

Lymphoma

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at <http://www.cms.gov> for additional information.

Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

DISCUSSION

Lymphoma is a cancer of the lymphatic system. The lymphatic system includes the lymph nodes, spleen, thymus gland, and bone marrow.¹ Lymphoma can affect all these areas as well as other organs throughout the body. Many types of lymphoma exist, and they are generally classified as either Hodgkin Lymphoma (HL) or Non-Hodgkin Lymphoma (NHL).¹

Hodgkin lymphoma is a cancer of the lymph system and is diagnosed by the identification of a characteristic cell under the microscope, the Reed-Sternberg cell. HL typically begins in the lymph nodes in one region of the body and then spreads through the lymph system in a predictable manner. Hodgkin lymphoma is a curable cancer for most patients with combination chemotherapy, targeted therapy, and/or radiation therapy. Mortality for HL has fallen more rapidly than for any other cancer over the last five decades.²

In 2022, an estimated 8,540 people will be diagnosed with HL disease in the United States, and 920 people will die. In 2019, it was estimated that 218,740 people were living with HL, and both men and women have the same 0.2% chance of being diagnosed with HL. Most patients are diagnosed between ages 15 and 35 years, followed by adults aged 55 and older.^{2,3}

According to the American Cancer Society (ACS), radiation therapy is used as part of the treatment for HL disease. The ACS classifies HL into two main types: classic Hodgkin lymphoma (cHL) and nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL). cHL accounts for 95% of the HL cases.²

Classic Hodgkin Lymphoma

Classic Hodgkin lymphoma accounts for approximately 95% of cases of Hodgkin lymphoma and is diagnosed when characteristic abnormal lymphocytes, known as Reed-Sternberg cells, are identified in the biopsy.² CHL is divided into four subtypes: nodular sclerosis Hodgkin, lymphocyte-rich classical Hodgkin lymphoma, mixed cellularity Hodgkin lymphoma, and lymphocyte-depleted Hodgkin lymphoma.

Nodular Lymphocyte-Predominant Hodgkin Lymphoma (NLPHL)

NLPHL represents approximately 5% of all HL and it often develops in the lymph nodes in the neck, groin, or armpit in younger patients. It is more like B-cell non-Hodgkin lymphoma and has characteristic “popcorn cells” or “LP cells” that have a marker called CD20 on their surface. NLPHL is often treated differently from cHL.²

Non-Hodgkin Lymphoma (NHL)

NHL is a general term for about 30 different types of lymphoma that differ from HL.³ Diffuse large B-cell lymphoma and follicular lymphoma are among the most common subtypes of NHL. NHL is eight times more common than HL. The American Cancer Society expects 80,470 people will be diagnosed with the disease in 2022.² Since the 1970s, the number of people with NHL has doubled.³ All types of NHL are treatable, and many are curable. NHL is usually treated with chemotherapy, biologic therapy, and/or radiation therapy. In some types of NHL, a stem cell transplant may be part of treatment.³

The most common treatment for lymphoma includes chemotherapy, radiotherapy, immunotherapy, stem cell transplant, and in rare cases, surgery.⁴ Chemoimmunotherapy, that is, rituximab, in combination with chemotherapy, is most used. Radiation is the main treatment for early-stage (I, II). Stage II with bulky disease, stage III, and IV are treated with chemotherapy along with immunotherapy, targeted therapy, and in some cases, radiation therapy.⁴

Radiation is typically delivered with photons. Results from studies have shown that significant dose reduction to organs at risk can be achieved with advanced radiation therapy planning including intensity-modulated radiation therapy (IMRT) and image-guided radiation therapy (IGRT). Involved site radiation therapy and involved node radiation are being used as alternatives to involved field radiation. Involved site radiation targets the originally involved nodal sites and is generally a smaller field than used historically. The optimized treatment plan for involved site radiation therapy (ISRT) is designed using conventional 3D conformal RT, or IMRT techniques.⁵

DEFINITIONS

- **External beam radiation therapy (EBRT)** - External radiation (or external beam radiation) is the most common type of radiation therapy used for cancer treatment. A machine is used to aim high-energy rays (or beams) from outside the body into the tumor.
- **Fractions** - A way of dividing a total dose of radiation into separate doses to be administered over a period of time.
- **Gray (Gy)** - One of the two units used to measure the amount of radiation absorbed by an object or person, known as the absorbed dose. One gray (Gy) is the international system of units (SI) equivalent of 100 rads, which is equal to an absorbed dose of 1 Joule/kilogram.
- **Image-guided radiation therapy (IGRT)** - Image-guided radiation therapy (IGRT) is the use of imaging during radiation therapy to improve the precision and accuracy of treatment delivery. IGRT is used to treat tumors in areas of the body that move, such as the lungs. Radiation therapy machines are equipped with imaging technology to allow your doctor to image the tumor before and during treatment. By comparing these images to the reference images taken during simulation, the patient's position and/or the radiation beams may be adjusted to target the radiation dose more precisely to the tumor. To help align and target the radiation equipment, some IGRT procedures may use fiducial markers, ultrasound, MRI, X-ray images of bone structure, CT scan, 3D body surface mapping, electromagnetic transponders, or colored ink tattoos on the skin.
- **Intensity-modulated radiotherapy (IMRT)** - Intensity-modulated radiation therapy (IMRT) is an advanced mode of high-precision radiotherapy that uses computer-controlled linear accelerators to deliver precise radiation doses to a malignant tumor or specific areas within the tumor. IMRT allows the radiation dose to conform more precisely to the three-dimensional shape of the tumor by controlling the intensity of the radiation beam in multiple small volumes. IMRT also allows higher radiation doses to be focused to regions within the tumor while minimizing the dose to surrounding normal critical structures.

- **Intraoperative radiation therapy (IORT)** - Intraoperative radiation therapy is radiation therapy that is administered during surgery directly in the operating room. Usually, therapeutic levels of radiation are delivered to the tumor bed while the area is exposed during surgery.
- **National Comprehensive Cancer Network® (NCCN®)** - An alliance of 32 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.
- **Stereotactic body radiation therapy (SBRT)** - Treatment outside the brain is called stereotactic body radiation therapy (SBRT). SBRT may be used for certain lung, spine, and liver tumors.
- **Volumetric modulated arc therapy (VMAT)** - Volumetric modulated arc therapy (VMAT) is an advanced form of intensity-modulated radiotherapy (IMRT) that delivers a targeted three-dimensional dose of radiation to a tumor in one or more treatments.

POLICY

The following table outlines the criteria that must be met for the number of fractions and dosing relative to Non-Hodgkin Lymphoma cancer radiation treatments. The following dosing table represents evidence-based doses and fractions for the designated type of cancer treatment. Variations outside of the ranges may indicate a deviation from standard treatment.

Non-Hodgkin Lymphoma			
	Number of Fractions	Total Dose	Technique
Definitive EBRT	12-24	24-36 Gy	3D, IMRT, IGRT
Consolidation EBRT	15-33	30-50 Gy	3D, IMRT, IGRT
Refractory Disease EBRT	20-36	40-55 Gy	3D, IMRT, IGRT
Palliative EBRT	1-10	4-30 Gy	3D, IMRT, IGRT

The following table outlines the criteria that must be met for the number of fractions and dosing relative to Hodgkin Lymphoma cancer radiation treatments. The below dosing table represents evidence-based doses and fractions for the designated type of cancer treatment. Variations outside of the ranges may indicate a deviation from standard treatment.

Hodgkin Lymphoma			
	Number of Fractions	Total Dose	Technique
Involved- Site Radiation Therapy (ISRT) Non- Bulky (Combined Modality)	10-20	20-30 Gy	3D, IMRT, IGRT
Involved- Site Radiation Therapy (ISRT) Bulky (Combined Modality)	15-24	30-36 Gy	3D, IMRT, IGRT
Partial Response to chemo	18-25	36-45 Gy	3D, IMRT, IGRT
Palliative EBRT	1-10	4-30 Gy	3D, IMRT, IGRT

REFERENCES

1. Lymphoma - Hodgkin - Introduction. Cancer.net. <https://www.cancer.net/cancer-types/lymphoma-hodgkin/introduction>. Accessed May 16, 2022.
2. What is Hodgkin lymphoma? American Cancer Society. <https://www.cancer.org/cancer/hodgkin-lymphoma/about/what-is-hodgkin-disease.html>. Accessed May 16, 2022.
3. Lymphomas – RTAnswers.Org. ASTRO. <https://www.rtanswers.org/Cancer-Types/Lymphomas>. Accessed May 16, 2022.

4. Sumina Sapkota, Shaikh H. Non-Hodgkin Lymphoma. Nih.gov. <https://www.ncbi.nlm.nih.gov/books/NBK559328/>. Accessed May 16, 2022.
5. Getting external beam radiation therapy. American Cancer Society. <https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/radiation/external-beam-radiation-therapy.html>. Accessed May 20, 2022.
6. Radiation therapy for Hodgkin lymphoma. American Cancer Society. <https://www.cancer.org/cancer/hodgkin-lymphoma/treating/radiation.html>. May 20, 2022.
7. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Hodgkin Lymphoma (Version 2.2022). Available at https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf. ©National Comprehensive Cancer Network, 2022.

Please see all related radiation therapy treatment policies for additional information on the treatment modalities. (3D-CRT, EBRT, IGRT and IMRT)

CODING [ICD-10, HCPCS]*

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, codes listed are not a guarantee of payment. CPT codes are available through the AMA.

Code	Description
C81.02	Nodular lymphocyte predominant Hodgkin lymphoma, intrathoracic lymph nodes
C81.12	Nodular sclerosis Hodgkin lymphoma, intrathoracic lymph nodes
C81.22	Mixed cellularity Hodgkin lymphoma, intrathoracic lymph nodes
C81.32	Lymphocyte depleted Hodgkin lymphoma, intrathoracic lymph nodes
C81.42	Lymphocyte-rich Hodgkin lymphoma, intrathoracic lymph nodes
C81.72	Other Hodgkin lymphoma, intrathoracic lymph nodes
C81.92	Hodgkin lymphoma, unspecified, intrathoracic lymph nodes
C82.02	Follicular lymphoma grade I, intrathoracic lymph nodes
C82.12	Follicular lymphoma grade II, intrathoracic lymph nodes
C82.22	Follicular lymphoma grade III, unspecified, intrathoracic lymph nodes
C82.32	Follicular lymphoma grade IIIa, intrathoracic lymph nodes
C82.42	Follicular lymphoma grade IIIb, intrathoracic lymph nodes
C82.52	Diffuse follicle center lymphoma, intrathoracic lymph nodes
C82.62	Cutaneous follicle center lymphoma, intrathoracic lymph nodes
C82.82	Other types of follicular lymphoma, intrathoracic lymph nodes
C82.92	Follicular lymphoma, unspecified, intrathoracic lymph nodes
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.12	Mantle cell lymphoma, intrathoracic lymph nodes
C83.32	Diffuse large B-cell lymphoma, intrathoracic lymph nodes
C83.52	Lymphoblastic (diffuse) lymphoma, intrathoracic lymph nodes
C83.72	Burkitt lymphoma, intrathoracic lymph nodes
C83.82	Other non-follicular lymphoma, intrathoracic lymph nodes
C83.92	Non-follicular (diffuse) lymphoma, unspecified, intrathoracic lymph nodes
C84.02	Mycosis fungoides, intrathoracic lymph nodes

Code	Description
C84.12	Sézary disease, intrathoracic lymph nodes
C84.42	Peripheral T-cell lymphoma, not classified, intrathoracic lymph nodes
C84.62	Anaplastic large cell lymphoma, ALK-positive, intrathoracic lymph nodes
C84.72	Anaplastic large cell lymphoma, ALK-negative, intrathoracic lymph nodes
C84.92	Mature T/NK-cell lymphomas, unspecified, intrathoracic lymph nodes
C84.A2	Cutaneous T-cell lymphoma, unspecified, intrathoracic lymph nodes
C84.Z2	Other mature T/NK-cell lymphomas, intrathoracic lymph nodes
C85.12	Unspecified B-cell lymphoma, intrathoracic lymph nodes
C85.22	Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes
C85.82	Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes
C85.92	Non-Hodgkin lymphoma, unspecified, intrathoracic lymph nodes
G6015	Intensity modulated treatment delivery, single or multiple fields/arcs, via narrow spatially and temporally modulated beams, binary, dynamic MLC, per treatment session
G6016	Compensator-based beam modulation treatment delivery of inverse planned treatment using 3 or more high resolution (milled or cast) compensator, convergent beam modulated fields, per treatment session
G0339	Image-guided robotic linear accelerator-based stereotactic radiosurgery, complete course of therapy in one session or first session of fractionated treatment
G0340	Image-guided robotic linear accelerator-based stereotactic radiosurgery, delivery including collimator changes and custom plugging, fractionated treatment, all lesions, per session, second through fifth sessions, maximum 5 sessions per course of treatment
Z92.3	Personal history of irradiation

REVISION AND REVIEW HISTORY

No.	Description	Metadata
1	Original Effective Date:	5/2022
2	Policy Review Dates:	5/20/2022, 5/24/2022, 6/2/2022, 7/20/2022
3	Policy Revision Dates:	5/20/2022, 5/24/2022, 6/2/2022, 7/20/2022
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval Dates:	5/24/2022, 6/2/2022
6	Revision Changes:	