose plans.
- Provide tissue constraints for both the target and affected critical structures.

Stereotactic Body Radiation Therapy[7]

Stereotactic Body Radiation Therapy (SBRT) is not currently a routine treatment option for the treatment of Hodgkin's lymphoma. SBRT may be appropriate for patients with tumors arising in or near a previously irradiated region to minimize risk to surrounding normal tissues.[7] If requested, this would require peer to peer review to determine medical necessity.

Proton Beam Radiation Therapy

Proton beam is not an approved treatment option for Non-Hodgkin's Lymphoma. Proton beam has not been proven superior treatment to conventional radiation therapy.

THE FOLLOWING APPLIES TO CMS (MEDICARE) MEMBERS ONLY:

For Proton Beam and Stereotactic Radiotherapy, refer to Local Coverage Determination (LCD), if applicable.

BACKGROUND

The incidence of non-Hodgkin's lymphomas has increased substantially over the past few decades due to age-related disease. The majority of non-Hodgkin's lymphoma originates in B-lymphocytes (80-85%)

with T-lymphocytes comprising 15-20%. Natural killer cell lymphomas are very rare. The classification of non-Hodgkin's lymphoma is based on the cell of origin (large B, large T, or large NK), precursor or mature lymphocytes, as well as genetic, immunophenotype, and clinical features. Radiation therapy is typically delivered to the involved field either alone or in consolidation following chemotherapy. CT-based simulation and 3-dimensional planning is typically advised.

The use of intensity modulated radiation therapy, as well as stereotactic body radiotherapy would be unusual. If requested, this would require peer to peer review to determine medical necessity. For nodal sites, radiation therapy alone or consolidation following chemotherapy should treat the involved field in most cases. Regional/ extended fields are typically not recommended.

REFERENCES

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): B-Cell Lymphomas Version 5.2022. National Comprehensive Cancer Network (NCCN). Updated July 12, 2022. Accessed December 6, 2022. https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf
2. American College of Radiology. ACR Appropriateness Criteria®: Diffuse Large B Cell Lymphoma. Updated 2014. Accessed December 6, 2022. https://acsearch.acr.org/docs/3091906/Narrative
3. American College of Radiology. ACR Appropriateness Criteria®: Localized Nodal Indolent Lymphoma. Updated 2013. Accessed December 6, 2022. https://acsearch.acr.org/docs/3082846/Narrative
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): T-Cell Lymphomas Version 2.2022. National Comprehensive Cancer Network (NCCN). Updated March 7, 2022. Accessed December 6, 2022. https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf
5. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 1.2023. National Comprehensive Cancer Network (NCCN). Updated August 30, 2022. Accessed December 10, 2022. https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf
6. Hartford AC, Palisca MG, Eichler TJ, et al. American Society for Therapeutic Radiology and Oncology (ASTRO) and American College of Radiology (ACR) Practice Guidelines for Intensity-Modulated Radiation Therapy (IMRT). *Int J Radiat Oncol Biol Phys*. Jan 1 2009;73(1):9-14. doi:10.1016/j.ijrobp.2008.04.049
7. American Society for Radiation Oncology. Model Policies: Stereotactic Body Radiation Therapy. American Society for Radiation Oncology (ASTRO). Updated June 2020. Accessed December 6, 2022, https://www.astro.org/ASTRO/media/ASTRO/Daily%20Practice/PDFs/ASTROSBRTModelPolicy.pdf

POLICY HISTORY

Date	Summary
May 2023	Clarified/updated radiation doses: • Definitive Radiation: ○ Follicular lymphoma (24-30Gy, or 36Gy if bulky) up to 24 fractions[1] ▪ Mantle cell lymphoma (24-36Gy) up to 24 fractions[1] ▪ MALT lymphoma – Marginal Zone (24-30Gy) up to 20 fractions[1] • Gastric: 24-30Gy up to 20 fractions • Orbital and Salivary Gland: 4Gy in 2 fractions for selected patients (e.g., elderly, patients with Sjogren syndrome, otherwise 24Gy up to 16 fractions ▪ Diffuse large B cell lymphoma (30-55Gy) up to 37 fractions[1] • Consolidation after chemotherapy: ○ CR (Deauville 1-3): 30-36Gy up to 20 fractions ○ PR (Deauville 4): 36-50Gy up to 28 fractions ○ Refractory Disease (Deauville 4-5): 40-55Gy up to 31 fractions • Primary treatment (without chemoimmunotherapy): 40-55Gy up to 30 fractions • In combination with hematopoietic cell transplantation: 20-36Gy up to 24 fractions depending on sites of disease and prior RT exposure • Prophylactic testicular irradiation: 25-30Gy up to 20 fractions ▪ Primary cutaneous anaplastic large cell lymphoma : • Consolidation after chemotherapy CR: 30-36Gy up to 24 fractions • Complementary after PR: 30-50Gy up to 28 fractions • Primary treatment for refractory or non-candidates for chemotherapy: 40-55Gy up to 31 fractions • In combination with hematopoietic cell transplantation: 20-36Gy up to 24 fractions depending on sites of disease and prior RT exposure • Hypofractionation for older patients and unfavorable prognosis: 12Gy in 6 fractions, 8Gy in 2 fractions both cautiously depending on the volume of the disease ▪ NK/T Lymphoma • primary treatment: 50-55Gy up to 31 fractions • combined modality: 45-56Gy up to 32 fractions • combined modality (non-asparaginase-based: ○ Sequential 45-50.4Gy up to 28 fractions ○ Sandwich: 56Gy up to 32 fractions

	○ Concurrent ▪ 50Gy up to 28 fractions in combination with DeVIC ▪ 50-54Gy up to 30 fractions in combination with Cisplatin followed by VIPD ▪ Localized chronic lymphocytic leukemia (CLL) and Small Lymphocytic Lymphoma (SLL): 24-30Gy up to 17 fractions • Palliative dose (up to 10 fractions) for symptom control ○ FL/MZL/MCL/SLL: 4Gy in 1-2 fractions maybe repeated as needed, doses up to 30Gy in 10 fractions may be appropriate in select circumstances (e.g., tumors ≥ 6cm, SUV ≥ 10) ○ DLBCL/HGBL/PMBL/Gray zone lymphoma with Burkitt lymphoma: 20-30Gy up to 10 fractions ○ NK/T lymphoma: 20-36Gy up to 18 fractions ○ AIDS-related B-cell lymphomas and PTLD: based on underlying histologic subtype and treatment intent • Deleted Additional Resources • Changed "Treatment options requiring physician review" to Treatment Options (will be reviewed on a case-by-case basis)
January 2022	Added Total Skin Electron Beam Therapy (TSEBT) along with dosage guidelines

Reviewed / Approved by NIA Clinical Guideline Committee

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