Hematopoietic and Lymphoid Neoplasm Coding Manual

Effective with Cases Diagnosed 1/1/2010 and Forward

Published October 2025

Editors: **Jennifer Ruhl, MSHCA, RHIT, CCS, ODS-C (NCI SEER)**
Carolyn Callaghan, ODS-C (SEER Seattle Registry)
Tiffany Janes, ODS-C (SEER Seattle Registry)
Suzanne Adams, BS, ODS-C (IMS)

Suggested citation: **Ruhl J, Callaghan C, Janes T, Adams S (October 2025). Hematopoietic and Lymphoid Neoplasm Coding Manual. National Cancer Institute, Bethesda, MD, 2025.**

Forward
by Jennifer Ruhl, NCI SEER (Manager for the Hematopoietic Manual and Database)

Hello everyone,

Welcome to the updated version of the Hematopoietic Manual. The last time the Hematopoietic manual had a significant update was in 2014. This update is long overdue. In preparation for this update, I came up with an idea for a complete overhaul of the manual. New look and everything. My trusted reviewers, Carolyn Callaghan and Tiffany Janes from Seattle, didn't like it. So, back to the drawing board.

Then I sent out a request for comments to the SEER registries. I received comments from representatives at many registries. Illinois sent 3 dense pages of comments. The first look at Illinois' comments I was ranting (in my head) and fussing. It was a bit overwhelming. The next morning, after I calmed down, I was able to review their comments and formulate a plan. Other comments, which were numerous and excellent, were easier to get through.

Illinois comments had my brain running in circles for several days. How was I going to incorporate some of their excellent comments and suggestions without exploding the manual, or adding any new rules? Even though this was going to be a major update, there were no plans to delete any of the current rules or modules, or add any. The rules as they are do work. The problem that registrars are having is that they are in the Heme Manual and DB so rarely that it's hard for them to become familiar with the rules (one of the comments that Iowa made). You just don't have the repetition of cases like you do with breast, prostate, colon and rectum, lung, and a few others. This is a problem that doesn't really have a solution.

So, where did Illinois comments take me? The "Steps for Using the Heme DB and Hematopoietic Coding Manual" got quite the overhaul. I don't know if this is what they imagined, but it's where I ended up. There are two tables that have been added, one for the M rules, and one for the PH rules. These are "roadmaps" to the rules, and hopefully will help you navigate through the rules more easily. Other sections that got an overhaul include Multiple Primaries Calculator, Transformations, Treatment, and Primary Site instructions.

Lots of formatting changes, and some rewording, additional comments, but the overall content is the same.

The Hematopoietic database has been updated based on the WHO Blue Book 5th edition of Hematolymphoid tumors. There are many new terms (See Appendix E).

Hope you find these updates helpful.

In Remembrance

SEER would like to take this opportunity to remember our colleague Carol Hahn Johnson, who worked for the SEER program, retired in 2012 and died December 2023. Carol was the brains and power behind the development of the Hematopoietic Manual and Database. Even after her retirement in 2012, she continued to provide assistance when asked and was instrumental in Jennifer Ruhl taking over managing the Hematopoietic manual and database.

In Appreciation

SEER would also like to take this opportunity to acknowledge the contributions of Lois Dickie, ODS-C and Peggy Adamo, ODS-C to the development of the Hematopoietic Manual and Database in 2010.

NCI SEER gratefully acknowledges the dedicated work of Drs, Charles Platz and Graca Dores since the inception of the Hematopoietic project. We deeply appreciate their willingness to serve as advisors for the rules within this manual for many years. The quality of this Hematopoietic project is directly related to their commitment.

NCI SEER would also like to acknowledge the following individuals who continue to provide support to all the SEER products through their working on SEER*Educate.

- Carolyn Callaghan, ODS-C (SEER Seattle Registry)
- Tiffany Janes, ODS-C (SEER Seattle Registry)

We would also like to give a special thanks to the following individuals at Information Management Services, Inc. (IMS) who provide us with document support and web development.

- Sean Brennan, BS
- Asya Melkonyan, MA
- Paul Stephenson, BS
- Jacob Tomlinson, BS

To our wonderful SEER Registries, many of whom provided excellent feedback on the Hematopoietic manual, we would like to express our sincere thanks. Their continued support of our efforts to provide comprehensive manuals for the registry community are greatly appreciated.

Dedication

The Hematopoietic and Lymphoid Neoplasm Coding Manual (Heme manual) and the companion Hematopoietic and Lymphoid Neoplasm Database (Heme DB) are dedicated to the hard-working cancer registrars across the world who meticulously identify, abstract, and code cancer data. Cancer registrars are the foundation for statewide, provincial, territorial, national, and international cancer surveillance programs which support cancer prevention and cancer control efforts worldwide.

A huge thank you to the registrars who submitted questions to Ask a SEER Registrar which resulted in changes to the manual and database.

Education

SEER*Educate provides training on how to use the Heme Manual and DB.

Questions about the Hematopoietic Manual and Database are to be sent to Ask a SEER Registrar - SEER Registrars. **Under Reporting Guidelines** choose Hematopoietic Rules (database and manual)

Notes for Use

Use this manual and the corresponding database to abstract and code cases diagnosed **January 1, 2010,** and forward.

Please note that these rules are for cancer registries and **are not followed by physicians**.

- Follow the rules as stated in this manual and abstract the number of primaries based on the rules. These rules were developed to provide standardized instructions on how to code multiple primaries, histology and primary site across the United States and Canada.
- **This may, or may not, agree with what the physician indicates in the patient record**.
- Physician interpretation can sometimes factor into determining reportability, diagnostic confirmation, or primary site; this is addressed in the specific coding instructions for those sections.

For cases diagnosed 2010+, use the current version of the Hematopoietic Manual found on the SEER website. Year based instructions will be noted in the manual and the database. Hematopoietic Project - SEER Registrars

Previous Releases

2010 Hematopoietic Coding Manual and Database (Effective dates 1/1/2010+)

- Release date: March 2010, Version 1.4 (initial release)
- Release date: April 2010, Version 1.5
- Release date: June 2010, Version 1.6
- Release date: May 4, 2012, Version 2.1
- Release date: May 23, 2012, Version 2.1
- Release date: February 25, 2013, Version 2.2
- Release date: January 2014
- Release date: January 2015
- Release date: May 2018
- Release date: January 2019
- Release date: September 2020
- Release date: August 2021
- Release date: November 2024

Please note: The SEER Training Website manual modules for Hematopoietic have also been updated

- Hematopoietic Module, Part I
- Hematopoietic Module, Part II

Contents

Revision History: 2026 Revisions

Hematopoietic Manual

1. No new modules or rules, no modules or rules deleted.
2. Overhaul of structure (content not changed).
3. New definitive terminology for assigning histology (See Histology Coding Instructions, #3)
4. New section introducing Hematopoietic neoplasms (overview of all the groups, lineage tables).
5. Overhaul of several sections, including Steps for Using the Heme Manual and DB, Multiple Primaries Calculator, Transformations, Primary site coding instructions (introduction, not the PH rules), and Treatment.
6. New section added for Coding Mets at Dx fields for Hematopoietic neoplasms.
7. Clarifications added on when and how to code histology based on positive immunophenotyping or genetics.
8. Updated lineage tables based on the WHO Blue Book, 5th edition for Hematolymphoid Tumors (2024).
9. Primary site assignments for each of the histologies have been removed from the Heme manual. This information is in the Heme DB.
10. Grade rules removed. The grade rules are no longer applicable for Heme neoplasms. For cases diagnosed prior to 2018, you can use the Heme DB to help assign grade. Make sure "Help me code for diagnosis year" is 2010-2017.
11. New examples added (courtesy of Ask a SEER Registrar questions).
12. New Appendix E: List of terms added to the Hematopoietic Database from the WHO 5th edition of Hematolymphoid Neoplasms.

Heme Database

1. New terms from the WHO Blue Book, 5th edition for Hematolymphoid Tumor (2024) added (see Appendix E: Terms added to the Hematopoietic Database from the WHO 5th edition of Hematolymphoid Tumors for a complete list)
2. Immunophenotyping and genetics updated based on the WHO Blue Book, 5th edition for Hematolymphoid Tumor. Only the most common immunophenotyping and genetics are included.
3. Definitive diagnosis field redone for all histologies (note: field previously included procedures, which were removed).
4. Abstractor notes updated based on the WHO Blue Book, 5th edition for Hematolymphoid Tumor (2024).
5. Definitions updated based on the WHO Blue Book, 5th edition for Hematolymphoid Tumor (2024).
6. Grade field hidden for cases diagnosed 2018+. For cases diagnosed prior to 2018 use "Help me code for diagnosis year" field and change the year to 2017.
7. Same primaries changed for Acute Lymphoblastic Leukemias (9811-9819). Any combination of these histologies is the same primary.
8. ICD-O-1 and ICD-O-2 fields were hidden for all diagnosis years.
9. ICD-9-CM field hidden for cases diagnosed 2015+. ICD-10-CM codes updated (when applicable).
10. Resources updated

For previous revisions, see Revision History for the Hematopoietic Project - SEER Registrars

Many of the revisions are based on questions submitted to Ask a SEER Registrar. Selected questions and answers from Ask a SEER Registrar are posted in SEER Inquiry System (SINQ), which is updated on a regular basis.

Introduction and Background

The Hematopoietic Working Group was led by the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI) and included members from many professional organizations: the National Cancer Registrars Association (NCRA), the North American Association of Central Cancer Registries (NAACCR), the National Program of Cancer Registries (NPCR) of the Centers for Disease Control and Prevention (CDC), the Commission on Cancer (CoC) of the American College of Surgeons (ACoS), and the Canadian Cancer Registries (CCR). The Working Group also included cancer registrars who work independently (contractors), hospital registrars, central cancer registry registrars, and clinical and research physicians who are experts in the hematopoietic and lymphoid neoplasm fields.

This working group has developed rules, guidelines and an interactive desktop Heme DB reference to assist registrars in determining case reportability, the number of primaries, as well as instructions for coding primary site, histology, grade, diagnostic confirmation and other therapy for a hematopoietic and/or lymphoid neoplasm. The rules, guidelines, and the Hematopoietic DB follow the *World Health Organization (WHO) Classification of Tumours of Haematopoietic and Lymphoid Tissues*, 4th Edition, 2008, also called the "WHO Blue Book." Both the *International Classification of Diseases for Oncology (ICD-O)* and the series of Blue Books are produced by the World Health Organization (WHO), but the content of the books are very different. Each has a prominent place in the oncology world.

The original ICD-O, the ICD-O-2, and the ICD-O-3 provide standard primary site and histology codes for specific benign, borderline, and malignant conditions. The ICD-O series also provides generic "not otherwise specified" or "NOS" codes for some conditions so registrars are able to code cases that have limited information, such as death-certificate-only cases and historic cases. When ICD-O assigns a code to a specific histology, the original code is rarely changed. The intent is that the code should never change; for example, code 8140/3 for adenocarcinoma, NOS has remained unchanged since the first edition of ICD-O. The ICD-O manuals are the standard for coding neoplasms throughout the world. To preserve the integrity of historical data and to allow for comparison of data over time, it is imperative that standard codes remain unchanged. Although the stability of these codes is necessary to interpret data over time, that process has some less-than-desirable results. When the clinical world reclassifies diseases to reflect the current state of science and knowledge about a particular disease or condition, that disease will remain in the same numeric position in ICD-O. When the ICD-O editors assign new codes for a neoplasm, the new code may not be placed in the desired category because there may not be room within that category to add a new code. An example of this problem is the placement of the non-Hodgkin lymphomas that were first added in ICD-O-3.

The WHO Blue Books, by contrast, are histo-pathology reference books used by pathologists and oncologists throughout the world. The Blue Books are revised and published when new information is available. The *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*, 4th Edition, a collaborative project of the Society for Hematopathology/European Association for Hematopathology was published in 2008. The reference includes new disease classifications, changes to existing classifications and cell lineages, and new conditions that reflect the state-of-the-science for these neoplasms. This reference was the primary source of information used to develop the *2010 Hematopoietic and Lymphoid Neoplasm Case Reportability and Coding Manual,* the *2012 Hematopoietic Coding Manual,* and the accompanying Hematopoietic DB as the WHO Blue Book is periodically updated with the current classification by cell lines or lineages and classification groupings. Using the WHO classifications gives the registrar reference material that is clinically relevant and compatible with current pathology reports and medical records. When the clinical field finds specific tumor markers, immunohistochemical testing, genetic testing, or other characteristics that define or refine a diagnosis or a particular histology, the WHO Blue Books introduce proposed new codes for new or more specific histologies, and these new histologies may be grouped or classified in categories based on information about the phenotype or behavior of the neoplasm.

Note: The WHO is the directing and coordinating authority for health within the United Nations system. It is responsible for providing leadership on global health matters, shaping the health research agenda, setting norms and standards, articulating evidence-based policy options, providing technical support to countries and monitoring and assessing health trends. (From http://www.who.int/about/en/)

The *Hematopoietic and Lymphoid Neoplasm Coding Manual* and Heme DB are designed to help the registrar understand and interpret the information written by pathologists and clinicians. The Heme DB will be updated as needed to ensure that the registrar has the most current information available to interpret and code a hematopoietic or lymphoid neoplasm.

The classification of the leukemias and lymphomas can be confusing because of the variety of cell types involved, the site of origin of the neoplastic process (bone marrow, lymph node, GI tract, etc.), and the relative frequency or infrequency of tumor cells circulating in the peripheral blood.

Leukemia and lymphoma are terms that reflect the primary behavior and often the site of a neoplasm. Leukemias have cells circulating in the peripheral blood, which can originate in lymph nodes or the marrow. Lymphomas generally form solid masses in lymph nodes or organs containing lymphoid tissue; they may occasionally have circulating tumor cells as well.

Leukemias and lymphomas may also be defined as being chronic or acute. Chronic neoplasms are of longer duration and are slowly progressive while acute neoplasms are of shorter duration and rapidly progressing.

Some examples of chronic and acute neoplasms include (not a complete list)

Cell Type	Chronic	Acute
Lymphocyte	Chronic lymphocytic leukemia/small lymphocytic leukemia (CLL/SLL); follicular lymphoma	Lymphoblastic leukemia (T or B cell); diffuse large B-cell lymphoma, plasma cell myeloma
Granulocyte	Chronic myeloid leukemia	Acute myeloid leukemia
Erythrocyte	Polycythemia vera	Acute erythroid leukemia
Megakaryocytic	Essential thrombocythemia	Acute megakaryocytic leukemia

Leukemias and Lymphomas

One of the differences between leukemia and lymphoma is that leukemia most commonly presents in the bone marrow and/or blood while lymphoma most commonly manifests in lymph nodes, lymphoid tissue, or lymphoid organs. When only the bone marrow is involved, the diagnosis is usually leukemia. Although rare, a lymphoma may present only in the bone marrow. (See PH rules, Modules 6 and 7, for instructions on coding primary site for lymphomas.)

Both leukemia and lymphoma patients may have splenomegaly (enlargement of the spleen). Patients with leukemia may have leukemic infiltrate of the spleen. Splenomegaly does not mean that the leukemia originated in the spleen or that this neoplasm is lymphoma. The spleen filters and stores blood cells. The spleen involvement is usually secondary, much like metastases in solid tumors. The rare histologies that are primary in the spleen are identified in the Heme DB. The Primary Site will be listed as C422.

Leukemias

Diagnostic Process for Leukemia

For most patients, the first suspicion or presentation of a hematopoietic neoplasm will be symptoms such as unexplained weight loss, weakness, chronic fatigue, easy bruising, etc. When the physician suspects leukemia, he/she usually orders a complete blood count (CBC) and/or a peripheral blood smear. The CBC will identify abnormalities of the platelets, hemoglobin, white blood cells or red blood cells. When an abnormality is identified in the blood cell analysis, a bone marrow (BM) biopsy is usually the next procedure.

The CBC or bone marrow alone seldom provide a definitive diagnosis; however, the results usually provide one or more provisional diagnoses such as: myeloproliferative neoplasms, myeloid neoplasms, myelodysplastic/myeloproliferative neoplasms, myelodysplastic syndromes, or leukemia. These non-specific diagnoses are differential or provisional. More testing is needed to identify the specific hematopoietic or lymphoid neoplasm. Follow back on these cases should be done.

Many of the neoplasms in the 2024 WHO 5th edition classification require immunophenotyping or genetic information to identify the specific histology. The Heme DB contains information on the types of diagnostic tests that are used to identify the specific histology for the hematopoietic or lymphoid neoplasm being abstracted. See the “Definitive Diagnostic Method” section in the Heme DB.

Leukemia cutis

Leukemia cutis is a rare manifestation of leukemia characterized by infiltration of malignant leukocytes into the skin (epidermis, dermis, or subcutis), producing visible, clinically recognizable lesions. Leukemia cutis may precede, follow, or occur concurrently with the diagnosis of systemic leukemia. It is an advanced phase of the leukemia having a poor prognosis that also strongly correlates with additional sites of extramedullary involvement. This can alter the appropriate treatment regimen for a patient. It is a type of "metastasis" or spread of the leukemia cells.

The "conventional" definition for leukemia cutis is the infiltration of skin from a bone marrow primary. It is most often diagnosed via skin biopsy—punch, shave, etc., utilizing IHC/biomarker testing and is commonly associated with chronic myelomonocytic leukemia (CMML) and acute myeloid leukemia (AML). As such, it a reportable condition especially when preceding a confirmed systemic leukemia diagnosis.

In rare cases, the leukemia cutis is diagnosed and there is no history of AML, and bone marrow biopsy is either not done or comes back negative. In this situation, the diagnosis date would be the date of the positive leukemia cutis skin bx—punch, shave, etc. The case should be coded to C421; 9800/3 Leukemia NOS until the official systemic leukemia diagnosis is rendered. If possible, follow back should be conducted to determine the specific systemic leukemia histology (CMML; AML) and the treatment received. If the leukemia cutis follows or occurs **concurrently** with the diagnosis of a systemic leukemia, it is NOT a separate primary but merely an advanced stage of the systemic leukemia diagnosis

Lymphomas

Biopsies
The most accessible involved lymph node or site is usually biopsied when lymphoma is suspected. For example, if a CT or PET scan identified enlarged cervical and mediastinal lymph nodes, the physician would biopsy the cervical lymph nodes because that would be the least invasive procedure; i.e. the cervical nodes are more accessible than the mediastinal nodes. Do **not** assume that the more accessible site chosen for biopsy is the primary site. Follow the primary site rules and instructions when coding Primary Site.

Hodgkin Lymphoma

A cancer of the immune system that is marked by the presence of a type of cell called the Reed-Sternberg cell. The two major types of *Hodgkin* lymphoma are classical *Hodgkin* lymphoma and nodular lymphocyte-predominant *Hodgkin* lymphoma. Symptoms include the painless enlargement of lymph nodes, spleen, or other immune tissue. Other symptoms, which are called B-symptoms, include fever, weight loss, fatigue, or night sweats.

See Table B16: Hodgkin lymphoma for a complete listing of Hodgkin lymphomas.

Non-Hodgkin Lymphoma
Non-Hodgkin lymphoma (NHL) comprises a diverse group of malignant neoplasms which include all lymphomas other than Hodgkin. NHL arises in lymphocytes (a type of white blood cell). Lymphocytes are present in lymph nodes and in lymphoid tissue throughout the body. NHL occurs in extranodal sites including tonsils, spleen, ileum (Peyer's patches), stomach, Waldeyer ring (WR), bone marrow, skin, bone, central nervous system, lung, gonads, conjunctiva, ocular adnexa, liver, kidneys, and uterus.

See Table B15: Mature B-cell neoplasms and Table B20: Mature T-cell and NK-cell neoplasms for a complete listing of non-Hodgkin lymphomas.

Hematopoietic Diseases

There are 5 major groupings for the Hematopoietic neoplasms per the 5th edition of WHO Blue Book for Hematolymphoid Tumors (2024). Presentation of these diseases will depend on the neoplasm. Below is a brief description of the different Hematopoietic groupings from the WHO Blue Book, 5th edition of Hematolymphoid Tumors. See Appendix B for a complete listing of histologies by their lineage table, or see the Hematopoietic Database for more information on the specific neoplasms.

1. Myeloid proliferations and neoplasms

Disease Group	Definition	Lineage Table
Myeloid precursor lesions	Clonal hematopoiesis is a broad term that is applicable to numerous entities. Several terms were introduced to describe clonality detected in people without a diagnosed hematological disorder. These are usually incidental findings.	Table B1: Myeloid precursor lesions (Not reportable)
Myeloproliferative neoplasms	Category of myeloid neoplasms characterized by excessive production of mature whole blood cells, erythrocytes, and/or platelets. This category is distinct from myelodysplastic/myeloproliferative neoplasms by virtue of the absence of myelodysplasia at presentation.	Table B2: Myeloproliferative neoplasms (MPNs)
Mastocytosis	Hematogenous diseases characterized by the accumulation of abnormal mast cells in various organs or tissues.	Table B3: Mastocytosis
Myelodysplastic neoplasms (MDN)	Previously myelodysplastic syndromes (MDS) Category of clonal hematopoietic stem cell neoplasms, defined by cytopenias and morphological dysplasia, and clinically characterized by progressively ineffective hematopoiesis and an increased risk of acute myeloid leukemia (AML).	Table B4: Myelodysplastic neoplasms
Myelodysplastic/ myeloproliferative neoplasms (MDS/MPN)	Category of myeloid neoplasms defined by overlapping pathological and molecular features of myelodysplastic neoplasms (MDSs) and myeloproliferative neoplasms (MPNs), often manifesting clinically with various combinations of cytopenias and cytoses. The definition of cytopenias is the same as that for MDS.	Table B5: Myelodysplastic/ myeloproliferative (MDS/MPN)
Acute Myeloid Leukemia (AML)	AML is a heterogenous group of blood cancers that result from clonal expansion of myeloid hematopoietic precursors in the bone marrow. Not only are circulating leukemia cells (also called blasts) seen in the peripheral blood, but granulocytopenia, anemia, and thrombocytopenia are also common as proliferating leukemia cells interfere with normal hematopoiesis.	Table B6: Acute myeloid leukemia
Secondary neoplasms	Myeloid neoplasms that arise secondary to exposure to cytotoxic therapy or germline disposition are grouped in this category.	Table B7: Secondary myeloid neoplasms
Myeloid/lymphoid neoplasms	Includes myeloid and lymphoid neoplasms driven by rearrangements involving genes encoding specific tyrosine kinases leading to fusion products in which the kinase domain is constitutively activated, resulting in cell signaling dysregulation that promotes proliferation and survival.	Table B8: Myeloid/lymphoid neoplasms

Disease Group	Definition	Lineage Table
Acute leukemias of mixed or ambiguous terminology	Leukemias composed of > 20% abnormal progenitors that do not show differentiation along a single lineage.	Table B9: Acute leukemias of mixed or ambiguous lineage

2. Histiocytic/Dendritic Cell Neoplasms

Disease Group	Definition	Lineage Table
Histiocytic/Dendritic Cell Neoplasms	Tumors originating from or showing differentiation towards cells of the mononuclear phagocyte system, which comprise monocytes, macrophages, and dendritic cells. The term "histiocyte" has been variable defined, either being equated with the macrophage or encompassing both the macrophage and the dendritic cell. There are 3 subgroups.	Table B10: Plasmacytoid dendritic cell neoplasms Table B11: Langerhans cell and other dendritic cell neoplasms Table B12: Histiocyte/macrophage neoplasms

3. B-cell lymphoid proliferations and lymphomas

The term "B-cell lymphoproliferative disorder" is used to describe both non-clonal and clonal expansions of B cells. Normal B-cell development begins in the bone marrow, with a hematopoietic stem cell (HSC) giving rise to a pro-B-cell, which later develops into an immature B cell via a pre-B-cell stage. These B-cell precursors, also known as B lymphoblasts, undergo immunoglobulin (IG) gene rearrangement and differentiate into mature but antigen-naïve B cells expressing surface immunoglobulin.

Disease Group	Definition	Lineage Table
Tumor-like lesions with B-cell predominance	Diseases are rich in B cells, and could be considered in the differential diagnosis of lymphoma, but that do not represent lymphoid neoplasms. These are included for the first time in a WHO edition. These are not reportable.	Table B13: Tumor like lesion with B-cell predominance (Not reportable)
Precursor B-cell neoplasm	Neoplasms of precursor lymphoid cells committed to the B-cell lineage, involving bone marrow and usually peripheral blood, and often involving nodal or extranodal sites.	Table B14: Precursor B-cell neoplasms
Mature B-cell lymphomas	Mature B-cell lymphomas includes the lymphoma that originate from the B-cells. The lymphomas are separated in indolent (i.e. CLL or SLL) or aggressive lymphomas (i.e. DLBCL)	Table B15: Mature B-cell neoplasms
Hodgkin lymphomas	Type of lymphoma originating in lymphocytes (a type of white blood cell). HL is characterized by the presence of Reed-Sternberg cells (RS cells) on microscopic examination	Table B16: Hodgkin lymphoma
Plasma cell neoplasms and other diseases with paraproteins	A number of conditions produce paraproteins or M proteins, which are either monoclonal intact immunoglobulins, light chains, or occasionally heavy chains or misfolded immunoglobulins that are deposited. The conditions range from mature B-cell neoplasms to plasma cell neoplasms.	Table B17: Plasma cell neoplasms and other diseases with paraproteins

4. T-cell and NK-cell lymphoid proliferations and Lymphomas

This group of diseases represent a broad spectrum of entities that range from non-clonal proliferations to highly aggressive lymphomas. They can arise in a variety of anatomical locations. Thirty-six distinct T-cell and NK-cell entities are recognized in this edition.

Disease Group	Definition	Lineage Table
Tumor-like lesions with T-cell predominance	These are T-cell lymphoid proliferations.	Table B18: Tumor-like lesions with T-cell predominance Not reportable
Precursor T-cell neoplasms	Neoplasms of precursor lymphoid cells committed to the T-cell lineage, involving bone marrow and usually peripheral blood, and often involving nodal or extranodal sites.	Table B19: Precursor T-cell neoplasms
Mature T-cell and NK-cell neoplasms	The category of mature T-cell and NK-cell leukemias includes six entities representative of T- and NK-cell proliferations that primarily present as leukemic disease. They are T-prolymphocytic leukemia, T-large granular lymphocytic leukemia (T-LGLL), NK-large granular lymphocytic leukemia (NK-LGLL), adult T-cell leukemia/lymphoma, Sézary syndrome, and aggressive NK-cell leukemia.	Table B20: Mature T-cell and NK-cell neoplasms

5. Stroma-derived neoplasms of lymphoid tissues

Disease Group	Definition	Lineage Table
Mesenchymal dendritic cell neoplasms	Follicular dendritic ell and fibroblastic reticular cell neoplasms have been moved from the "histiocytic and dendritic cell neoplasms" category to this new category, because follicular dendritic cells and fibroblastic reticular cells are not derived from hematopoietic stem cells but are of mesenchymal origin.	Table B21: Mesenchymal dendritic cell neoplasms

First Course of Treatment for Hematopoietic Neoplasms

Treatment varies by the type of hematopoietic neoplasm.

Lymphomas can be treated with surgery (extranodal or nodal), chemotherapy, radiation, hormones and immunotherapy, while leukemias are often treated with chemotherapy, immunotherapy and bone marrow/stem cell transplants. In addition, immunotherapy (biologic response modifiers) and hormones are frequently used to treat hematopoietic and lymphoid neoplasms. Also, for many of these diseases, the principal treatment is either supportive care, observation, or another type of treatment that does not meet the usual definition of treatment that "modifies, controls, removes or destroys proliferating cancer tissue."

Starting in 2010, some neoplasms that have undergone a transformation are reported as new primaries (see rules M10-M13 for specific instructions), and treatment can affect this. For purposes of determining multiple primaries in the Hematopoietic diseases, "treatment" refers to the patient receiving at least one form of cancer-directed treatment such as surgery or systemic therapy, not passive treatment plans like supportive care or observation.

There are three main phases for treatment of Hematopoietic neoplasms, specifically leukemias. These phases may differ based on the histology, age of the patient, risk factors and comorbidities.

1. **Induction**
   The goal of induction therapy is to get the leukemia to go into remission. This is achieved by finding no leukemia cells in a bone marrow biopsy. Induction is not a cure as there may still be leukemia cells in the body. Induction chemotherapy usually last for a month. Several different treatment regimens may be used during this phase to achieve remission.

2. **Consolidation/Intensification**
   If remission is achieved through the induction phase, another phase of chemotherapy is given. This phase usually includes the same drugs that were given for the induction phase. This phase usually lasts for several months. Drugs are given in high doses, and the treatment is fairly intense. During this phase patients may also have a bone marrow or stem cell transplant

3. **Maintenance**
   Maintenance therapy can last up to two years.

4. **Palliative therapy**
   This type of therapy is given to patients whose treatments have failed to achieve remission. At this phase, the main goal is controlling the cancer and its symptoms, rather than to cure it.

Coding Instructions for Treatment

1. When there is only one neoplasm (one primary), use the documented first course of therapy (treatment plan) from the medical record. **First course of therapy ends when the treatment plan is completed or remission is achieved, no matter how long it takes to complete the plan.**
   - ***Example 1***: Patient clinically diagnosed with plasma cell myeloma. The patient begins treatment. Several months later treating physician states that levels are still high, that the treatment plan is changed. This is still first course treatment since remission has not been achieved. The statement that "levels are still high," is stating that the first group of drugs were not working. This is not progression.
   - ***Example 2:*** Patient diagnosed with leukemia. Patient had induction therapy but did not achieve complete remission. Disease progressed and the patient received autologous stem cell transplant. This is still first course treatment since the patient had not achieved remission.
2. Chronic neoplasm followed by an acute neoplasm
   a. The presence/absence of treatment **DOES NOT** affect the number of primaries when a chronic neoplasm transforms to an acute neoplasm
   b. First course of treatment for the chronic neoplasm may or may not be completed when the chronic neoplasm transforms to the acute neoplasm.
   - ***Example****:* Patient diagnosed in 2020 with follicular lymphoma. Patient refused treatment. Patient returns in 2025 with DLBCL. Abstract the DLBCL as a second primary even though there was no treatment for the follicular lymphoma.
3. Acute neoplasm followed by a chronic neoplasm
   a. The presence/absence of treatment **DOES** impact the determination of the number of primaries when the acute neoplasm reverts to a chronic neoplasm (see Rules M12 and M13).
   b. The planned first course of therapy may not have been completed when a biopsy/pathologic specimen shows only chronic neoplasm after an initial diagnosis of an acute neoplasm.
   c. The patient may have completed the first course of treatment and have been cancer free (clinically, no evidence of the acute neoplasm) for an interim when diagnosed with the chronic neoplasm.
   d. The patient may not have been cancer free, but completed the first course of treatment and biopsy/pathology shows only chronic neoplasm.
4. Code the treatment on both abstracts when a patient has multiple primaries and the treatment given for one primary also affects/treats the other primary.
   - ***Example***: Patient is diagnosed in May 2025 with both multiple myeloma (9732/3) and mantle cell lymphoma (9673/3), which are separate primaries per rule M15. The oncologist states she began Velcade chemotherapy for the lymphoma. Velcade would affect both primaries, so it should be coded on both abstracts.

Reporting Phlebotomy, Blood-Thinners/Anti-Clotting Medications, and Transfusions as Other Therapy (NAACCR Item #1420)

Note: These instructions apply to cases diagnosed 2010 and forward.

Do **not** collect **blood transfusions** (whole blood, platelets, etc.) as treatment. Blood transfusions are widely used to treat anemia, and it is not possible to collect this procedure in a meaningful way.

Collect **phlebotomy ONLY** for polycythemia vera (9950/3).

Collect **blood-thinners** and/or **anti-clotting agents ONLY** for essential thrombocythemia (9962/3).

Previously, instructions stated that blood thinners and/or anti-clotting agents were also collected for certain histologies. Review of current treatment protocols for these histologies shows that these are no longer defined as treatment for the histologies listed below. This change is effective for cases diagnosed 1/1/2010 and forward; however, there is no requirement to change cases already abstracted

- 9740/3 Mast cell sarcoma
- 9741/3 Systemic mastocytosis with an associated hematological neoplasm
- 9742/3 Mast cell leukemia
- 9875/3 Chronic myeloid leukemia *BCR-ABL1*-positive
- 9950/3 Polycythemia vera
- 9961/3 Primary myelofibrosis
- 9963/3 Chronic neutrophilic leukemia
- 9975/3 Myelodysplastic/myeloproliferative neoplasm, unclassifiable

Donor Leukocyte Infusions

The use of donor leukocyte infusions for treatment of hematopoietic neoplasms, specifically leukemias, is increasing. Abstract as immunotherapy when a reportable hematopoietic neoplasm is treated with donor leukocyte infusion, even if it is not listed in the treatment section of the Heme DB for the specific neoplasm. See the Glossary for Registrars for a definition of donor leukocyte infusions.

Coding Diagnostic Confirmation (NAACCR Item #490)

Peripheral Blood Smears

Peripheral blood smears are commonly done when there is a suspected blood or bone marrow disorder. Peripheral blood smears can be used to diagnosis a hematopoietic neoplasm. Flow cytometry is frequently done with the peripheral blood smear tissue.

Immunophenotyping and Genetics

The immunophenotyping and genetics information in the Hematopoietic Database are to be used **only to code the data item diagnostic confirmation**. They are **not to be used by registrars to assign a more specific histology**. Registrars are to record the diagnosis provided on the pathology report or stated by the managing physician.

Codes for Hematopoietic and Lymphoid Neoplasms (9590/3-9993/3)

Microscopically Confirmed

Code	Description
1	Positive histology Includes: peripheral blood smear only
2	Positive cytology
3	Positive histology PLUS: • Positive immunophenotyping AND/OR • Positive genetic studies Includes: peripheral blood smear followed by flow cytometry (***Effective for cases diagnosed 1/1/2010 and later)***
4	Positive microscopic confirmation, method not specified

Not Microscopically Confirmed

Code	Description
5	Positive laboratory test/marker study ***Note 1***: Includes cases with positive immunophenotyping or genetic studies and ***no*** histological confirmation ***Note 2:*** This does **not** include cases where a peripheral blood smear is done (code 1) and peripheral blood smear followed by flow cytometry (code 3)
6	Direct visualization without microscopic confirmation
7	Radiology and other imaging techniques without microscopic confirmation
8	Clinical diagnosis only (other than 5, 6 or 7)

Confirmation Unknown

Code	Description
9	Unknown whether or not microscopically confirmed; death certificate only

Diagnostic Confirmation Coding Instructions for Hematopoietic and Lymphoid Neoplasms (9590/3-9993/3)

1. **Hierarchical order**
   Other than microscopic confirmation (1-4) taking priority over clinical diagnosis only (5-8), there is no priority order or hierarchy for coding the diagnostic confirmation for hematopoietic or lymphoid neoplasms. Most commonly the bone marrow biopsy provides several provisional diagnoses, and the specific histologic type is determined through immunophenotyping or genetic testing.

2. **Diagnostic confirmation code 1**
   - Coded when ONLY tissue, bone marrow, or blood was used to diagnose the specific histology
     - Use code 1 for peripheral blood smears
   - Do not use code 1 if the provisional diagnosis was based on tissue or bone marrow, and the final diagnosis was based on positive genetics or immunophenotyping that identified a specific hematopoietic neoplasm (see code 3)

3. **Original diagnosis confirmed by histology, later has positive genetics and immunophenotyping**
   If a neoplasm is originally confirmed by histology (code 1), and later has immunophenotyping, genetic testing or JAK2 which confirms a more specific neoplasm, **and the specific histology is confirmed/documented by the pathologist/managing physician** and there is no evidence of transformation, change the histology code to the more specific neoplasm and change the diagnostic confirmation to code 3.
   - See Histology Coding Instructions, Note 6 for more information on assigning histology when there is positive immunophenotyping or genetics.

Diagnostic confirmation codes

Code 1: Positive histology

Code 1 includes a provisional diagnosis and/or several provisional (differential) diagnoses which may or may not be preceded by approved ambiguous terminology. Includes the following

- **Hematopoietic histologies (9590/3-9993/3)**
  - Tissue from lymph node(s), organ(s) or other tissue specimens from biopsy, frozen section, surgery, or autopsy
  - Bone marrow specimens (aspiration and biopsy)
  - IHC studies are done, but the patient has a provisional (NOS) diagnosis or one or more provisional diagnoses
  - Peripheral blood smear
    - CLL/SLL (9823/3) is commonly diagnosed via peripheral blood smear. Flow cytometry will be done, which will provide the diagnosis.
  - Historical cases not already in the database if information states that there was histologic confirmation

- **Leukemia** only (9800/3-9948/3)
  - Positive histology also includes complete blood count (CBC) or white blood count (WBC)
    - A registrar may **NOT** abstract a hematopoietic neoplasm based on a CBC or WBC with abnormal counts alone. **There must be a diagnosis of a reportable Heme neoplasm by the managing physician based on the CBC or WBC report.**
    - If immunophenotyping, genetic testing, or JAK2 is done and positive, see code 3
      - Code 1 is applicable if immunophenotyping, genetic testing, or JAK2 are done and not diagnostic, or if unknown if these were done
  - ***Example 1:*** Bone marrow biopsy positive for plasma cell neoplasm. Medical oncologist states plasma cell myeloma based on the bone marrow biopsy.
  - ***Example 2:*** Acute myelomonocytic leukemia (9867/3) CD7 negative. CD7 positive is listed under Immunophenotyping for this histology in the hematopoietic database and this case is CD7 negative, so diagnostic confirmation should be 1.
  - ***Example 3:*** Peripheral Smear Review: Atypical lymphocytosis. Comments state macrocytosis, consistent with chronic lymphocytic leukemia
  - ***Example 4:*** Peripheral smear demonstrated lymphocytosis with no obvious abnormalities. This is consistent with CLL.
  - ***Example 5:*** Bone marrow positive for plasma cell neoplasm. Medical oncologist states plasma cell myeloma based on the bone marrow biopsy
  - ***Example 6:*** Patient diagnosed in 2025 with Stage III mantle cell lymphoma, diagnosed by LN biopsy. Mantle cell lymphoma not in the database. Now presents with DLBCL

Code 2: Positive cytology

Code 2 is rarely used for Hematopoietic and Lymphoid neoplasms, but would include the following

- Examination of fluid such as spinal fluid, peritoneal fluid, or pleural fluid
- Paraffin block specimens from concentrated spinal fluid, peritoneal fluid, or pleural fluid
- A specimen that fails to provide enough tissue to do a histologic examination-in this case, the report will be a cytology report rather than a pathology report

Code 3: Positive histology PLUS positive immunophenotyping or genetic testing

Code 3 can be used for cases diagnosed **2010+** with histologic confirmation (see code 1) **AND** immunophenotyping, genetic testing, or JAK2 confirmation

- Certain histologies will ALWAYS have a diagnostic confirmation code 3. These ICD-O codes/terms are defined by genetics, meaning the only way they can be diagnosed is through genetic testing.
    - The following histologies are diagnosed based on immunophenotyping or genetics and therefore should only be diagnostic confirmation 3: 9806/3, 9807/3, 9808/3, 9809/3, 9812/3, 9813/3, 9814/3, 9815/3, 9816/3, 9817/3, 9818/3, 9819/3, 9865/3, 9866/3, 9869/3, 9871/3, 9877/3, 9878/3, 9879/3, 9896/3, 9897/3, 9911/3, 9912/3, 9965/3, 9966/3, 9967/3, 9968/3, 9986/3.

- Histologies that are NEVER confirmation code 3
  The following histologies should never be assigned diagnostic confirmation 3 since they are non-specific codes and neither genetic testing or immunophenotyping are listed as Definitive Diagnostic Methods for these histologies in the Hematopoietic database: 9590/3, 9655/3, 9800/3, 9820/3, 9860/3, 9863/3, 9975/3, 9980/3, 9982/3, 9989/3, 9991/3.
    - If there is immunophenotyping or genetics available, then a more specific histology code may be able to be assigned

- **2026 updates**
  The immunophenotyping and genetics sections were redone. Only the **most common** immunophenotyping and genetics were included.

  If immunophenotyping or genetics are used by the pathologist/managing physician to identify and document a **specific** neoplasm and specific immunophenotyping or genetics are not included in the Hematopoietic database **AND** cytogenetics/genetic testing and/or immunophenotyping/immunohistochemistry are listed as Definitive Diagnostic methods for that histology, go ahead and use these to code diagnostic confirmation code 3.

  Note that just because a marker may be listed in the immunophenotyping or genetics fields, it does not mean that one marker is confirming the diagnosis. For many of the neoplasms, especially the B-cell lymphomas, there is a wide range of immunophenotyping results that are shared. Genetics are the more definitive way to identify or confirm a specific neoplasm.

- **Assign code 3 for**
    - Cases with positive histology for the neoplasm being abstracted (including acceptable ambiguous terminology and provisional diagnosis) **AND** immunophenotyping, genetic testing, or JAK2 are listed as Definitive Diagnosis methods in the Hematopoietic Database
        - **AND** the testing confirms the neoplasm **OR**
        - Pathologist/managing physician Identifies a more specific histology (not preceded by ambiguous terminology)
    - NOS histology diagnosed and not a provisional diagnosis and genetics/immunophenotyping was performed and pathologist/managing physician identifies a more specific histology

- Peripheral blood smear followed by flow cytometry (most commonly done with CLL/SLL, 9823/3) and pathologist/managing physician identifies a more specific histology
    - Flow cytometry studies are normally done based on an abnormal blood smear. If unable to find documentation that a peripheral blood smear was done first, assume that it was and code 3

Do <u>not</u> use code 3 for positive immunophenotyping or genetic testing identifying a more specific histology when a test result is proceeded by

- **Ambiguous terminology**
- **Patchy weak staining**

- ***Example 1 (identifying a specific histology)***: Peripheral blood flow cytometry report: Flow cytometry express HLA-DR, CD5, CD19, moderate CD20, CD22, bright CD45, bright CD200 and exhibit lambda immunoglobin light chain restriction by intracellular staging. These cells lack expression of CD38. Taken together, these results demonstrate the presence of a clonal population of B-cell, immunophenotypically diagnostic of CLL/SLL.

- ***Example 2 (Identifying a more specific histology):*** Bone marrow biopsy positive for acute myeloid leukemia (9861/3). Genetic testing positive for AML with inv (16) (p13.1q22) (9871/3). Code Diagnostic Confirmation code 3, positive histology and positive genetic testing, which identified a more specific histology.

- ***Example 3 (Identifying a more specific histology):*** Peripheral blood smear with lymphoblastic lymphoma (9671/3). Bone marrow biopsy with immunophenotyping showing CD5 negative and IgM positive, diagnosis Waldenstrom Macroglobulinemia (9761/3). Code Diagnostic Confirmation code 3, positive histology and positive immunophenotyping testing which identified a more specific histology.

- ***Example 4 (confirming the histologic diagnosis):*** Bone marrow biopsy diagnosis is plasma cell dyscrasia. Peripheral blood smear is compatible with plasma cell leukemia. FISH and chromosome analysis revealed plasma cell myeloma. Both plasma cell leukemia and plasma cell myeloma are coded to the same ICD-O code, 9732/3, so there is only one disease process. The peripheral blood smear is histologic diagnosis for plasma cell leukemia and FISH confirmed the diagnosis of multiple myeloma/plasma cell myeloma per pathologist. Code diagnostic confirmation 3, positive histology and positive genetic testing.

- ***Example 5 (Histologic confirmation plus genetic and immunophenotyping confirmation):*** Patient diagnosed with CLL by CBC and flow cytometry that was positive for both the genetic and CD antigens (immunophenotyping) for CLL per pathologist. A bone marrow biopsy was not performed. Since this is leukemia, the CBC is histologic confirmation, so this patient had histologic confirmation, genetic, and immunophenotyping positive for CLL. Code diagnostic confirmation 3, positive histology and positive genetic testing/immunophenotyping.

- ***Example 6 (ambiguous terminology used with immunophenotyping):*** Bone marrow biopsy shows B lymphoblastic leukemia. Abnormal FISH results most likely represent a hyperdiploid clone. Code the histology to 9811/3 (B-ALL, NOS) and assign a diagnostic confirmation code of 1. Neither diagnostic confirmation code 3 nor the specific hyperdiploidy histology is coded because the associated FISH result is preceded by ambiguous terminology.

- ***Example 7 (updating diagnostic confirmation code)*****:** Patient presented to physician for annual exam and noted to be anemic. An electrophoresis was done, which showed the Bence-jones protein. A bone marrow biopsy was done which was non-diagnostic. Based on the electrophoresis, physician diagnosed patient with early stage multiple myeloma (diagnostic confirmation code 8). Patient monitored for several years and then was noted to have increasing bone pain. Skeletal survey was done which showed osseous lesions. A repeat bone marrow biopsy was done, which was diagnostic of plasma cell myeloma, confirmed by immunophenotyping per pathologist. Based on this finding, the diagnostic confirmation code should be changed from an 8 to a 3.

Code 4: Positive microscopic confirmation, method not specified

Code 4 is rarely used for Hematopoietic and Lymphoid neoplasms.

- Assign code 4 when there is information that the diagnosis of cancer was microscopically confirmed, but the type of confirmation is unknown

Code 5: Positive laboratory test/marker study

Assign code 5 when the diagnosis of cancer is based on laboratory tests, tumor marker studies, genetics or immunophenotyping that are diagnostic for that specific cancer as listed under Definitive Diagnostic Methods in the Hematopoietic Database.

- Common laboratory test include Bence-Jones protein or SPEP for multiple myeloma
- Common genetic marker JAK2 is used for Myeloproliferative neoplasms (Table B2: Myeloproliferative neoplasms (MPNs)

Do not use this code when there is a histological confirmation, which includes a peripheral blood smear is done (which qualifies for a code 1), or a peripheral blood smear followed by flow cytometry (which may qualify for a code 3). Flow cytometry studies are normally done based on an abnormal peripheral blood smear. If unable to find documentation that a peripheral blood smear was done first, assume that it was and code 3

- ***Example 1:*** CT scan consistent with plasma cell myeloma (9732/3). Twenty-four-hour urine protein elevated with the presence of Bence-Jones kappa. Assign code 5 because the diagnosis is based on the positive Bence-Jones and there is no histologic confirmation in this case. Bence-Jones protein is a lab test listed in the Heme DB as one of the definitive diagnostic methods for plasma cell myeloma.
- ***Example 2:*** There is no histological examination; however, a JAK2 is done, which is positive for ET. Assign code 5 because the diagnosis is based on the positive JAK2 and there is no histological confirmation in this case. JAK2 is listed as genetics in the Heme DB and genetics are listed as a definitive diagnosis method for Essential Thrombocythemia.
- ***Exception:*** Patient only had a JAK2 which was positive, but there was no indication positive for what. Physician later stated in his impression that the patient probably had Polycythemia Vera and treated as such. **Diagnostic Confirmation 5 cannot be used in this situation since the JAK2 only stated positive, NOS and the physician's clinical diagnosis is preceded by ambiguous terminology.** Since the diagnosis was made by the physician clinically, the diagnostic confirmation would be coded to 8.

Code 6: Direct visualization without microscopic confirmation

- Code 6 is rarely used for Hematopoietic and Lymphoid neoplasms, includes the following
  - Operative report states the patient had lymphoma, but no biopsy or cytology was done
  - The diagnosis is determined by gross autopsy findings (no tissue or cytologic confirmation)

Code 7: Radiology and other imaging techniques without microscopic confirmation

- Code 7 is rarely used for Hematopoietic and Lymphoid neoplasms, includes the following
    - The diagnosis is confirmed by radiology or other imaging techniques only
        - ***Example***: Terminally ill patient who has a CT scan with the impression: suspicious for lymphoma. The patient refused further workup.

Code 8: Clinical diagnosis only (other than 5, 6, or 7)

While clinical diagnosis is seldom used for solid tumors, it is a valid diagnostic method for certain hematopoietic neoplasms. Clinical diagnoses are generally made when all the workup (biopsy, flow cytometry, immunophenotyping, genetics) don't point to a specific hematopoietic neoplasm.

Code 8 includes the following situations

- The Heme DB will list Clinical Diagnosis as a definitive diagnostic method for the hematopoietic neoplasm.
- The diagnosis is determined based on the physician's clinical expertise, combined with the information from the biopsy, equivocal or negative tests, and the clinical symptoms. This is called a "diagnosis of exclusion" because the physician's judgment and the work-up literally exclude all other possible diagnoses, leaving one diagnosis. Ambiguous terminology may precede the diagnosis.
    - ***Example:*** Bone marrow biopsy shows anemia, NOS; physician notes states the patient's overall clinical presentation of hypercalcemia, fever, and anemia is consistent with Myelodysplastic Syndrome, unclassifiable (9989/3). Code Diagnostic confirmation 8, clinical diagnosis only

Code 9: Unknown whether or not microscopically confirmed; death certificate only

- Code 9 is used for the following
    - When it is unknown if the diagnosis was confirmed microscopically.
    - For death-certificate-only (DCO) cases.
    - For historical/history of cases not already in the registry database when there is no information available about the diagnostic confirmation.
        - ***Example****:* "History of follicular lymphoma in 2010, now presents with DLBCL." Follicular lymphoma not in the registry database. Assign diagnostic confirmation of 9 for the follicular lymphoma.

Transformations: Chronic and Acute Neoplasms

Transformations are defined as chronic (indolent) neoplasms that transform (change) to an acute (aggressive) neoplasm. Transformations occur within the Myeloid neoplasms and the B-cell Lymphoid neoplasms.

> ***Note:*** The use of the terms "chronic" or "acute" in the disease name (e.g., Chronic Myeloid Leukemia) does not imply that one transforms into the other. Always refer to the "Transformations to/from" fields in the Hematopoietic Database to determine transformation status.

Myeloid neoplasms

Chronic myeloid neoplasms	Acute myeloid neoplasms
Myelodysplastic syndromes (MDS)	Acute myeloid leukemia, includes all subtypes of AML
Myeloproliferative neoplasms (MPN)	
Myelodysplastic/myeloproliferative neoplasms (MDS/MPN)	

Lymphoid neoplasms

Indolent (Chronic) lymphoid neoplasms	Aggressive (Acute) lymphoid neoplasms
Chronic lymphocytic leukemia/small lymphocytic lymphoma	Diffuse Large B-cell lymphoma
Extranodal marginal zone B-cell lymphoma	
Follicular lymphoma	
Hairy cell leukemia	
Lymphoplasmacytic lymphoma	
Mantle cell lymphoma	
Splenic marginal zone lymphoma	
Plasmacytomas	Plasma cell myeloma

Only the most common transformations are listed in the Heme DB.

As a reminder, physician's use the word "transformation" differently than the cancer registry field. Follow the instructions provided in the Hematopoietic Manual and Database regarding transformations. If a physician states that a histology has transformed, yet there is no information in the "transformation to" or "transformation from" fields, do not use the Chronic/Acute rules (M8-M13).

IMPORTANT NOTE: ALWAYS REVIEW TRANSFORMATION INFORMATION BEFORE GOING TO THE M RULES.

When determining if you have multiple primaries, always check the "Transformations to" and the "Transformation from" fields in the hematopoietic database. The acute neoplasm is listed in the **"Transformations to"** section; whereas histologies listed in the **"Transformations from"** section are the chronic neoplasms.

***Case Scenario from Ask a SEER Registrar*:** Patient diagnosed from a single bone marrow biopsy with two histologies: IgG lambda ISS I Multiple Myeloma and lymphoplasmacytic lymphoma. The treating physician states "these are two separate processes, will treat the multiple myeloma (DaraDex and Velcade) and continue to monitor IgM levels for the lymphoplasmacytic lymphoma. Logically it seems like these are 2 primaries - one myeloma and one lymphoma. When I look these up in the HDB, the myeloma is an acute process while the lymphoplasmacytic lymphoma is a chronic one.

Based on Rule M8: Abstract a single primary and code the acute neoplasm when both a chronic and an acute neoplasm are diagnosed simultaneously or within 21 days and there is only one positive BM biopsy. Should M8 only refer to a chronic and acute of the same line - or is it any chronic and acute?

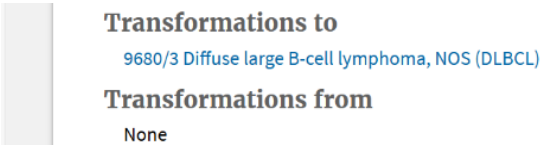
***Response**:* First, registrars are not to determine what is acute or chronic this way. Secondly, multiple myeloma is not listed as a "transformation from" in Lymphoplasmacytic lymphoma, and Lymphoplasmacytic lymphoma is not listed in the "transformations to" in Multiple Myeloma. The chronic/acute rules do not apply to this situation.

The only histologies that transform to Multiple Myeloma are the Plasmacytomas. For the lymphoplasmacytic lymphoma, it transforms only to DLBCL.

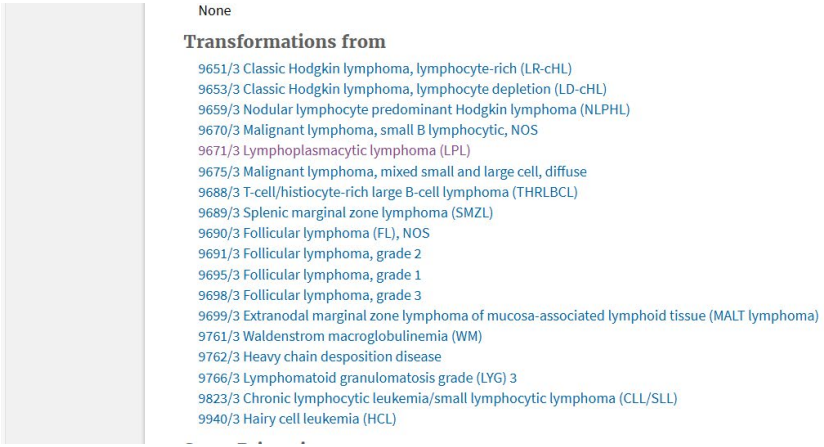
The correct rule in this case is M15, which states to use the multiple primaries calculator. That shows two primaries, which matches with the physician's statement.

Transformations to (Acute neoplasm)
If a chronic/indolent neoplasm can transform to an acute/ aggressive neoplasm, the Heme DB will show the **acute** neoplasm in the **"Transformations to"** section. For example, if you search the Heme DB for Follicular lymphoma, NOS (9690/3), the "Transformations to" section shows that Follicular lymphoma transforms to Diffuse Large B-cell lymphoma (9680/3). This indicates that Follicular lymphoma is a chronic or indolent neoplasm and Diffuse large B-cell lymphoma is an acute or aggressive neoplasm.

The Hematopoietic database snapshot here is from histology 9690/3 and shows what is included in the "transformations to" field. The NONE listed in the "transformations from" field means that there are no Hematopoietic neoplasms that transform to Follicular lymphoma.



Transformations from (Chronic neoplasm)
Information in this field is also intended to help registrars determine which histologies are chronic/indolent and which are acute/aggressive. Acute neoplasms may have multiple histologies listed in the "Transformations from" field. Histologies listed in the **"Transformations from"** field are **chronic**. For example, in the Heme DB under DLBCL, the "Transformations from" field list all the chronic (indolent) B-cell neoplasms that transform to DLBCL. This indicates that DLBCL is an acute or aggressive neoplasm, and all the B-cell neoplasms listed are chronic or indolent neoplasms.


None

Transformations from

9651/3 Classic Hodgkin lymphoma, lymphocyte-rich (LR-cHL)
9653/3 Classic Hodgkin lymphoma, lymphocyte depletion (LD-cHL)
9659/3 Nodular lymphocyte predominant Hodgkin lymphoma (NLPHL)
9670/3 Malignant lymphoma, small B lymphocytic, NOS
9671/3 Lymphoplasmacytic lymphoma (LPL)
9675/3 Malignant lymphoma, mixed small and large cell, diffuse
9688/3 T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL)
9689/3 Splenic marginal zone lymphoma (SMZL)
9690/3 Follicular lymphoma (FL), NOS
9691/3 Follicular lymphoma, grade 2
9695/3 Follicular lymphoma, grade 1
9698/3 Follicular lymphoma, grade 3
9699/3 Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma)
9761/3 Waldenstrom macroglobulinemia (WM)
9762/3 Heavy chain desposition disease
9766/3 Lymphomatoid granulomatosis grade (LYG) 3
9823/3 Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)
9940/3 Hairy cell leukemia (HCL)

If the "transformation to" AND "transformation from" fields are BOTH "**none**," then the neoplasm is **NOT a chronic or an acute neoplasm** per our rules **AND Rules M8-M13 will not apply**. Physicians may still document a transformation though.

Rules M8-M13

These rules are only for the histologies that have transformations listed in the Heme DB.

The most common form of transformation is when a neoplasm progresses from chronic to acute (Rules M8-M11); however, neoplasms may be diagnosed in an acute phase and transform to a less aggressive or indolent (chronic) phase after treatment (Rules M12-M13).

Rule M8: Single primary, both chronic and acute diagnosed in the clinical work up and there is only one biopsy

In this situation, there is one biopsy, and the diagnosis lists both neoplasms, for example, Follicular grade lymphoma 3A with presence of DLBCL, OR Myelodysplastic syndrome transforming to Acute Myeloid Leukemia. In this situation, *the acute neoplasm is coded as a single primary.*

Rule M9: Single primary, both chronic and acute diagnosed in the clinical work up and there is no documentation on biopsy

This rule very rarely applies. This type of situation may be a facility that a patient has been referred to and the diagnosis is "follicular lymphoma/DLBCL" or "MDS/AML." In this situation, *the acute neoplasm is coded as a single primary.*

- ***Note:*** *This is a change from previous instructions, which stated to code the later diagnosis. This change is based on consultation with our expert hematopathologist*

Rule M10: Multiple primaries, original diagnosis a chronic neoplasm, after initial clinical work up completed, the acute neoplasm is diagnosed
This happens commonly with indolent B-cell neoplasms and DLBCL, or MDS and AML. In this situation, the patient is initially worked up and found to have the chronic neoplasm. Treatment is determined. Then sometime later, months or even years, they are diagnosed with the aggressive neoplasm. Treatment for the chronic neoplasm does not have to be started or completed to use this rule. ***The key to this rule is that there are two biopsies confirming both diagnoses.*** In this situation, *the acute neoplasm is coded as a second primary.*

Rule M11: Multiple primaries, both chronic and acute diagnosed in the clinical work up and there are two biopsies
In this situation, a patient has two biopsies, one confirming the chronic neoplasm, the other confirming the acute neoplasm. Commonly seen with the indolent B-cell lymphomas and DLBCL. A lymph node biopsy will show follicular lymphoma, while a bone marrow biopsy will show DLBLC. In this situation, *both the chronic and acute are coded as new primaries.*

Rule M12: Single primary, original diagnosis an acute neoplasm, after initial clinical work up completed, the chronic neoplasm is diagnosed
It is possible for a patient to be diagnosed with an acute neoplasm, and then later on (after initial clinical workup is completed), be diagnosed with a chronic neoplasm. This is a rare occurrence, but it does happen. This rarely used rule deals with this situation when there is **no treatment, or it's unknown if there is treatment.** For example, patient diagnosed with AML, several months later, repeat bone marrow biopsy shows MDS; however, there is no indication of treatment. In this situation, *only the acute neoplasm is abstracted.*

Rule M13: Multiple primaries, original diagnosis an acute neoplasm, after initial clinical work up completed, the chronic neoplasm is diagnosed
This rule and M12 deal with the same situation; however, **in M13, it is known that the patient had treatment, or is currently undergoing treatment**. In this situation, *the chronic neoplasm is coded as a second primary.*

IMPORTANT NOTE: There have been several scenarios where a chronic neoplasm is diagnosed (1st primary) and then an acute neoplasm follows (2nd primary). Then the patient comes back and is diagnosed with the chronic neoplasm again. **Rules M12 and M13 do not apply to this situation. The chronic neoplasm would be the same primary based on Rule M2.**

The Hematopoietic Database (Heme DB)

The Heme DB is available online through the SEER website. Access the database at http://seer.cancer.gov/seertools/hemelymph/. An internet connection is required. Please note that the online version cannot be downloaded onto a PC or laptop.

The Hematopoietic database contains the following information

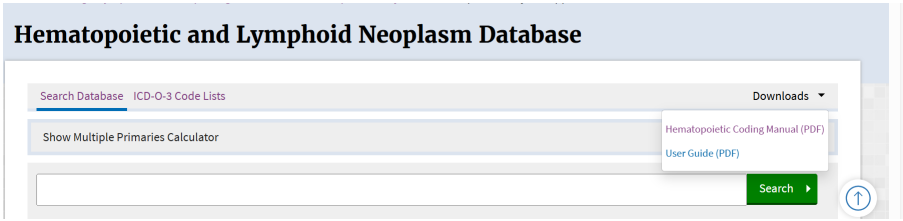
Field	Description	Comments
Name	Generated by the ICD-O-3 Morphology field	Preferred term depends on the WHO edition
ICD-O-1 Morphology	Displays historical codes	Informational only (now hidden on public website)
ICD-O-2 Morphology	Displays historical codes	Informational only (now hidden on public website)
ICD-O-3 Morphology	Displays the current ICD-O morphology code	
Reportable	Displays the reportability status	
Primary site	Displays information regarding primary site	Contains helpful information in coding primary site, note that the final primary site determination is not limited to listed sites, unless there is a default primary site (i.e., leukemias, C421)
Help me code for diagnosis year	Allows registrars to the choose the year of diagnosis for their case (drop down menu)	Defaults to the current year when you open the database
Coding Manual	Hematopoietic Coding Manual (PDF)	The Hematopoietic manual can be accessed within the Hematopoietic database
Abstractor Notes	Displays histology specific information helpful for registrars	Contains information on primary site, nuances associated with the histology, when the histology code became valid (or discontinued) and crosswalks to other codes when applicable
Diagnostic Confirmation	How was the neoplasm diagnosed	Diagnostic confirmation records how a neoplasm was diagnosed- microscopically, with or without immunophenotyping/genetics, imaging, or a physician's (clinical) diagnosis
Grade	Displays grade of the neoplasm	Only be shown for cases diagnosed prior to 2018.
Module Rule	Displays specific rules in the Hematopoietic Manual that might be relevant for the case	Not all histologies have a module rule listed, not all cases end up using the listed module rule
Alternate terms	Displays additional terms assigned to the histology code	The alternate names are based on terms from ICD-O-3 - ICD-O-3.2, and WHO 5th edition Blue Book for Hematolymphoid tumors
Definition	Displays the definition from the current WHO Blue Book	Not all histology codes are included in the WHO 5th edition

Field	Description	Comments
Definitive Diagnostic Methods	Displays the diagnostic methods used to diagnose the neoplasm	Includes cytogenetics/genetics, histologic confirmation, immunohistochemistry/ immunophenotyping, clinical diagnosis
Genetics Data	Displays genetics used in the diagnosis of the neoplasm	If a neoplasm is confirmed by positive genetics, diagnostic confirmation is 3
Immunophenotyping	Displays immunophenotyping used in the diagnosis of the neoplasm	If a neoplasm is confirmed by positive immunophenotyping, diagnostic confirmation is 3
Treatments	Displays general treatments categories	See SEER*RX for additional information
Transformations to	Displays the histology code & name of neoplasms that the neoplasm can transform to	See the Hematopoietic database for information on transformations, or review Transformations: Chronic and Acute Neoplasms
Transformations from	Displays the histology code & name of neoplasms that can transform to the neoplasm	See the Hematopoietic database for information on transformations, or review Transformations: Chronic and Acute Neoplasms
Same primaries	Displays the histology code & name of neoplasms determined to be a same primary	This information is used for Rules M7, M15, PH28, PH29
Corresponding ICD-9-CM Codes	Displays the applicable ICD-9-CM code(s) for this neoplasm	ICD-9-CM was discontinued in 2014 when ICD-10-CM was implemented. The field will only show when the date of diagnosis is prior to 2015
Corresponding ICD-10 Codes	Displays the applicable ICD- 10 code(s) for this neoplasm	These are cause of death codes. They are not the same thing as ICD-10-CM codes. These are effective 1/1/1999
Corresponding ICD-10-CM Codes	Displays applicable ICD-10-CM code(s) for this neoplasm	These are effective 1/1/2015
Signs and symptoms	Displays common symptoms for neoplasm	
Diagnostic exams	Displays common diagnostic exams and tests used in the clinical workup	
Progression/Transformation	Displays comments about progression/transformation	Source of information: Current WHO Blue Book (5th ed)
Epidemiology	Displays epidemiological information	Source of information: Current WHO Blue Book (5th ed)
Sources	Displays the sources used to populate the Hematopoietic Database	

Steps for Using the Heme DB and Hematopoietic Coding Manual

Follow each step in the order listed below:

1. **Locate the User Guide**

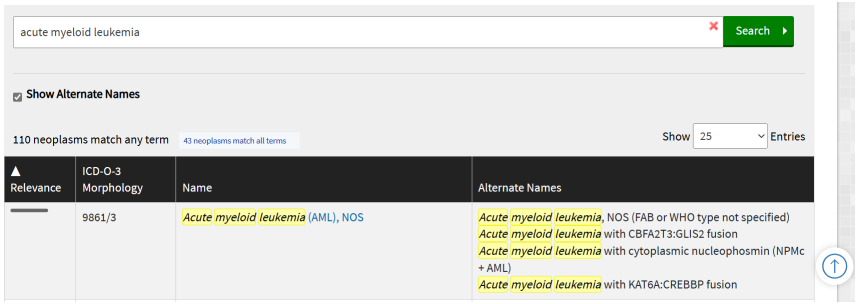


The user guide, which can be found in the upper right corner can be accessed by clicking on the "Download" button and then clicking on the "user guide." Also available from the "Download" button is the current copy of the Hematopoietic manual. A separate tab in your web browser will open up. Both the user guide and Hematopoietic manual can be downloaded as PDF's.

2. **Identify the working (preliminary) histology code(s)**
   a. Search the Heme DB using a unique word, abbreviation, or acronym
      i. Use "precursor" if the diagnosis is Precursor Acute Lymphoblastic Leukemia
      ii. Use "MECOM" if the diagnosis is Acute Myeloid Leukemia with MECOM rearrangement
      iii. Abbreviations, or acronyms can also be used. For example, using AML for acute myeloid leukemia, or CMML for chronic myelomonocytic leukemia, or DLBCL for diffuse large B-cell leukemia

   b. Avoid searching on
      i. General terms such as "leukemia" or "lymphoma." This type of search will return too many results
      ii. Complete names. For some histologies this may result in what you are looking, for others, too many results will return. For example searching on acute myeloid leukemia will return 117 terms

3. **Searching alternate names**



   a. The display of Alternate terms can be turned on by clicking the "Show Alternate Names" box as seen in the screenshot. If this box is checked, the results will include an additional column that shows where the alternate terms that include the search criteria. This function will be selected/displayed by default and will remain selected until it is turned off
   b. Below the "show alternate terms" it shows how many different ICD-O codes appear on a search. For acute myeloid leukemia, 110 names were found. The results include any term that has acute, myeloid, or leukemia. Next to that is a result showing only those ICD-O codes that include "acute myeloid leukemia," which is 43.

4. **Viewing the desired histology**
   a. Once the desired histology is found, click on the preferred terminology (third column in above screenshot).
   b. Once you are in the histology, use the database to find specific information for that neoplasm (see Table above that explains each of the fields in the database).
   c. Don't forget to check the "transformations to" and "transformations from" fields (See Transformations: Chronic Neoplasms and Acute Neoplasms for more information). **This NEEDS to be reviewed BEFORE using the M rules.**

5. **Reviewing the Hematopoietic manual**
   a. Once you retrieve all the relevant information from the Hematopoietic database, move over to the Hematopoietic manual to go through the rules.
   b. Familiarize yourself with the different sections of the Hematopoietic Manual
   c. These sections include general information on leukemias and lymphomas, different groups of Hematopoietic disease, reportability, treatment information, coding diagnostic confirmation, transformations, and how to code the Mets at Dx data items for Hematopoietic neoplasms.

6. **The Multiple primary rules (M rules)**
   a. Start with rule M1, move through the rules in consecutive order and **STOP** at the first rule that applies.
      i. The M rule references in the Heme DB are to be used as a guide only.
      ii. Some of the rules are histology specific. If the working histology(ies) aren't included, continue on to the next rule
   b. Make sure that you are using the rules correctly by carefully READING EACH rule. Many registrars end up at Rule M15 when another rule is applicable.

Summary of the Multiple Primary Rules

Use this as a guide only, do not use this summary to determine the appropriate M rule.

Multiple Primary Rule	Covers	Comments
M1 (Single primary)	Limited information, death certificate only cases	
M2 (Single primary)	Same histology, same primary	Exception for 9699/3, need to review
M3 (Single primary)	Myeloid sarcoma and Acute Myeloid leukemia or Mast cell sarcoma and Mast cell leukemia	Histologies: 9740, 9742, 9930, and all AML histologies
M4 (Single primary)	Two or more NHL's diagnosed in the same biopsy	See PH11 or PH15 for histology
M5 (Single primary)	Hodgkin and non-Hodgkin in the same biopsy	See PH14 for histology
M6 (Multiple primaries)	Hodgkin and non-Hodgkin in different biopsies	
M7 (Single primary)	More specific histology and NOS histology	*Example:* Follicular lymphoma (specific histology) and NHL, NOS (NOS histology) Review same primaries section in the Hematopoietic database
M8 (Single primary)	Chronic and acute neoplasm diagnosed at the same time and there is one biopsy	Histologies must have information in the Transformation to or Transformation from field in the database
M9 (Single primary)	Chronic and acute neoplasm diagnosed at the same time and there is no documentation of the biopsy(ies)	Histologies must have information in the Transformation to or Transformation from field in the database
M10 (Multiple primaries)	Chronic and acute neoplasm diagnosed at different times	Histologies must have information in the Transformation to or Transformation from field in the database
M11 (Multiple primaries)	Chronic and acute neoplasm diagnosed at the same time and there are two biopsies	Histologies must have information in the Transformation to or Transformation from field in the database
M12 (Single primary)	Acute neoplasm reverts to chronic neoplasm, no (or unknown), treatment given for acute neoplasm	Histologies must have information in the Transformation to or Transformation from field in the database
M13 (Multiple primaries)	Acute neoplasm reverts to chronic neoplasm and treatment given for the acute neoplasm	Histologies must have information in the Transformation to or Transformation from field in the database
M14 (Single Primary)	Post transplant lymphoproliferative disorder (9971/3) with an accompanying hematopoietic neoplasm	See PH1 for coding histology
M15 (Multiple primaries calculator)		See Multiple Primaries Calculator

7. **Primary Site and Histology rules (PH rules)**
    a. Verify or revise the working histology code(s) using the Primary Site and Histology (PH) Rules (Primary Site and Histology Coding Rules)
    b. When the PH rules lead you to a **different** histology code, enter that code in the Heme DB search box and display the record for that histology
    c. The PH rules referenced in the Heme DB are the most common rule(s) used to code Primary Site and Histology for the selected histology. More than one Module/PH Rule may be needed to code Primary Site and Histology.
    d. Primary site coding instructions are found in the manual. See Primary Site Coding Instructions.
    e. Primary site can also be found in the Hematopoietic database
        i. For certain histologies, only one primary site code is displayed in the primary site field.
            - **All leukemias, myelodysplastic syndromes and chronic myeloproliferative diseases are assigned primary site bone marrow C421.** There are **NO** exceptions. This rule was implemented in ICD-O-2 in 1992.
        ii. For the remaining histologies, the most common primary sites are listed in the primary site text field. Additional notes may be included regarding sites that cannot be used.
            - This list is not hierarchical. The most common primary sites are from the current version of the WHO Blue Book for Hematolymphoid tumors. Uncommon primary sites can also occur.
        iii. Additional information may be found in the Abstractor Notes, which can be used to confirm that the site/histology combination indicated by the involvement documented in the medical record is possible.
        iv. A physician's statement of the primary site can be used.

Summary of the PH rules

Use this as a guide only, do not use this summary to determine the appropriate PH rule.

The PH rules are separated into 9 different modules. **Modules 1-6 are histology specific.** The rules included in these will instruct you on how to code histology, sometimes primary site.

Many of the rules in Modules 1-6 will direct you to Module 7 to assign primary site. Module 7 is used mostly for assigning primary site for Lymphomas, but can also be used for Langerhans, Dendritic, and other miscellaneous neoplasms. **Do not use Module 7 for Leukemias, Myelodysplastic Syndromes, Myeloproliferative neoplasms, or other bone marrow neoplasms.**

Module	Module Title	Rules	Histology(ies)	Comments
1	Post-Transplant Lymphoproliferative Disorder	PH1	TBD	See also Rule M14
2	Plasmacytomas	PH2-PH4	9731/3, 9734/3	
3	Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)	PH5-PH6	9823/3	
4	Leukemia/lymphomas (Acute Lymphoblastic Leukemias)	PH7-PH8	9811/3-9819/3, 9827/3, 9837/3	

Module	Module Title	Rules	Histology(ies)	Comments
5	Myeloid Neoplasms and Mast Cell Neoplasm	PH9-PH10	9740/3, 9742/3, 9930/3, All AML histologies	See also Rule M3
6	Non-Hodgkin Lymphoma	PH11-PH17	All non-Hodgkin lymphomas	PH11: 9680/3 (see also M4) PH12: 9597/3 PH13: 9680/3 (skin involvement) PH14: 9596/3 (see also M5) PH15: (see also M4) PH16: 9761/3 (WM) PH17: 9671/3 (LpL)
7	Coding Primary Site	PH18-PH27	All lymphomas, extraosseous plasmacytomas, histiocytic and dendritic cell neoplasms, mast cell sarcoma, heavy chain disease, myeloid sarcoma and post-transplant lymphoproliferative disease (PTLD)	Module 7 provides instructions on how to code primary site
8	NOS and More Specific Histology	PH28-PH29	All hematopoietic neoplasms (NOS and more specified histologies)	Use Multiple Primaries Calculator
9	Coding Primary site and histology	PH30-PH31	All hematopoietic neoplasms	Use the Heme DB to determine primary site

NOTE: For some cases, you may have to go through the M and/or PH rules twice.

Multiple Primaries Calculator

⚠ Do not start with the Multiple Primaries Calculator. Rule M15 is not a default and should only be used if none of the earlier rules (M1–M14) apply.

1. Start with the database first and gather as much information on your histology as you can.
2. Determine if you have a histology that transforms to another histology, or a histology that has another histology transforming to it. If you have either one of these, rules M8-M13 would apply.
   - **Do NOT apply Rule M15 to histologies that have transformation information.** See Transformations: Chronic and Acute Neoplasms.
3. Carefully go through all the rules (M1-M14) in chronological order to determine which one is applicable. STOP at the FIRST applicable rule
   - Some registrars are getting to rule M15 when one of the other rules from M1-M14 actually apply, so read the rules carefully.

⚠ Do NOT compare the number of primaries determined from Rule M1-M14 with the Multiple Primaries Calculator.

- **It is only appropriate to use the Multiple Primaries Calculator when the applicable M rule specifically instructs one to use it**

Examples of when M15 DOES apply (Case Scenarios from Ask a SEER Registrar)

1. Patient with diagnosis of Myeloid sarcoma in February 2025. In March 2025, bone marrow biopsy shows Chronic myeloid leukemia in chronic phase. BCR-ABL1 fusion is detected.
   - There are no rules that apply to Myeloid Sarcoma and Chronic Myeloid leukemia (only have rules that apply to Myeloid Sarcoma and Acute myeloid Leukemia).
   - Rules M1-M14 are not applicable. Rule M15 says to use the multiple primaries calculator. Two primaries.
2. Patient had bone marrow biopsy, which showed smoldering myeloma and hairy cell leukemia.
   - There is a rule for when two lymphomas occur in the same diagnostic biopsy; however, there are no rules for myeloma and leukemia.
   - Rules M1-M14 do not apply. Rule M15 says to use the multiple primaries calculator. Two primaries.
3. Bone marrow biopsy involved by acute myeloid leukemia, chronic lymphocytic leukemia and underlying myelodysplastic syndrome
   - For this case, you must go through the rules twice
   - The AML is an acute neoplasm, and the MDS is a chronic neoplasm. MDS transforms to AML. Rule M8 applies to this, which states that when a chronic and an acute occur within the initial clinical workup, and there is only one biopsy, code the acute, which would be the AML (9861/3)
   - THEN compare the AML (9861/3) and CLL/SLL (9823/3). Although CLL is a “chronic” neoplasm, it does not transform to AML.
   - Rules M1-M14 don’t apply. Rule M15 applies. This is two primaries, CLL/SLL (9823/3) and AML (9861/3)
4. Patient diagnosed with T-ALL (T-acute lymphoblastic leukemia). Several months later presents with multiple subcutaneous skin nodules and right eye conjunctive lesion. Both biopsied and positive for myeloid sarcoma.
   - Registrar stated that Rule M3 applied. Rule M3 applies only to Acute myeloid leukemias, this is an acute lymphoblastic leukemia.
   - Thus Rule M15 is the first rule that applies. Two primaries.

Examples of when M15 DOES NOT apply (Case Scenarios from Ask a SEER Registrar)

1. Patient with diagnosis of MDS with excess blasts in June 2025. In October 2025, patient returns for bone marrow biopsy, which states AML.
    - Registrar asks if Rule M15 is correct and that the histologies are 9861/3 and 9983/3. Rule M15 is NOT correct.
    - Prior to reviewing the M rules, you need to go to the Heme DB and look up both histologies. Scroll down to the "transformation to" section for MDS and the "transformation from" section for AML and you'll see that MDS transforms to AML.
    - This means that Rules M8-M13 apply.
    - The diagnoses are about 6 months apart. Rule M10 applies, which states to code the AML as a second primary
2. Patient diagnosed in November 2024 with AML. In December 2024, a debridement of the ring finger shows myeloid sarcoma
    - Registrar asked why the calculator didn't say this was the same primary.
    - Prior to reviewing the M rules, go to the Heme DB and look up both histologies. Scroll down to the abstractor notes. In both histologies, 9861/3 (AML) and 9930/3 (Myeloid Sarcoma), there is a note explaining that if Myeloid Sarcoma is diagnosed at the same time as AML or after AML, that Rule M3 applies, and it is the same primary.
    - The reason the multiple primaries calculator does not show this as the same primary is because if Myeloid Sarcoma is diagnosed first, then the AML is diagnosed at a later time, Rule M15 does apply, and it is two primaries.
3. Lymph node pathology shows two types of NH lymphomas, CLL/SLL and follicular. Peripheral blood only shows CLL/SLL.
    - To determine how many primaries, you must go through the rules twice
    - Rule M4 applies to the lymph node biopsy where CLL/SLL and follicular lymphoma are diagnosed. Per Rule PH15, the higher histology is coded, which is the CLL/SLL, 9823/3.
    - THEN a second pass through the rules stops at Rule M2, which states same histology is same primary. The peripheral blood showed CLL/SLL, which is the same histology as the lymph nodes. Rule M15 would not be used.

Case Reportability Instructions

This section is for reportability only. It does not cover rules for assigning histology. (See Histology Coding Instructions). Make inquiries to the physician's office to confirm the diagnosis whenever possible. Unless that type of follow-back is done, hematopoietic cases will be underreported.

1. Search the Heme DB to determine case reportability.
   a. There is a field called "reportable" in the database. Review this field to determine if the term you are seeking is reportable.
      Note: All terms covered in the latest WHO Blue Book for Hematolymphoid tumors are included in the Hematopoietic database. This includes reportable and non-reportable terms, as well as terms that have no ICD-O code.
   b. If a term cannot be found in the Heme DB, search the Glossary for Registrars
2. Report all cases with morphology codes **9590-9993** with a **/3 behavior.**
   a. There are several histologies in the Heme DB that are a /1. These are not reportable for U.S.
      Note: For **Canadians**, please refer to your specific province for reportability requirements.
   b. /1 neoplasms include in situ lymphomas (mantle cell and follicular). These are **NOT** reportable
3. Report hematopoietic and lymphoid neoplasms with morphology codes **9590-9993** listed in ICD-O as **/1** that are **described as malignant** by a physician. Apply the matrix rule and change the behavior code to /3.
4. Report the case when the diagnosis of a hematopoietic neoplasm is preceded by one or more of the **ambiguous terms listed below:**
   a. **This instruction pertains to reportability and case finding only. See the Histology Coding Instructions, #3-5 for instructions on assigning histology with ambiguous terminology.**
      - Apparently
      - Appears
      - Comparable with
      - Compatible with
      - Favor(s)
      - Malignant appearing
      - Most likely
      - Presumed
      - Probable
      - Suspect(ed)
      - Suspicious (for)
      - Typical (of)

b. Use these terms when screening all reports other than cytology and tumor markers.
c. Report cases that use only the word on the list or an equivalent word such as “favored” rather than “favor(s)””.
d. Do NOT substitute synonyms such as “supposed” for “presumed” or “equal” for “comparable with,” OR “likely” for “most likely”
    - See Registry Operations - SEER Registrars for the SEER Coding Manual and review the reportability section
e. Accept the reportable term and report the case when one part of the medical record uses a reportable ambiguous term such as “apparently” and another section of the medical record(s) uses a term that is not on the reportable list.
f. Follow back is recommended for diagnoses based on ambiguous terminology to see if the diagnosis has been confirmed or proven to be incorrect (see #5).
g. Do **NOT** report the case when biopsy or physician’s statement confirms a non-reportable condition or proves the ambiguous diagnosis is **wrong**.

5. Do **not** report cases diagnosed only by ambiguous **cytology** (cytology diagnosis preceded by ambiguous terminology)
    a. Report the case when the patient is treated for a reportable neoplasm
    b. Report the case even if the diagnostic tests are inconclusive, equivocal, or negative
    c. For treatment information see the National Cancer Institute’s Physicians’ Data Query (PDQ) or the SEER*Rx Antineoplastic Drugs Database.
6. Report the case when the patient is **treated** for a reportable neoplasm.
    a. Report the case even if the diagnostic tests are inconclusive, equivocal, or negative.
    b. For treatment information see the National Cancer Institute’s Physicians’ Data Query (PDQ) or the SEER*Rx Antineoplastic Drugs Database.
7. Report the case when there is a **clinical diagnosis** (physician’s statement) of reportable hematopoietic or lymphoid neoplasm.
    a. The clinical diagnosis may be a final diagnosis found within the medical record or recorded on a scan (CT, MRI for example).
    b. Report the case even if the diagnostic tests are equivocal. A number of hematopoietic neoplasms are “diagnoses of exclusion” in which the diagnostic tests are equivocal, and the physician makes the clinical diagnosis based on the equivocal tests and the clinical picture. See the Heme DB for definitive diagnostic methods for the specific neoplasm being abstracted.
8. Report the case when a reportable diagnosis appears in any text or report described as a **Definitive Diagnostic Method** in the Heme DB.
    a. Definitive diagnostic methods differ depending upon the histology. See the Heme DB for details.
        - ***Example 1***: CT scan shows enlarged lymph nodes suspicious for lymphoma. Subsequent biopsies of the lymph nodes thought to be involved with a neoplasm are negative for malignancy. The pathology is more reliable than the scan; the negative biopsy proves that the ambiguous diagnosis was wrong. Do **not** report the case.
        - ***Example 2***: Parotid ultrasound guided FNA: consistent with non-Hodgkin’s lymphoma. This case was diagnosed based on cytology/fine needle aspiration (FNA) preceded by ambiguous terminology (**consistent with**). Do not report this case based on ambiguous cytology.

Multiple Primary Rules

Initial Clinical Workup

Several of the M rules now refer to "initial clinical workup." This is the timeframe of when patients are first diagnosed. The initial clinical workup may include blood work, imaging, biopsies (including bone marrow), and genetic testing. In some situations, treatment may be started before the full workup is completed.

General Instructions for Multiple Primary Rules

1. Start with M1 for each case, move through the rules and stop at the first rule that applies. Use the M rule references in the Heme DB as a guide only.
    a. Some of the M rules are histology specific. See the Summary of the Multiple Primary Rules that may help you narrow down the applicable rules
2. Review the Transformations: Chronic and Acute Neoplasms to determine if Rules M8-M13 are applicable for your case
3. The registrar must recognize that during the diagnostic workup the physician may start with a provisional or several provisional (differential) diagnoses (NOS) and as testing is completed, a more specific diagnosis may be identified. These diagnoses are not multiple primaries; they represent steps in the diagnostic work-up.
4. If there have been more than two diagnoses of Heme/lymphoid neoplasms, you may need to go through the M rules more than once to determine the number of primaries.
    - ***Example:*** 11/2016 L retroperitoneal node bx: 9695/3 (follicular lymphoma gr 1 of 3). Tx was active surveillance, 7/2019 L inguinal node FNA, 9680/3 (DLBCL). Tx was R-CHOP. Per M10, this is 2nd primary. 7/2023 L neck, Level 2 node excision: 9691/3 (Follicular lymphoma, gr 1-2 of 3)
        i. Compare the diagnosis from 2016 (FL, G1) to the 2019 diagnosis (DLBCL). Per Rule M10, the DLBCL is a second primary
        ii. For the 2023 occurrence, compare the FL G2 to the FL G1. Per Rule M2, this is the same primary (all Follicular lymphomas are the same primary). This is still 2 primaries.
5. The Heme DB Multiple Primaries Calculator is to be used **only** when the rules instruct you to do so.
    a. Do NOT automatically go to M15 when there are two or more histologies. You must step through rules M1-M14 first, to see if one applies. Going directly to the multiple primaries calculator may result in the wrong number of primaries, and/or the wrong histology.
    b. See Multiple Primaries Calculator for more information regarding the use of M15.
6. In some cases, treatment may start before the full work up is completed.

The M Rules

Do not query the Multiple Primaries calculator unless specifically instructed to (See Multiple Primaries Calculator)

Rule M1: Minimal information, death certificate only case

1. Abstract a single primary when minimal information is available (such as a death certificate only [DCO] case or a pathology-report only case)

Rule M2: Single Histology

1. Abstract a single primary when there is a single histology.
   a. Recurrence of the same histology is always the same primary (timing is not relevant) (see #4 for 9699/3).
      - ***Example:*** Patient diagnosed in 2020 with DLBCL of the left Renal Pelvis. Presented in 2024 for a prostate needle biopsy positive for DLBCL.
   b. Bilateral involvement of lymph nodes and/or organs with a single histology is a single primary.
      - ***Example:*** Right and left breast both involved with diffuse large B-cell lymphoma (9680/3). Abstract as a single primary .
2. ***Exception:*** The occurrence of multiple MALT primaries are **not always the same primary.**
   a. Abstract multiple primaries when a nodal MALT (C770-C779, 9699/3) occurs before or after an extranodal MALT (all other sites, 9699/3). These are two distinct lymphomas that have the same histology code.
      - ***Example***: Marginal zone lymphoma (MALT) of right inguinal node (C774) diagnosed in 2018. Stage I with no recurrence. In 2025, patient diagnosed with Stage III ocular marginal zone lymphoma. Abstract a new primary.
3. A single histology is diagnosed by the definitive diagnostic method as defined in the Heme DB.
   a. For example, the patient had several provisional diagnoses, but the definitive diagnostic method identified a single histology. Abstract as a single primary.
4. Follicular lymphomas (9690/3, 9691/3, 9695/3, 9698/3) are ALWAYS the same primary.
   a. Follicular lymphomas have 3 different grades and a NOS. If there are multiple follicular lymphomas, update the histology as needed to reflect the highest grade.
      - ***Example:*** Patient diagnosed with follicular lymphoma, grade 1 (9695/3), in 2023. In 2025, patient was diagnosed with follicular lymphoma, grade 3. This is the same primary. Since the second primary was a grade 3, change the histology code to 9698/3.
5. **There are no timing rules for M2**.

- ***Case Scenario from Ask a SEER Registrar:*** Patient was diagnosed with DLBCL of Lt Renal Pelvis at OSH in 2010 and treated with surgery and systemic treatment. Patient came to our facility in 2024, and a prostate needle biopsy showed DLBCL and HoLEP confirmed as well. No lymphadenopathy was involved during each incidence. Is this a recurrence in 2024? or a new primary based on site and timing?
  - Same histology always same primary per Rule M2 (except for 9699/3). Primary site and timing are irrelevant.
  - As a reminder, Heme rules are very different than Solid Tumor Rules. Sounds like you are referring to the timing rules for Solid Tumors. The only timing rules in the Heme Manual are for chronic/acute neoplasms. This is not one of those situations.

Rule M3: Acute myeloid leukemia/myeloid sarcoma or Mast cell leukemia/mast cell sarcoma

1. Abstract a single primary when a myeloid or mast cell **sarcoma** is diagnosed during the initial clinical workup **OR** after a leukemia of the same lineage.
   a. Acute myeloid leukemia (Table B6: Acute myeloid leukemia), and myeloid sarcoma are diagnosed during the same clinical workup.
      - ***Example 1:*** Patient noted to have a solid tumor mass. Biopsy revealed myeloid sarcoma. Further workup included labs which were concerning for AML. Bone marrow biopsy positive for AML. Abstract one primary, the AML (See PH Rules, Module 5). This is the same primary since both the myeloid sarcoma and AML were diagnosed during the clinical workup.

   b. Acute myeloid leukemia initially diagnosed (Table B6: Acute myeloid leukemia), and myeloid sarcoma diagnosed at a later time.
      - ***Example 2:*** Acute myeloid leukemia (AML) diagnosed in 2024. In 2025, a soft tissue mass was biopsied, and the pathology report final diagnosis was myeloid sarcoma. This is the same primary. Presence of the myeloid sarcoma is a manifestation of the acute myeloid leukemia.

   c. Mast cell leukemia and mast cell sarcoma diagnosed during the same clinical workup.
   d. Mast cell leukemia diagnosed first followed by mast cell sarcoma diagnosed at a later time.
2. The myeloid/mast cell sarcoma is a manifestation of the leukemia (AML, Mast cell leukemia). The presence of the sarcoma indicates progression of the leukemia. This is not a second primary; it is a direct result of the myeloid cells circulating in the blood. It is similar in concept to a solid tumor in the colon metastasizing to the liver.
3. This rule **does not** apply to Chronic myeloid leukemia: 9863/3, 9875/3, 9876/3. These leukemias are not the same lineage as the myeloid sarcoma.
4. Do not apply this rule to other situations where Myeloid or Mast cell sarcoma may be diagnosed after another histology.
   - ***Example:*** Patient with h/o Acute Lymphoblastic leukemia (ALL) (9811/3) in 2023. Presents in 2025 with multiple subcutaneous skin nodules and right eye conjunctiva lesion, both biopsied and positive for myeloid sarcoma. Rule M3 does not apply. Rule M15 applies. The sarcoma would be a second primary.
5. See Module 5 for assigning primary site and histology.
6. It is possible for a myeloid/mast cell sarcoma to occur without the presence of leukemia. In this situation, abstract the sarcoma as a new primary. If the patient is diagnosed later with the leukemia, abstract a new primary (Rule M15).

Rule M4: Two or more non-Hodgkin lymphomas diagnosed in the same specimen (biopsy, surgical resection)

1. Abstract a single primary when two or more types of non-Hodgkin B-cell lymphomas are present in the same biopsy specimen (same lymph node, same organ or same tissue specimen).
   - ***Example***: Biopsy of cervical lymph node shows follicular lymphoma and DLBCL. Abstract as a single primary.
2. This rule **does not apply** to situations where a lymphoma is diagnosed, and the patient returns later to have a biopsy of the **same site,** and another lymphoma is diagnosed. In this situation, see Rule M7 to continue through the rules.

3. For the purpose of using the rules, a non-Hodgkin lymphoma is any lymphoma (including the leukemia/lymphomas) not stated to be Hodgkin lymphoma, NOS or a type of Hodgkin lymphoma.
    a. Hodgkin lymphomas are: 9650/3-9653/3, 9655/3, 9659/3, 9663/3.
4. Do **not** use this rule for **cutaneous lymphomas**. Simultaneous occurrences of two or more cutaneous lymphomas, other than an NOS and more specific, are extremely rare. If there are simultaneous cutaneous lymphomas, **DO NOT** use this rule; proceed to **rule** M15 **(Multiple primaries calculator).**
    a. Cutaneous lymphomas include 9597/3, 9700/3, 9701/3, 9708/3, 9709/3, 9718/3, 9719/3, 9726/3.
5. Early stage lymphomas have involved lymph node(s) in the same region as defined by ICD-O.
    a. See Appendix C for help identifying lymph node names, chains, regions and codes.
6. In advanced stage lymphomas, both non-Hodgkin B-cell lymphomas may be present in multiple lymph nodes in the same regions as defined by ICD-O, or in an organ and that organ's regional lymph nodes, or in multiple organs.
    a. If the physician biopsies one of the involved sites and diagnoses the combination of two or more types of non-Hodgkin lymphoma, assume that all of the nodes, tissues, and/or organs and associated lymph nodes are involved with the same combination of non-Hodgkin lymphomas.
7. See Rules PH11 and PH15 for assigning primary site and histology.
    - **Case Scenario from Ask a SEER Registrar:** LN Path: DLBCL. Follicular lymphoma, G1-2. When I looked up the rules, Rule M4 seemed to apply; however, when I plugged DLCBL & follicular into the calculator in that order, it said follicular was new primary. I'm assuming I go by the rule before the calculator. The same w/B-cell lymphoma w/the others. So, why lump them all under 1 abstract when the histology is different?
        - Rule M4 applies, one primary. Then PH11 applies for the histology, which is DLBCL (9680/3).
        - Never use the calculator unless the rules tell you to do so. See Multiple Primaries Calculator

Rule M5: Hodgkin and non-Hodgkin B-cell lymphoma in same specimen (biopsy, surgical resection)

1. Abstract a single primary when both **Hodgkin and non-Hodgkin B-cell lymphoma (Table B15: Mature B-cell neoplasms)** are present in **the same anatomic location(s) at the same time**, such as the same lymph node or same lymph node region(s), the same organ(s), and/or the same tissue(s).
    a. ***Example:*** Biopsy of cervical lymph node shows Hodgkin and non-Hodgkin B-cell lymphoma. Abstract as a single primary.
2. This rule **does NOT apply to** T-cell and NK-cell lymphomas.
    a. See Rule M15 (multiple primaries calculator), if you have a T-cell or NK-cell lymphoma (Table B20: Mature T-cell and NK-cell neoplasms) and Hodgkin lymphoma. (Table B16: Hodgkin lymphoma)
    Note: This is a change in rules based on consultation with our expert hematopathologist.
3. For the purpose of using the rules, a non-Hodgkin lymphoma is any lymphoma (including the leukemia/lymphomas) not stated to be Hodgkin lymphoma, NOS or a type of Hodgkin lymphoma. (Table B16: Hodgkin lymphoma).
4. Early stage lymphomas have involved lymph node(s) in the same region as defined by ICD-O.
    a. See Appendix C for help identifying lymph node names, chains, regions and codes.
5. In advanced stage lymphomas, both non-Hodgkin B-cell lymphomas may be present in multiple lymph nodes in the same regions as defined by ICD-O, or in an organ and that organ's regional lymph nodes, or in multiple organs.

6. If the physician biopsies one of the involved sites and diagnoses the Hodgkin and non-Hodgkin B-cell lymphoma, assume that all of the nodes, tissues, and/or organs and associated lymph nodes are involved with the same combination of Hodgkin and non-Hodgkin B-cell lymphomas.
7. See PH14 for information regarding primary site and histology.
8. Do not apply this rule when the diagnoses are not during the initial clinical workup.
    - ***Example of when M5 would NOT apply:*** Pt presented with anterior mediastinum mass. Diagnosed with classical Hodgkin lymphoma, stage 2B in 2024 per HemOnc w/ ABVD regimen. Persistent disease after 4 cycles on PET. Re-biopsy of the anterior mediastinum mass in March 2025 showed Grey Zone lymphoma.
        - Rule M5 does **NOT** apply in this situation since the Grey Zone Lymphoma was not diagnosed during the initial clinical workup. **See Rule M15.**

Rule M6: Hodgkin and non-Hodgkin lymphoma in different specimen (biopsy, surgical resection)

1. Abstract as multiple primaries when **Hodgkin lymphoma** is diagnosed in one anatomic location and **non-Hodgkin lymphoma (includes B, T and NK cell lymphomas)** is diagnosed in another anatomic location.
    - ***Example 1***: Patient diagnosed with HL in the cervical lymph nodes and with NHL in the GI tract. Abstract as multiple primaries.
    - ***Example 2:*** Hodgkin lymphoma diagnosed in a mediastinal mass and non-Hodgkin lymphoma in the tonsil. Abstract as multiple primaries.
    - ***Example 3:*** NHL diagnosed in a right cervical node and HL in a left cervical node. Abstract as multiple primaries. Left and right node chains are separate regions. See Appendix C.
2. For the purpose of using the rules, a non-Hodgkin lymphoma is any lymphoma (including the leukemia/lymphomas) not stated to be Hodgkin lymphoma, NOS or a type of Hodgkin lymphoma. (Table B16: Hodgkin lymphoma)

Rule M7: More specific histology diagnosed after an NOS histology

1. Abstract as a single primary when a more specific histology is diagnosed after an NOS **ONLY** when the Heme DB Multiple Primaries Calculator confirms that the NOS and the more specific histology are the same primary.
    a. See Appendix B WHO Classification of Haematolymphoid Tumors Histology Lineage to determine NOS histologies, or look at the same primaries for either the NOS or specific histology.
2. The more specific histology confirmation does not have to occur in the same anatomic location
3. There are no time restrictions on these diagnoses; the interval between the NOS and the more specific histology does not affect this rule.
4. The Heme DB Multiple Primaries Calculator will identify these histologies as the same primary.
5. Change the histology code on the original abstract to the more specific histology when the original diagnosis is in your registry database. Use previous editions of ICD-O (i.e. ICD-O-1, ICD-O-2) or the Heme DB to assign the code applicable to the year of diagnosis for the more specific histology.
    - ***Example 1:*** Patient diagnosed with non-Hodgkin lymphoma (9591/3) in 2003. Patient returns in 2013 with a diagnosis of CD30 positive lymphoproliferative disorder (9718/3). 9591/3 is an NOS histology and 9718/3 is more specific.
        - Per the Multiple Primaries Calculator, 9591/3 and 9718/3 are the same primary. 9718/3 was a valid code in 2003; change the histology to 9718/3 for the 2003 diagnosis.

- ***Example 2:*** CT guided core biopsy pelvic mass positive for lymphoma (9590/3) diagnosed in 2008. In November 2014, lymph node biopsy shows T-cell/histiocyte rich large B-cell lymphoma (9688/3). 9590/3 is an NOS histology and 9688/3 is more specific.
    - Per the Multiple Primaries Calculator, 9590/3 and 9688/3 are the same primary. Per the Hematopoietic Database, 9688/3 was not valid until 2010. Since the original diagnosis was in 2008, 9688/3 cannot be used. Keep the original code of 9590/3.

CHRONIC/ACUTE RULES: Rules M8-M13 are for neoplasms that Transform (see Transformations: Chronic and Acute Neoplasms)

1. "Transformations to" (acute neoplasms) and "Transformations from" (chronic neoplasms) are defined for each applicable histology in the database. If the neoplasms in question are not listed as "Transformations to" or "Transformations from" each other, then these rules do not apply. Go to Rule M14 to continue through the rules.
2. The phrase "initial clinical workup" has been incorporated into the chronic/acute rules (replaces simultaneously and the 21 day criteria).

Rule M8: Chronic and acute diagnosed during the initial clinical workup with one specimen

1. Abstract as a single primary and code the acute neoplasm when both a **chronic** and an **acute** neoplasm are diagnosed during the initial clinical workup **AND** there is documentation of **only one** positive biopsy (bone marrow biopsy, lymph node biopsy, or tissue biopsy).
2. See Rule M12 if there are two or more biopsies.
3. When these diagnoses occur within the initial clinical workup, it is most likely that one diagnosis was provisional, and the biopsy identified the correct diagnosis. Abstract the acute neoplasm.
    - ***Example 1***: Pt with T9 bone lesion 6/7/24 bx c/w plasmacytoma. Imaging at the time showed multiple other metabolically active but less so and at the time the dx was plasmacytoma vs multiple myeloma. Negative bone marrow and a 7/5/24 bx of a femur lesion that was negative on 7/24/24. On 8/16/24, imaging showed progression of the other lesions, and they determined the patient had multiple myeloma.
        - Per the WHO Classification of Hematolymphoid Tumors, the presence of multiple plasmacytomas is multiple myeloma. The working diagnosis was plasmacytoma versus multiple myeloma. The multiple myeloma was confirmed in August. This is all part of the initial clinical workup and therefore is one primary, the multiple myeloma (9732/3).
            - ***Note:*** Even though the bone marrow biopsy was negative, primary site is still assigned to C421.
    - ***Example 2****:* Excisional LN biopsy, large B-cell lymphoma arising from nodular lymphocyte predominant Hodgkin lymphoma.
        - Nodular Lymphocyte Predominant Hodgkin Lymphoma transforms to DLBCL. Per Rule M8, when you have a chronic and acute neoplasm simultaneously and there is only one biopsy, you code the acute neoplasm, which is the DLBCL.

Rule M9: Chronic and acute neoplasm diagnosed in the initial clinical workup and there is no available documentation of biopsy(ies).

1. Abstract a single primary and **code the acute neoplasm** when both a **chronic** and an **acute** neoplasm are diagnosed during the initial clinical workup **AND** there is **no available documentation** on biopsy (lymph node biopsy, tissue biopsy and/or bone marrow biopsy)

   Note 1: This rule should rarely be used.

   Note 2: This is a change in rules based on consultation with our expert hematopathologist.

Rule M10: Chronic neoplasm followed by acute neoplasm

1. Abstract as multiple primaries when a neoplasm is originally diagnosed as a chronic neoplasm during the initial clinical workup AND there is a second diagnosis of an acute neoplasm after the initial clinical workup is completed.
   - ***Example 1:*** Patient was diagnosed with MDS, unclassifiable in 2019. The patient presents in 2024 with a diagnosis of acute myeloid leukemia (AML) (9861/3).
     - This is a MDS (chronic neoplasm) followed by AML (acute neoplasm). The AML was diagnosed 5 years after the diagnosis of the myelodysplastic syndrome. This is two primaries: MDS (2019), AML (2024).
   - ***Example 2:*** Patient had a biopsy of the T4 vertebra in Dec 2024, path-plasma cell neoplasm with kappa restriction. No other bone lesions were seen on imaging. a Bone marrow biopsy, path: kappa predominant plasma cell population identified by IHC, 5-10. The medical oncologist stated "Patient has a plasmacytoma. " The patient received radiation therapy to the spine as the only treatment. Patient returns 5/25 and the physician states “labs consistent with multiple myeloma.” Bone marrow biopsy positive for multiple myeloma.
     - This is a plasmacytoma (chronic neoplasm) followed by multiple myeloma (acute neoplasm). The multiple myeloma was diagnosed after the initial clinical workup, diagnosis and treatment of the plasmacytoma. This is two primaries: plasmacytoma (12/24), multiple myeloma (5/25).

Rule M11: Chronic and acute diagnosed during initial workup with two biopsies

1. Abstract as multiple primaries when both a **chronic** and **acute** neoplasm are diagnosed during the initial clinical workup **AND** there **is documentation of two biopsies**: bone marrow, lymph node, or tissue, one confirming the chronic neoplasm and another confirming the acute neoplasm.
   - ***Example 1:*** 10/25/25, left pelvic mass, biopsy, diffuse large B-cell lymphoma. 11/3/23, bone marrow biopsy, low grade B-cell lymphoma, favor low grade follicular lymphoma, negative for large B-cell lymphoma.
     - This is a case of an acute neoplasm (DLBCL) and a chronic neoplasm (Follicular) and two different biopsies.
     - Two primaries: 1: 9680/3 (DLBCL), 2: 9690/3 (Follicular lymphoma, NOS).

     Note: The NOS code was chosen since it said “favor low grade follicular lymphoma.
   - ***Example 2:*** Patient noted to have bilateral lung nodules and bilateral breast masses. 4/21/21 biopsy of the right breast showed DLBCL arising in a background of MALT lymphoma. 4/21/21 left breast biopsy showed MALT lymphoma only. 5/18/21 biopsy of one of the right lung nodules showed MALT only.
     - This would be two primaries, the MALT and the DLBCL, per Rule M11. You have more than one biopsy, one confirming the MALT (chronic neoplasm), the other the DLBCL (acute neoplasm).

Rule M12: Acute neoplasm followed by chronic with no treatment or unknown if treatment

1. Abstract a single primary when a neoplasm is originally diagnosed as acute AND reverts to a related chronic neoplasm after the initial clinical workup been completed AND there is no confirmation available that the patient has been treated for the acute neoplasm. If there was treatment after the acute neoplasm, see Rule M13.
   - If the two diagnoses occur within the initial clinical workup, see Rules M8-M11.

- ***Example:*** 3/16/2025 biopsy of cervical nodes positive for diffuse large B-cell lymphoma (DLBCL) (9680/3). 4/18/2025 bone marrow biopsy done shows follicular lymphoma (9690/3). No treatment given between the diagnoses of acute neoplasm (DLBCL) and chronic (follicular). Abstract one primary, DLBCL (9680/3). Rule M8 applies to this case.

- When the chronic diagnosis occurs after the initial clinical workup of the acute neoplasm, it is important to follow back to obtain information on treatment or a subsequent bone marrow biopsy that negates the diagnosis of the acute neoplasm.

Rule M13: Acute neoplasm followed by chronic with treatment

1. Abstract multiple primaries when a neoplasm is originally diagnosed as acute and reverts to a chronic neoplasm after treatment.
   a. Only abstract as multiple primaries when the patient has been treated for the acute neoplasm. If it is unknown if patient was treated, see Rule M12
      - ***Example:*** Patient was diagnosed in 2022 with AML, NOS (9861/3). The patient was treated with chemotherapy and a subsequent stem cell transplant. In 2025, a bone marrow biopsy was positive for myelodysplastic syndrome. Abstract a second primary with the histology MDS, unclassifiable (9989/3).

   b. Apply this rule even when treatment for the acute neoplasm has not been completed
      - ***Example:*** Patient diagnosed with AML (9861/3). Plan of treatment chemotherapy. Remission is achieved, followed by bone marrow transplant. After chemotherapy, bone marrow biopsy is done and shows a complete remission regarding the AML, but the bone marrow shows MDS, unclassifiable (9989/3). The MDS is a second primary even though the planned first course of treatment was not completed prior to the diagnosis of the MDS.

- ***Exception:*** This does not apply to plasmacytoma(s) (9731/3, 9734/3) occurring after a diagnosis of plasma cell myeloma (9732/3). The presence of the plasmacytomas after a diagnosis of plasma cell myeloma is evidence of advanced disease and not a separate primary. Abstract one primary, plasma cell myeloma, 9732/3.

THIS IS THE END OF THE CHRONIC/ACUTE RULES

Rule M14: Post-transplant lymphoproliferative disorder

1. Abstract a single primary when post-transplant lymphoproliferative disorder is diagnosed in the same biopsy or surgical pathology report with any B-cell lymphoma, T-cell lymphoma, Hodgkin lymphoma or plasmacytoma/myeloma.
   a. Post-transplant lymphoproliferative disorders include, but are not limited to, monomorphic PTLD, Classic Hodgkin Lymphoma PTLD, Burkitt-type PTLD.

- ***Example 1:*** Biopsy of a nasopharyngeal mass shows EBV positive DLBCL consistent with monomorphic PTLD.
  - This is one primary. Histology would be coded to the accompanying lymphoma, DLBCL (9680/3).

- ***Example 2: Case Scenario from Ask a SEER Registrar (Rule M14 doesn't apply):*** Patient is diagnosed with post-transplant lymphoproliferative disorder 9971/3 in 2019 and a T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL) 9688/3 in 2025. Rule M14 of the HEME manual says to abstract a single primary when post-transplant lymphoproliferative disorder is diagnosed simultaneously with any B-cell lymphoma, T-cell lymphoma, Hodgkin lymphoma or plasmacytoma/myeloma. Once the lymphoma in 2025 is diagnosed, you no longer have a monomorphic PTLD.

What is the timing rule for simultaneously? Does this mean the same day, month, year? The heme calculator considers them a new primary. Is this a conflict with M14?

- Rule M14 applies to the same biopsy or surgical pathology report, same location, same time. This presentation is 6 years apart. This does not conflict with the multiple primaries calculator because of the timing. The T-cell/histiocyte-rich large B-cell lymphoma is a new primary per Rule M15.

b. Code the histology to the B-cell lymphoma, T-cell lymphoma, Hodgkin lymphoma, plasmacytoma, or myeloma.
c. See Rule PH1 for assigning histology.
d. See **Module 7** for assigning primary site.
e. This rule does not apply to polymorphic PTLD (PTLD without an accompanying Hematopoietic neoplasm). See 9971/3 (2010-2020, 2025+) and 9971/1 (2021-2024) in the Hematopoietic database for information on coding polymorphic PTLD.

- ***Example***: Patient with history of kidney transplant. 2025 mass biopsied showed posttransplant lymphoproliferative disorder. Rule M14 does not apply to this case. This is PTLD by itself, which is 9971/3. See Rule M2 (single histology).

Rule M15: Rules M1-M14 are not applicable

1. Use the Heme DB Multiple Primaries Calculator to determine the number of primaries for all cases that do not meet the criteria of M1-M14.
2. Before using this rule
   a. Check the Heme DB first, if both histologies include transformation information, review rules M8-M13
   b. See Multiple Primaries Calculator section which includes additional information and examples on when Rule M15 applies.
3. If both histologies include transformation information in the Heme DB, review rules M8-M13.

This is the end of the rules for determining the number of primaries.

Primary Site Coding Instructions

Unlike solid tumors, primary site does not play a huge role for Hematopoietic neoplasms; however, all cases abstracted in the registry must have a primary site. For Hematopoietic neoplasms, the most important information is the histology, and for lymphomas, this also includes stage as well. The primary site rules for the Hematopoietic neoplasms were created to provide a standardized way of collecting primary site information. This ensures that registrars are coding the same way. **As with other registry rules, the primary site rules may not agree with the physician.**

In order to avoid duplicate information, the listing of all the histologies with their primary site information has been removed from this section. **This information is now solely contained in the Hematopoietic database.** This decision was made based on the future implementation of ICD-O-4 (2028), which has >200 new Hematopoietic codes being added.

Primary site coding tips

In terms of coding primary site for Hematopoietic neoplasms, *Lymphomas are the most complex,* especially when there is extensive involvement throughout the body. Most of the primary site coding tips are geared towards lymphomas, but can be used for the other hematopoietic neoplasms (excludes histologies that have an assigned primary site).

Note: There is no hierarchy within the primary site rules. Find the one that fits your case and stop there.

1. Primary site codes C420 (Blood), C423 (Reticuloendothelial system), and C424 (Hematopoietic, NOS) are not used for Hematopoietic neoplasms.
    a. These codes are invalid because they are non-specific and don't represent the actual tumor origin. Always assign a specific primary site based on clinical, imaging, pathology, or database information.
2. Code primary site using
    a. Scans
    b. Medical record documentation
    c. Pathology report
    d. Hematopoietic database
    e. Physician statement (if available)
3. The hematopoietic database has two fields related to primary site: primary site (includes the C codes) and primary site text.
    a. The primary site field will be used when a hematopoietic neoplasm has a default primary site. A common example of this is for all the Leukemias, primary site is C421. That is the only primary site allowed.
    b. The primary site text field provides additional information on assigning primary site, such as the most common sites for a particular histology, or primary sites that cannot be used. For example, C422 cannot be used for 9699/3.
4. Do **not** simply code the primary site based on the location of the biopsy. **The purpose of the biopsy is to get the histological information; it is not used to determine primary site.** The biopsy is usually done on the most accessible site. Bone marrow biopsies may also be done based on other factors, but never assume that the primary site is the bone marrow based on that.
5. Imaging information is critical for assigning primary site. Review your imaging to determine involvement.

6. Remember that bone, brain, liver, lung, and bone marrow (see #11) are common metastatic sites. If these are involved, put those aside and see what else is involved. Involvement of these organs are commonly recorded in stage.

7. Once the common metastatic sites are put aside, look for any other organ involvement.
    a. If there is a **single** organ involved.
        i. See #10 if the spleen is involved.
        ii. Look to see if there are any involved regional nodes for that organ.
            - (The US follows how AJCC defines regional nodes. Review the AJCC manual or EOD Regional Nodes for the specific organ to determine if you have regional or distant nodes for that organ).
        iii. See Rules PH24 (single organ WITHOUT regional lymph node involvement) or PH25 (single organ WITH regional lymph node involvement).
            - Note that distant lymph nodes for that organ may also be involved; however, that factors into stage and not primary site.
    b. If there are **multiple** non-metastatic organs involved.
        i. WITH lymph node involvement, code to C779 (See Rule PH22).
        ii. WITHOUT lymph nodes involved, then your primary site may be C809, OR one of the organs may be your primary site and the other(s) metastatic.

8. A common statement on an imaging report is **"lymph nodes above and below the diaphragm."** This is important stage information, but it is also important for assigning primary site. In this situation, primary site may be C778 (See Rule PH21).
    a. Determine if an organ and its regional nodes are involved first.
    b. Other involvement in this situation would be recorded into stage.

9. **If unable to determine if organ involvement is metastatic disease,** use the following guidelines
    a. Code C778 when there are multiple lymph nodes/lymph node chains involved.
    b. Code C779 when there is lymph node involvement, but unknown if multiple lymph node chains involved.
    c. If there is no lymph node involvement, your primary site may be C809.

10. **Spleen** involvement
    a. Splenomegaly or spleen infiltration does not mean that the lymphoma originated in the spleen. Infiltration refers to deposits of lymphoma or leukemia in the spleen as a result of the spleen filtering the blood.
    b. Spleen involvement does not factor into primary site; it is recorded in stage.
        i. ***Exception****:* A primary spleen lymphoma can happen (see 9689/3, 9716/3); however, for ALL other histologies, if there is other involvement, the spleen would not be primary site. Diffuse large B-cell lymphoma (9680/3) can also originate in the spleen.

11. **Bone marrow** involvement
    a. If bone marrow is the ONLY anatomical location involved, code to bone marrow. (See Rule PH26).
    b. If bone marrow is involved, AND there are organs and/or lymph nodes involved, bone marrow involvement is recorded in stage.

Coding the Mets at Dx fields for Lymphomas and Leukemias

The Mets at Dx fields (bone, brain, liver, lung, distant lymph nodes, other) are applicable for lymphomas, and some other Hematopoietic neoplasms. **See the SEER Program Coding Manual for the complete instructions regarding these data items.**

1. Primary site C421
   a. If primary site is **C421**, ALL Mets at Dx fields **must be coded to 8 (not applicable)**.
   b. This applies to all leukemias, MDS, MPN and other bone marrow neoplasms.
   c. This also applies to lymphomas when the primary site is C421.
2. Lymph node primaries and Mets at Dx-Distant lymph nodes
   a. When the primary site is **C770-C779,** Mets at Dx-Distant lymph nodes **must be coded 8 (not applicable)**.
3. Lymphomas
   a. Coding Mets at dx for lymphomas follows the exact same concept as solid tumors. Just like solid tumors, common metastatic sites for lymphomas include the bone (Mets at Dx-Bone), brain/CNS (Mets at Dx-Brain), liver (Mets at Dx-Liver), and lung (Mets at Dx lung). Like Solid Tumors, these can also be primary sites; however, lymphomas originating in these sites is much rarer than it is for Solid Tumors
   b. These sites are usually secondary involvement (See Primary Site Coding Instructions) and are recorded as mets.
   c. When determining primary site, if bone, brain/CNS, liver, lung or bone marrow (mets at Dx Other code 1) are involved, look for other areas/sites involvement first, such as lymph nodes.
   Note: **The term "mets" or "metastatic disease" may not be used by physicians or radiologists. "Mets" in this context is used solely for the purpose of determining the appropriate primary site based on the rules.**

Remember: When trying to determine primary site, if any of the common metastatic sites are involved [bone, brain (CNS), liver, lung, distant lymph nodes (except for C77 primaries), and other (bone marrow)], set those aside and work with the remaining sites/lymph nodes that are involved.

See the SEER Manual for the full instructions for coding the Mets at Dx data items.

- ***Example 1:*** Colon biopsy, Aggressive non-Hodgkin B-cell lymphoma, germinal center type (9680/3). PET Scan large mass in ascending colon. Mass like fullness in infra hilar region. Small densities seen in bilateral lungs consistent with lung mets. Retroperitoneal/mesenteric LAD, bilateral inguinal lymph nodes, bulky mediastinal LAD. Enlarged bilateral cervical and axillary LNs.
  - First determine what is probably metastatic: Lung is a common metastatic site.
  - That leaves us with the colon, and mesenteric lymph nodes, which are regional for colon
    - **Rule PH25** applies which is code the primary site to the organ when an organ and its lymph nodes are involved. Primary site colon.
  - **Mets at Dx Lung: 1, Mets at Dx Distant Lymph nodes: 1. Remaining Mets at Dx fields coded as 0.**
- ***Example 2:*** CT Abdomen and Pelvis: Large mass in cecum, multiple regional lymph nodes involved. Right hemicolectomy, DLBCL, non-germinal center lymphoma. PET CT: nodal mets above and below the diaphragm. Skeletal mets. Bone marrow positive for DLBCL.
  - First determine what is probably metastatic: Bone (Skeletal mets) and Bone marrow, lymph nodes
  - That leaves us with the colon, and regional lymph nodes

        - **Rule PH25** applies which is code the primary site to the organ when an organ and its lymph nodes are involved. Primary site cecum
    - **Mets at Dx Bone: 1, Mets at Dx Distant Lymph Nodes: 1, Mets at Dx Other: 1, other Mets at Dx fields 0.**
- ***Example 3****:* Scans reveal 6 cm mass in the RLL lung, large mediastinal mass, right axillary ln positive for classical Hodgkin lymphoma.
    - Per the Hematopoietic database, Hodgkin lymphomas usually start in the lymph nodes. There are positive mediastinal lymph nodes (described as mediastinal mass) and axillary lymph nodes.
        - **Rule PH22** which states code to C778 when there are multiple lymph nodes.
    - **Mets at Dx Lung: 1, Mets at Dx Distant Lymph Nodes 8, other Mets at Dx fields 0.**
        - Distant lymph nodes are coded to 8 because this is a lymph node primary, and when there is a lymph node primary, you cannot distinguish between regional and distant lymph nodes
    - This case was coded differently due to Hodgkin being a lymphoma that usually presents in the lymph nodes.
- ***Example 4:*** Left middle ear biopsy: CLL/SLL. CT Scan: Abnormal soft tissue in the middle ear. This extends to involved the mastoid air cells. PET Scan: adenopathy noted within the cervical, supraclavicular, mediastinal, abdominal, and superficial inguinal regions.
    - First determine what is probably metastatic: Supraclavicular, mediastinal, abdominal and inguinal lymph nodes
    - That leaves us with the middle ear and cervical lymph nodes, which are regional nodes.
        - **Rule PH25** applies which is code the primary site to the organ when an organ and its lymph nodes are involved. Primary site middle ear.
        - **Mets at Dx Distant Lymph Nodes: 1, other Mets at Dx fields 0**

Coding Histology

The results from the immunophenotyping and genetic studies may not be on the original pathology report, but on an addendum and in some cases, on a totally separate report from the genomics lab itself. Registrars are encouraged to look for addendums when they are reviewing Hematopoietic neoplasms. Once the results from immunophenotyping and genetics are received, the pathologist or managing physician should update the diagnosis if needed.

Registrars are NOT to update the diagnosis based on positive immunophenotyping and genetics results only. The updated diagnosis based on positive genetics or immunophenotyping MUST be provided by the pathologist or the managing physician. See Note 6.

1. Code the **histology** that was identified by the method(s) listed under the **Definitive Diagnostic Method(s)** section of the Heme DB. Definitive diagnostic method(s) may be any of the following

   Note: There is no hierarchy among the items on this list.
   - Clinical diagnosis
   - Cytology
   - Genetic/Cytogenetic testing
   - Immunophenotyping/Immunohistochemistry testing
   - Addendum to final diagnosis (addendums will usually include results from the genetics and immunophenotyping, along with an updated diagnosis)
   - Pathology
   - CAP protocol/synoptic report
   - Final diagnosis (including the comments)

2. When tests or reports defined as Definitive Diagnostic Method(s) are **not available**, code histology using the following documentation in hierarchical order.
   - **Medical record documentation** (H&P, Progress or consult Notes, etc.) **where physician is referring to the** original scans, genetic testing, immunophenotyping, or pathology reports, OR histology.
   - Death certificate (central or regional registries only).

3. When the test or report lists a specific histology with **ambiguous term(s)** and an "NOS" histology, code the **NOS histology**. This prevents coding a temporary/provisional histology that could change with further testing which may not appear in the patient's chart, such as subsequent flow cytometry sent from the physician's office to an outside lab. (See also Rule PH28).
   - Ambiguous terminology can be used for case finding and reportability, or to assign a provisional histology code. For instruction on using ambiguous terminology for casefinding and reportability, go to the "Case Reportability Instructions, #4" at the beginning of the manual.
   - **For hematopoietic and lymphoid neoplasms, ambiguous terminology may NOT be used when a specific histology has not been confirmed (see #4 for exceptions)**. In this situation, there is not enough proof for the physician to definitely diagnose the specific histology. **If there is no further information regarding the more specific histology, the registrar is to assign the NOS equivalent for that histology.**
   - A specific histology can be assigned if there is documentation that the physician is treating the patient for the specific disease.

- ***Example:*** Biopsy, B-cell lymphoma, suspicious for DLBLC. Subsequent documentation from the physician indicates that the patient is being treated for DLBCL. Code the histology to DLBCL.

4. Update to Ambiguous terminology for **coding histology ONLY**
   - The following terms are now "definitive diagnoses" and are no longer on the ambiguous terminology list for assigning histology.
     - Comparable with
     - Compatible with
     - Consistent with
     - Most likely
     - Probable
     - Typical (of)

     Note: Do not apply these changes to casefinding, reportability or staging.

   - ***Example 1:*** Left first rib, soft tissue mass: plasma cell neoplasm (kappa light chain restricted) compatible with Multiple Myeloma. Code 9732/3 for Plasma Cell Myeloma/Multiple Myeloma.
   - ***Example 2:*** Myelodysplastic neoplasm most likely MDS with low blasts and isolated 5q deletion (MDS-5q-). Code 9986/3 for Myelodysplastic neoplasm with low blasts and 5q deletion (MDS-5q).
   - ***Example 3:*** Findings are consistent with myelodysplastic syndrome secondary to previously treated MPN, which may be best classified as myelodysplastic syndrome post cytotoxic therapy (MDS-pCT) according to new WHO classification. Code to 9920/3 for Myeloid neoplasm post cytotoxic therapy (MN-pCTs).

5. If there is **only one histology** available and it is **preceded by ambiguous terminology (see #4 for changes in what is ambiguous terminology for histology)**, review the Abstractor Notes in the Heme DB for that histology to see if other information can be used to confirm the diagnosis.
   - ***Example:*** CBC states abnormal lymphocytosis, no histology or provisional diagnosis on the CBC or peripheral blood smear. Flow cytometry states suspicious for CLL. No other workup done. Per the Abstractor Notes in the database, "abnormal lymphocytosis" is present in CLL. Assign histology CLL (9823/3) since "abnormal lymphocytosis" is part of the CLL/SLL definition.

6. If relevant immunophenotyping or genetics information is present in Abstractor Notes, and the only histology available is preceded by ambiguous terminology, code the ambiguous histology so that the case can be reported for incidence. (See Case Reportability Instructions, #4). Follow back to the physician's office or other sources at a later date to determine if subsequent testing confirmed the specific histology or the patient was diagnosed with a different histology.

7. **Registrars are NOT to update the histology based on genetics or immunophenotyping without a pathologist's/physician's statement.**
    - Pathologist's/physician statement can be found in the final diagnosis, synoptic report, or in the comments section
    - Registrars have been picking positive genetics out from pathology reports and trying to figure out which code to use, sometimes listing 4-5 different codes (especially for Acute Myeloid Leukemia) based on the genetics
    - This is not how a histology is determined and why registrars are not to assign a more specific histology based on genetics or immunophenotyping **UNLESS** the pathologist/managing physician documents it
        - **Case Scenario from Ask a SEER Registrar:** Final diagnosis: Acute myeloid leukemia with monocytic differentiation. Note: The combined morphologic and immunophenotypic findings are consistent with involvement by an acute myeloid leukemia with monocytic differentiation. Cytogenetics: RUNX1, RUNX1T1 POS. NPM1+ FLT3 TKD+. No revised diagnosis available. Registrar asks which of the AML codes should be used: RUNX1, NPM1, or FLT3.
            - Pathologist has clearly stated the diagnosis **as acute myeloid leukemia with monocytic differentiation** based on the pathology report. The positive genetics cannot be used to assign histology since there is no statement from the pathologist/managing physician. Diagnostic confirmation would be 1.
            - This is a prime example of how registrars have been misreading the rules. **You take the pathologist's diagnosis. Never use the genetics to determine the appropriate histology code.**
        - **Case Scenario from Ask a SEER Registrar:** Bone marrow biopsy shows Acute myeloid leukemia with inv(3)(q21q26) MECOM rearrangement. In addition, has complex karyotype 45,XY,-7[2]/45,idem,t(inv(3);15)(q25;q11.2)inv(3)(q21q26)[18]/46,idem,t(inv(3);15),+der(15)t(inv(3);15)[5]. NGS identified pathogenic mutations in DNMT3A, IDH2, JAK2 and RUNX1. Registrar states: Since the patient has multiple genetic abnormalities that can be coded to different histologies, I wasn't sure what histology code to assign. I narrowed it down to AML w/ mutated RUNX1 9879/3 or AML w/ MECOM rearrangement 9869/3. Do I use the higher code? I couldn't find anywhere in the Heme manual that talked about histologies with multiple genetic abnormalities.
            - The pathologist has clearly stated the diagnosis: **Acute myeloid leukemia with inv(3)(q21q26) MECOM rearrangement.**
            - This is a prime example of how registrars have been misreading the rules. You take the pathologist's diagnosis. Never use the genetics to determine the appropriate histology code.
            - Note: There are no combination codes for AML when there are multiple genetic abnormalities.

1. The primary site and histology coding rules are divided into nine modules. Each **module** covers a group of **related** hematopoietic or lymphoid neoplasms. However, a specific histology may be covered in more than one module.
2. The modules are **NOT** hierarchical, but the rules within each module are in hierarchical order. Apply the rules within each module in order. Stop at the first rule that applies.
3. For further information, such as primary sites, on the specific histologies listed in the PH rules, see the Hematopoietic database.

Module 1: Post-Transplant Lymphoproliferative Disorder (PTLD)
WITH an accompanying lymphoma or plasmacytoma/myeloma
(including, but not limited to: Monomorphic PTLD, Classic Hodgkin lymphoma-PTLD type, Burkitt type PTLD)

Rule PH1: Post-transplant lymphoproliferative disorder

1. Code the **histology of the accompanying hematopoietic neoplasm** when the diagnosis is post-transplant lymphoproliferative disorder and any lymphoma, plasmacytoma, or plasma cell myeloma diagnosed in the same biopsy**.** Code primary site to the **site of origin**, (lymph nodes, tissues, or organs). See Rule M14.
   - Rule PH1 applies to post-transplant lymphoproliferative disorders, which include, but are not limited to monomorphic PTLD, Classic Hodgkin Lymphoma-PTLD Type, Burkitt type PTLD.
     i. The patient **must** have a history of a solid organ transplant or an allogeneic bone marrow transplant in order to have a PTLD.
     ii. Most cases of PTLD occur within a year of transplantation; however, they can occur any time after the transplant.
     iii. Monomorphic PTLD is also caused by the immunosuppressant drugs. Patients are treated for the lymphoma or plasmacytoma/myeloma.
   - **This rule does not apply to polymorphic PTLD** (PTLD without an accompanying Hematopoietic neoplasm).
     i. See 9971/1 and 9971/3 in the Hematopoietic Database for information on coding polymorphic PTLD.
2. Effective with diagnosis year 2025+, a new SSDI has been added to capture the presence of the PTLD. See the SSDI Manual, Version 3.3, for more information.
3. See Appendix C for help identifying lymph node names, chains, regions and codes.
4. See Module 7 and the Hematopoietic database to determine primary site.
   - ***Example:*** Previous history of kidney transplant. Now presents for bone marrow biopsy. BM positive for B-cell lymphoma. Abdominal mass biopsy was positive for PTLD, monomorphic type and aggressive B-cell malignancy. Immunohistochemistry shows the B-cell malignancy to be Burkitt lymphoma. Code the histology to Burkitt lymphoma and primary site to the abdominal lymph nodes (C77.2).

Module 2: Plasmacytomas PH2 – PH4
Extramedullary plasmacytoma (EMP) (9734/3)
Solitary plasmacytoma of bone (SPB) (9731/3)

See the Hematopoietic Database for Plasma Cell Myeloma, 9732/3. Code 9732/3 if there are multiple plasmacytomas or the bone marrow is involved.

Rule PH2: Extraosseous (non-bone) primaries for plasmacytoma (see PH3 for bone primaries)

1. Code the histology to extramedullary plasmacytoma (9734/3) when there is a single plasmacytoma only in a site other than bone
   a. Extraosseous plasmacytoma
   b. Plasmacytoma, NOS (occurring outside of bone)
   c. Solitary plasmacytoma (occurring outside of bone)
2. This plasmacytoma is a localized **solitary** tumor outside the bone. Complete skeletal radiographs (preferably MRI) show no other lesions. If additional lesions or tumors are found on the MRI or CT (or other radiological surveys) during the initial clinical workup, this is diagnostic of **plasma cell myeloma** (see 9732/3).
3. See Primary site coding tips **for additional information on coding primary site.**
4. See Appendix C for help identifying lymph node names, chains, regions and codes.
5. See Module 7 and the Hematopoietic database to determine primary site.
   - ***Example 1***: Pathology reports a solitary plasmacytoma wrapped around L4 vertebrae, no invasion of vertebrae. Code the primary site as soft tissue of back (C496) and histology to plasmacytoma (9734/3).
   - ***Example 2***: Scan shows a plasmacytoma in the nasopharyngeal wall. Biopsy confirms plasmacytoma. Code the primary site nasopharynx (C119) and histology to plasmacytoma (9734/3).

Rule PH3: Bone primaries for plasmacytoma (see PH2 for non-bone primaries)

1. Code the histology to **solitary plasmacytoma of bone** (**9731/3)** and the **primary site to** the **specific bone site (C400-C419)** where the plasmacytoma originated when the diagnosis is:
   a. Osseous (medullary) plasmacytoma
   b. Plasma cell tumor
   c. Plasmacytoma, NOS (occurring in bone)
   d. Solitary plasmacytoma (occurring in bone)

2. This plasmacytoma is a localized **solitary** tumor of the bone. Complete skeletal radiographs (preferably MRI) show no other lesions. If additional lesions or tumors are found on the MRI or CT (or other radiological surveys) during the initial clinical workup, this is diagnostic of **plasma cell myeloma** (see 9732/3)
3. Most common sites are bones with active bone marrow hematopoiesis, which include vertebrae, ribs, skull, pelvis, femur, clavicle, and scapula.
4. **Plasma cell neoplasm** is not the same thing as plasma cell tumor or plasmacytoma of bone.
    a. See the Hematopoietic database for more information on plasma cell neoplasm.

Rule PH4: Plasmacytoma, NOS and no primary site

1. Code the histology to **solitary plasmacytoma (9731/3**) and **primary site bone, NOS (C419)** when the only information is that the patient had a plasmacytoma, NOS or a solitary plasmacytoma, NOS and there is no indication of bone or extramedullary involvement.
2. Death-certificate only case (central or regional registry only) with underlying cause of death listed as plasmacytoma.

Module 3: Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) PH5-PH6
Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) 9823/3

Rule PH5: Bone marrow and/or peripheral blood involved (WITH or WITHOUT lymph node(s), tissue(s), and/or organ(s))

1. Code the primary site to bone marrow (C421) when the bone marrow and/or peripheral blood are involved.
    a. Involvement of lymph node(s), tissue(s), and/or organ(s) is not taken into account.
    b. If the bone marrow and/or peripheral blood are not involved, or it's unknown if they are involved, **see Rule PH6** .

Rule PH6: Bone marrow AND peripheral blood NOT involved, or UNKNOWN if involved

1. Code the **primary site to the involved lymph nodes, organs, or tissue** when there is no bone marrow and/or peripheral blood involvement, **OR** when it is unknown if there is bone marrow and/or peripheral blood involvement.
2. If the bone marrow and/or the peripheral blood are involved, see Rule **PH5.**
3. See Primary site coding tips **for additional information on coding primary site.**
4. See Appendix C for help identifying lymph node names, chains, regions and codes.
5. See Module 7 and the Hematopoietic database to determine primary site.

Module 4: Leukemia/Lymphoma
(Specific neoplasms that can manifest as either leukemia or lymphoma or both leukemia and lymphoma) PH7 – PH8
(9811/3-9819/3, 9827/3, 9837/3)

See Table B14: Precursor B-cell neoplasms and Table B19: Precursor T-cell neoplasms

Rule PH7: ONLY Bone marrow or peripheral blood involved

1. For the histologies above, code the primary site to bone marrow (C421) when the only site involved is bone marrow and/or peripheral blood
   a. If lymph node(s), tissue(s), and/or organ(s) are involved, see **PH8.**

Rule PH8: Lymph node(s), organ(s), and/or tissue(s) involved (WITH OR WITHOUT bone marrow and/or peripheral blood).

1. For the histologies listed above, code the **primary site** to the site of origin when lymph node(s), tissue(s), and/or organ(s), are involved
2. Do not simply code the site of a biopsy; also use the information available from scans to determine the correct primary site.
3. See Primary site coding tips **for additional information on coding primary site.**
4. See Appendix C for help identifying lymph node names, chains, regions and codes.
5. See Module 7 and the Hematopoietic database to determine primary site.

Module 5: Myeloid Neoplasms and Mast Cell Neoplasms PH9 - PH10
Mast cell sarcoma (9740/3)
Mast cell leukemia (9742/3)
Myeloid sarcoma (9930/3)

9861/3 and **Table B6: Acute myeloid leukemia**

Rule PH9: Mast cell leukemia/Mast cell sarcoma

1. Code the histology to **mast cell leukemia (9742/3)** and **primary site to C421** when the diagnosis is mast cell sarcoma (9740/3) **AND** there is a simultaneous or previous diagnosis of mast cell leukemia. See Rule M3.
2. When mast cell sarcoma (9740/3) follows a diagnosis of mast cell leukemia (9742/3), the sarcoma is a manifestation of late-stage leukemia.

Rule PH10: Acute myeloid leukemia/Myeloid sarcoma

1. Code the histology to **acute myeloid leukemia (9861/3) or any of the specific AML histologies** (Table B6: Acute myeloid leukemia) and **primary site to bone marrow (C421)** when the diagnosis is myeloid sarcoma (9930/3) AND Acute myeloid leukemia, or there was a previous diagnosis of acute myeloid leukemia.
2. When myeloid sarcoma (9930/3) follows a diagnosis of acute myeloid leukemia (any subtype), the sarcoma is a manifestation of late-stage leukemia.

Module 6: Non-Hodgkin Lymphomas (NHL) PH11 – PH17
Diffuse large B-cell lymphoma (9680/3)
Primary cutaneous follicle centre lymphoma (9597/3)
B-cell lymphoma, with features intermediate between diffuse large B-cell lymphoma and classic Hodgkin lymphoma (9596/3)
Waldenstrom Macroglobulinemia (9761/3)
Lymphoplasmacytic lymphoma (9671/3)

See Primary site coding tips **for additional information on coding primary site**

Rule PH11: DLBCL and other non-Hodgkin lymphoma in same site of origin

1. Code the histology to **diffuse large B-cell lymphoma, when DLBCL (9680/3)** and any other non-Hodgkin lymphoma are present in the same lymph node, organ, tissue, or bone marrow at the same time. See Rule M4.
   a. Non-Hodgkin lymphomas can be found in Table B14: Precursor B-cell neoplasms, Table B15: Mature B-cell neoplasms, Table B19: Precursor T-cell neoplasms and Table B20: Mature T-cell and NK-cell neoplasms.
   b. This rule does not apply to Table B16: Hodgkin lymphoma.
2. Do **not** use this rule if DLBCL is not one of the two non-Hodgkin lymphomas, see rule PH15.
3. See Primary site coding tips **for additional information on coding primary site.**
4. See Appendix C for help identifying lymph node names, chains, regions and codes.
5. See Module 7 and the Hematopoietic database to determine primary site.

Rule PH12: Primary cutaneous follicle center cell lymphoma

1. Code the histology to **primary cutaneous follicle center cell lymphoma (9597/3)** and primary site to **skin** (C44_) when there is **skin infiltration** with follicle cell lymphoma, or B-cell lymphoma, follicle type and the involvement is
   a. Limited to skin WITH or WITHOUT regional lymph nodes for the specific skin site.
2. **Follicular lymphomas (NOS, grades 1, 2, 3A, 3B)** were once called follicle center lymphoma, and this term may still be used. If the term follicle center is used
   a. If the term follicle center lymphoma is used, code to follicular lymphoma (9690/3, 9691/3, 9695/3, 9698/3) when
      i. Lymph nodes and extranodal sites are involved **OR**
      ii. There is involvement of lymph nodes that are NOT regional for the skin site involved, OR involvement of bone marrow or other organs
   b. Code to primary cutaneous follicle center lymphoma (9597/3) if the skin is involved WITH or WITHOUT the regional lymph nodes for that specific skin site.

Rule PH13: Skin infiltration by large B-cell lymphoma

1. Code the histology to **diffuse large B-cell lymphoma (9680/3)** and **primary site skin (C44_)** when there is **skin infiltration** with large B-cell lymphoma, large cell type, or large cell lymphoma and the involvement is
   a. Limited to skin WITH or WITHOUT regional lymph node(s) for the specific skin site.
2. Do **not** code skin (C44_) as the primary site when there is involvement of lymph node(s) that are not regional for the skin site involved.
   a. See Summary Stage Chapter "Skin" for a listing of regional lymph nodes for skin primary sites.

Rule PH14: Composite Hodgkin and non-Hodgkin lymphoma

1. Code the histology to **B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and classic Hodgkin lymphoma/composite Hodgkin and non-Hodgkin B-cell lymphoma (9596/3) (See M5) when**
   a. Both a B-cell non-Hodgkin lymphoma and Hodgkin lymphoma are present in one lymph node or multiple lymph nodes in one lymph node region **OR**
   b. Both a B-cell non-Hodgkin lymphoma and Hodgkin lymphoma are present in multiple lymph node regions as defined by ICD-O. e.g., NHL and HL present in superior hilum and superior rectal nodes.
2. When only one node is biopsied, assume all lymph nodes are involved with both NHL and HL.
3. Histologies include Table B16: Hodgkin lymphoma and Table B14: Precursor B-cell neoplasms or Table B15: Mature B-cell neoplasms
4. See Rule M15 for a combination of Hodgkin lymphoma and Table B19: Precursor T-cell neoplasms or Table B20: Mature T-cell and NK-cell neoplasms.
5. See Primary site coding tips **for additional information on coding primary site.**
6. See Appendix C for help identifying lymph node names, chains, regions and codes.
7. See Module 7 and the Hematopoietic database to determine primary site.

Rule PH15: Coding histology when two or more non-Hodgkin lymphomas (excluding DLBCL) in same lymph node(s), tissue(s), organ(s).

1. Code the histology to the **numerically highest ICD-O code** when two or more non-Hodgkin lymphomas are present in the same lymph node(s), tissue(s), organ(s), and/or bone marrow. See Rule M4.
   a. Non-Hodgkin lymphomas can be found in Table B14: Precursor B-cell neoplasms, Table B15: Mature B-cell neoplasms, Table B19: Precursor T-cell neoplasms and Table B20: Mature T-cell and NK-cell neoplasms.
      - ***Example***: Biopsy revealed both small lymphocytic lymphoma (9823/3) and follicular lymphoma grade 2 (9691/3) in the same lymph node. Per Rule M4, this is one primary. Code histology to 9823/3 since it is the numerically higher ICD-O code.

   b. This rule does not apply to Table B16: Hodgkin lymphoma.
2. Do **not** use this rule if
   a. DLBCL is one of the two non-Hodgkin lymphomas, see rule PH11.
   b. When different non-Hodgkin lymphomas are present in different sites (see Rule M15)
      - ***Example*:** B-cell lymphoma is present in the intrathoracic lymph nodes and peripheral T-cell in the liver. 2 primaries.

   c. When there is an NOS histology AND a more specific histology (see Rule M7)
      - ***Example*:** Non-Hodgkin lymphoma, NOS and Follicular lymphoma (code the follicular lymphoma)
3. See Primary site coding tips **for additional information on coding primary site.**
4. See Appendix C for help identifying lymph node names, chains, regions and codes.
5. See Module 7 and the Hematopoietic database to determine primary site.

Rule PH16: Waldenstrom macroglobulinemia

1. Code the histology to **Waldenstrom macroglobulinemia (9761/3)** and primary site to **bone marrow (C421)** when
   a. Lymphoplasmacytic lymphoma (LpL) is found in the bone marrow biopsy blood AND clinical diagnosis of WM

      OR
   b. Waldenstrom macroglobulinemia found in the bone marrow biopsy or blood (There may be a clinical diagnosis and/or histologic confirmation of lymphoplasmacytic lymphoma (LpL) as well)

      OR
   c. Clinical diagnosis of Waldenstrom Macroglobulinemia, including a diagnosis of Lymphoplasmacytic lymphoma/Waldenstrom Macroglobulinemia

Rule PH17: Lymphoplasmacytic lymphoma

1. Code the histology to **lymphoplasmacytic lymphoma** (9671/3) when
   - Lymphoplasmacytic lymphoma (LPL) confirmed by biopsy (bone marrow, peripheral blood, lymph nodes, or organs) **AND**
   - There is no mention of Waldenstrom Macroglobulinemia.
2. See Primary site coding tips **for additional information on coding primary site.**
3. See Appendix C for help identifying lymph node names, chains, regions and codes.
4. See Module 7 and the Hematopoietic database to determine primary site.

Module 7: Coding Primary Site PH18 - PH27

Hodgkin lymphomas: Table B16: Hodgkin lymphoma

Non- Hodgkin lymphomas: Table B15: Mature B-cell neoplasms, Table B20: Mature T-cell and NK-cell neoplasms

Extraosseous (not occurring in bone) plasmacytomas-9734/3

Mast cell sarcoma-9740/3

Histiocytic and dendritic cell neoplasms: Table B10: Plasmacytoid dendritic cell neoplasms, Table B11: Langerhans cell and other dendritic cell neoplasms, Table B21: Mesenchymal dendritic cell neoplasms

Heavy chain disease-9762/3

Myeloid sarcoma-9930/3

Polymorphic post-transplant lymphoproliferative disorders (polymorphic only)-9971/3 (2010-2020, 2025+ only)

See Primary site coding tips **for additional information on coding primary site**

Rule PH18: Nodal Lymphomas described as a "mass"

1. **Applicable for Hodgkin & non-Hodgkin lymphomas only:** Code the primary site to the specified **lymph node region** when the site of the lymphoma is described ONLY as a mass and there is no additional lymph node involvement.
   a. Mediastinal lymph nodes (C771) when the site of the lymphoma is described only as a mediastinal mass.
      - ***Example:*** *L*ymphoplasmacytic lymphoma with an anterior mediastinal mass. No other involvement. Rule PH18 applies. Primary site C771.
   b. Intra-abdominal lymph nodes (C772) when the site of the lymphoma is described only as a **retroperitoneal mass or mesenteric mass.**
   c. Inguinal lymph nodes (C774) when the site of the lymphoma is described only as an **inguinal mass.**
   d. Pelvic lymph nodes (C775) when the site of the lymphoma is described only as a **pelvic mass.**

2. Do **not** apply this rule to any other descriptions of "mass."
    a. ***Example*:** LT Paravertebral Mass. Imaging describes the location of a soft tissue lesion to the LT of T11-T12. Paravertebral mass is not covered in Rule PH18, so this cannot be used for this case scenario. (Note: This is a mass surrounding the vertebra, assign primary site to vertebrae).
3. Do **not** apply this rule when multiple lymph nodes are involved. **See PH21.**
    a. ***Example*:** 2023 patient has CT scan showing a bulky mediastinal mass, PET shows mediastinal mass and hypermetabolic nodal tissue throughout the cervical, supraclavicular, subpectoral and axillary nodal stations. Mediastinal mass bx showed classic Hodgkin lymphoma nodular sclerosis subtype 9663/3, and bone marrow bx was negative. Rule PH18 **does not apply** since multiple lymph node areas are involved

Rule PH19: One lymph node chain/region involved

1. Code the primary site to the **specific lymph node region** when only one lymph node or region is involved.
    a. There is no other involvement found during the workup.
2. See Rule PH21 if multiple lymph node regions are involved.
3. See Appendix C for help identifying lymph node names, chains, regions and codes.

Rule PH20: Multiple lymph node chains/same region

1. Code the primary site to the specific lymph node region when multiple lymph node chains within the same region as defined by ICD-O are involved.
    a. Use this rule where there is bilateral involvement of lymph nodes in the same region.
2. See Rule PH21 if multiple lymph node regions are involved.
3. See Primary site coding tips **for additional information on coding primary site.**
4. See Appendix C for help identifying lymph node names, chains, regions and codes.
    - ***Example 1***: Code involvement of intra-abdominal, hepatic, and para-aortic lymph node chains to intra-abdominal lymph nodes (C772).
    - ***Example 2***: Code involvement of cervical lymph node chain and mandibular lymph node chain to lymph nodes of head, face and neck (C770).
    - ***Example 3***: Code to mediastinal lymph nodes (C771) when bilateral mediastinal lymph nodes are involved.

Rule PH21: Multiple lymph node regions

1. Code the primary site to lymph nodes of multiple regions (C778) when multiple lymph node regions are involved.
    a. If a physician documents that the lymphoma originated in a specific lymph node region, code that as the primary site (this is very rare).
    b. If imaging, or the physician states "lymph nodes above and below the diaphragm," code to C778.
    Note: Multiple lymph nodes regions involved can be on the same side or both sides of the diaphragm
2. See Primary site coding tips **for additional information on coding primary site.**

3. See Appendix C for help identifying lymph node names, chains, regions and codes.
    - ***Example 1***: Cervical (C770) and intra-thoracic (C771) lymph nodes involved with B-cell lymphoma. No indication of site of origin. Code the primary site to lymph nodes of multiple regions (C778).
    - ***Example 2***: Biopsy of an axillary lymph node (C773) confirmed lymphoma. CT scans showed involvement of the axillary lymph nodes (C773) and the pelvic lymph nodes (C775). No additional involvement was identified during the work-up and no indication of site of origin. Code the primary site to lymph nodes of multiple regions (C778).
    - ***Example 3***: Documentation at diagnosis includes mediastinal lymphadenopathy, unilateral left sided pleural effusion, questionable left lung nodular abnormality, splenomegaly, thrombocytopenia, and nodes present above and below the diaphragm, pleural fluid involvement. Pericardial soft tissue abnormality. Code the primary site to lymph nodes of multiple regions (C778).
    - ***Example 4:*** PT was originally diagnosed on imaging w/ a small bowel primary 4cm mass & multiple LNs within the omentum were noted. PT was urgently taken to the OR for a small bowel resection. Patho from resection showed "follicular lymphoma involving mesentery, muscularis propria & submucosa of small intestine. 9 LNS (+)". On her PET scan following the surgery she had LNS(+) above and below the diaphragm, "susp for follicular lymphoma."
        - Even though the phrase “above and below the diaphragm” is used, the primary site would still be small intestine since the positive lymph nodes were regional for small intestine. The “above and below the diaphragm” would be recorded in stage.

Rule PH22: Lymph nodes, NOS

1. **This rule does not apply if there is no lymph node involvement (continue with PH24).**
    a. ***Exception***: This rule may only be used for lymphomas for historical, history of, death certificate cases OR when there is no information available.
        - ***Example***: Patient presents for biopsy of lymph node region which is positive for lymphoma. No other information available.
2. Code the primary site to lymph nodes, NOS (C779) when
    a. **Single organ and non-regional (distant) lymph node involvement OR**
        i. Lymphoma can spread from organs to regional lymph nodes, but does not spread from the organ directly to distant lymph nodes.
        ii. If a **single organ** and its regional lymph nodes are involved, see PH25.
    b. **Multiple organs and lymph nodes involved**
        i. Before using this rule, determine if multiple organs are truly involved. When determining the number of organs, exclude the following: bone marrow, spleen and usual metastatic sites such as bone, brain, liver, lung (see Primary site coding tips). If these have been ruled out, apply this rule to
            - Multiple organs and regional nodes for all involved organs **OR**
            - Multiple organs and combination of regional/distant nodes for the involved organs **OR**
            - Organ(s) and lymph node(s) involved, and no primary site/particular lymph node region is identified.
3. Do not use this rule for extraosseous plasmacytomas (9734/3) or Langerhans cell histiocytosis, disseminated (9751/3).
    a. See Hematopoietic database
4. See Primary site coding tips **for additional information on coding primary site.**

5. See Appendix C for help identifying lymph node names, chains, regions and codes.
    - ***Example 1:*** The patient has positive mediastinal lymph nodes (C771) and cervical lymph nodes (C770) and involvement of the stomach (C169). No further information is available. Code to lymph node, NOS (C779).
    - ***Example 2:*** The patient has involvement of two extranodal sites and regional lymph nodes for only one of those sites. If the site of origin cannot be determined, code the primary site to lymph nodes, NOS (C779).
    - ***Example 3:*** The patient has a history of Stage II lymphoma. No other information is available. Code to lymph nodes, NOS (C779).

Rule PH23: Proof of extension from regional lymph nodes into an organ

1. **Applicable for Hodgkin & non-Hodgkin Lymphomas only.** Code the primary site to the lymph node region as defined by ICD-O when there is proof of extension from the regional lymph nodes into an organ. In rare cases a lymphoma may spread from lymph nodes to an extranodal site.
2. If there is additional involvement, this rule may not apply.
    - ***Example***: Patient presents with abdominal adenopathy. Surgical exploration documents direct invasion of the stomach from the regional lymph nodes. Code abdominal lymph nodes (C772). *Other involvement would be recorded in stage*.

Rule PH24: Organ involvement only

1. Code the primary site to the organ when the neoplasm is present only in an organ.
    a. This rule does **not** apply to bone marrow, or metastatic sites. (See Primary site coding tips). These are recorded in stage.
    b. If there is lymph node involvement, see Rule PH25.
2. **Includes lymphomas that are primary in the spleen.**
    a. Splenic primaries are rare. Histologies that arise in the spleen include splenic marginal zone lymphoma (9689/3); hepatosplenic T-cell lymphoma (9716/3); splenic B-cell lymphoma/leukemia, unclassifiable (9591/3); splenic diffuse red pulp small B-cell lymphoma (9591/3); splenic marginal zone diffuse variant (9591/3); splenic EBV-associated B-cell lymphoproliferative disorder (9680/3).
    b. If there is splenic involvement and the histology is none of those listed above, review all documentation to determine if there is involvement elsewhere. If the only information available is from the biopsy, or the physician states that spleen is the origin, code to spleen (C422).
    c. Follow-back for additional information when the histology is other than those listed.

    - **Case Scenario from Ask a SEER Registrar:** Bone marrow biopsy shows Mantle cell lymphoma, blastoid variant. (9673/3). MRI ABD lesion involving the midportion and spleen has characteristics suggestive of evolving infarct, which may be secondary to splenomegaly. My coworker stops at PH24 and calls it a Spleen Primary (C422). I stop at PH27 for Unknown Primary because I consider the bone marrow as separate "organ", and there is no evidence of lymphadenopathy and there was no biopsy of the spleen done.
        - You are both wrong. There are only 3 lymphomas that will originate in the spleen: the two splenic lymphomas and DLBCL. Spleen is factored into stage, not primary site. So, you have ruled out spleen as the primary site. Then, all you have left is the bone marrow. Primary site is bone marrow (C421). It's uncommon for lymphomas to originate in the bone marrow, but mantle cell does (see the Hematopoietic database).
    - ***Example*:** Diffuse large B-cell lymphoma present in splenic lesions, upper abdominal lymph nodes, pelvic lymph nodes, and multiple osseous lesion. Bone biopsy of right pelvic bone consistent with DLBCL.

- DLBCL is one of the few lymphomas that can occur de novo in the bone. This would be primary site C419 for Bone, NOS since there are multiple lesions involved. The lymph nodes are regional for the right pelvic bone, so this would be counted as regional lymph node involvement, even though the pelvic bone is not recorded as the primary site.
- Splenic involvement is recorded in stage.

3. **See Primary site coding tips for additional information on coding primary site.**

Rule PH25: Organ involvement with regional lymph nodes

1. Code the primary site to the organ when a neoplasm is present in an **organ** and that **organ's regional lymph nodes.**
   a. This rule does **not** apply to bone marrow. Bone marrow involvement is usually recorded in stage.
   - ***Example 1***: Lymphoma is present in the kidney and peri-renal lymph nodes. Code the primary site to kidney (C649).
   - ***Example 2***: Lymphoma is present in the stomach and the gastric lymph nodes. Code the primary site to stomach, NOS (C169).
   - ***Example 3***: Lymphoma is present in the spleen and the splenic lymph nodes. Code the primary site to spleen (C422).
2. In Stage II, III, and IV disease, distant lymph nodes or other organs, such as spleen, may be involved. Disregard the distant lymph nodes and splenic involvement. Secondary involvement of distant lymph nodes, spleen, and/or bone marrow are recorded in stage.
3. If there are multiple organs involved within a body system that share the same regional lymph nodes, an NOS code can be used to indicate which body system the lymphoma is in.
   - ***Example 1:*** Retroperitoneal biopsy positive for diffuse large B-cel lymphoma. CT Abdomen and Thoracic shows bilateral adrenal masses and diffuse retroperitoneal adenopathy with positive periaortic and perigastric lymph nodes. Enhancing lesions in spleen. PET/CT Scan shows cervical lymph node involvement.
     - Code primary site to Adrenal Gland. Retroperitoneal lymph nodes are regional for Adrenal Gland. Cervical lymph nodes are recorded in stage and the mets at dx field.
     - ***Note:*** Bilateral organs are counted as one organ for purposes of assigning primary site.
   - ***Example 2:*** Left cervical lymph nodes positive for DLBCL. PET scan also showed involvement of the thyroid gland and the lung, plus positive hilar, pelvic and abdominal lymph nodes.
     - Code primary site to Thyroid. Cervical lymph nodes are regional for Thyroid. Record the lung involvement and other lymph nodes in stage and the mets at diagnosis fields.
   - ***Example 3:*** Left tonsil, follicular dendritic cell sarcoma. CT neck imaging revealed cervical lymph nodes and tonsillar mass. No other involvement. Code primary site to tonsil.
   - ***Example 4:*** CT Abdomen and Pelvis. Multiple hepatic masses. Bulky gastrohepatic, porta hepatis, retroperitoneal and retrocrural adenopathy. Liver biopsy positive for DLBCL
     - Liver and its regional lymph nodes are involved. Assign primary site to liver and the remaining lymph nodes are recorded in stage.
   - **Case Scenario from Ask a SEER Registrar:** CT scan shows masses in the parotid gland bilaterally, and base of tongue, with bilateral cervical lymph node enlargement. Enlarged hilar lymph nodes and lesion seen in liver. Multiple lesion involving the hepatic lobe suspicious for mets.
     - Registrar thought this was a C779; however, this is a head and neck lymphoma with regional lymph node involvement (bilateral cervical nodes) with mets to distant lymph nodes (hilar), lung, and the liver. Assign primary site C148. Lung, liver, and the distant lymph nodes would be recorded in the mets at diagnosis fields.

- **Case Scenario from Ask a SEER Registrar**: Involvement of two extralymphatic sites: small intestine (terminal ileum) and colon (cecum).Involvement of extranodal site: spleen. No involvement of LN's on imaging. No bone marrow bx done. In following the Hematopoietic manual rules, I stop at PH27 and am instructed to code C809 Unknown Primary. Is this correct?
    - Small intestine and colon are both in the GI tract. A primary site of C269 is much better than coding C809.

4. **See Primary site coding tips for additional information on coding primary site.**

Rule PH26: ONLY bone marrow and/or peripheral blood involvement

1. Leukemias, Myelodysplastic Syndromes, Myeloproliferative neoplasms, and other bone marrow diseases, are ALWAYS coded to C421
    a. See the Hematopoietic database.
2. For lymphomas, bone marrow is only assigned as primary site when a neoplasm is present **ONLY** in the bone marrow and/or peripheral blood
    a. All available physical exams, scans, and other work-up must be **negative** for lymph node(s), tissue(s) and/or organ(s) involvement **OR** no other work-up was done **OR** unknown if other work-up was done.
    b. ***Excludes*** splenic involvement. See Primary site coding tips, #10
    c. Check registry database to see if patient had a previous lymphoma, if so, this is either progression or transformation.
3. Code primary site to C421 when the **only** information available is a positive peripheral blood smear.
4. **See Primary site coding tips for additional information on coding primary site.**
    - ***Example:*** Bone marrow biopsy is positive for diffuse B-cell lymphoma (DLBCL). No other work up performed.
        - Code primary site to C421 (bone marrow). If further workup is done that identifies a primary site, reassign primary site.

Rule PH27: Multiple organs involved WITHOUT lymph node involvement (C809)

Note: For several histologies, a specific primary site can be assigned when there is not enough information to assign primary site. See the Hematopoietic database for this information, which will be in the Primary Site field.

1. **This rule only applies to cases where there is no lymph node involvement. See PH22 if there is lymph node involvement.**
2. For purposes of these rules, bone marrow is not an organ. Bone marrow involvement is recorded in stage.
3. The following are coded to C809
    a. Multiple organs involved and there is NO lymph node involvement
        i. Excludes bone marrow, spleen and common metastatic sites (see Primary site coding tips)
    b. Unknown where the lymphoma originated and there is NO lymph node involvement.
    c. Physician does not document site of origin (Physician's documentation of primary site can be used).

- ***Example 1:*** MALT lymphoma involved in the bone and a breast nodule. No evidence of lymph node involvement. No documentation from the physician for primary site. Assign primary site C809.
- ***Example 2:*** BM bx found diffuse large B-cell lymphoma; CT C/A/P IMP: Osseous mets. No evidence of lymphadenopathy or organ involvement. MD statement that PET scan revealed diffuse skeletal mets and hepatic mets. Assign primary site C809.

- ***Example 3:*** Bone marrow bx: B-lymphoblastic leukemia KMTIA rearrangement, Cerebrospinal fluid: positive for B-ALL involvement
  - **PH27 does not apply**. For this case, the cerebrospinal fluid (CSF) is metastatic disease and does not factor into primary site. Primary site is C421 (bone marrow)
- ***Example 4:*** Per imaging, the patient had widespread bone lesions through the body, with extension of the bone lesions into surrounding soft tissue. There were no organs or lymph nodes involved. Bone marrow bx was negative. Bone biopsy showed DLBCL
  - **PH27 does not apply.** Although there is widespread bone involvement, and there is no indication where it started, primary site would be C419 (Bone, NOS) instead of C809. DLBCL does occur de novo in the bones.

Module 8: NOS and More Specific Histology PH28 – PH29

All hematopoietic and lymphoid neoplasms 9590/3-9993/3

Rule PH28: Non-specific (NOS) histologies

1. Code the non-specific (NOS) histology when the diagnosis is
   - One non-specific histology **AND**
   - Two or more specific histologies **AND**
   - The Heme DB Multiple Primaries Calculator **CONFIRMS** the specific histologies and NOS are the **same primary AND**
     - If the Heme DB Multiple Primaries calculator returns with "new primary," then this is not the correct rule.
   - There is no further information regarding the physician's final diagnosis.
   - Physician may document "differential diagnoses."
2. See Appendix B WHO Classification of Haematolymphoid Tumors Histology Lineage to determine NOS histologies, or look at the same primaries for either the NOS or specific histology, which are found in the Hematopoietic database.
3. See Instructions #3-5 in the Histology Coding Rules for cases with ambiguous terminology.
   - ***Example 1***: The diagnosis is myelodysplastic/myeloproliferative neoplasm unclassifiable (9975/3), polycythemia vera (9950/3), essential thrombocythemia (9962/3). The Heme DB Multiple Primaries Calculator shows that myelodysplastic/myeloproliferative neoplasm unclassifiable and polycythemia vera are the same primary. The Multiple Primaries Calculator also shows that myelodysplastic/myeloproliferative neoplasm unclassifiable and essential thrombocythemia are the same primary. Follow-back produces no additional information. Code the histology myelodysplastic/myeloproliferative neoplasm, unclassifiable (9975/3).
   - ***Example 2***: Pathology report states morphologic features and immunophenotype of low grade B-cell lymphoma are most compatible with lymphoplasmacytic lymphoma or marginal zone lymphoma. The term "compatible with LPL (9671/3) or MZL (9699/3)" means that the immunophenotype was not definitely diagnostic for either specific disease. Default to the NOS diagnosis, the B-cell lymphoma, (9591/3).

Rule PH29: Specific and non-specific histologies

1. Code the specific histology when the diagnosis is
   - One non-specific (NOS) histology **AND**
   - One specific histology AND.
   - Use the Heme DB Multiple Primaries Calculator to confirm that the NOS and specific histology are the same primary.
2. See Appendix B WHO Classification of Haematolymphoid Tumors Histology Lineage to determine NOS histologies or look at the same primaries for either the NOS or specific histology.
3. See Instructions #3-5 in the Histology Coding Rules for cases with ambiguous terminology. If the specific histology diagnosis includes ambiguous terminology, code the NOS histology.

Module 9: Coding Primary Site and Histology PH30 – PH31

All hematopoietic and lymphoid neoplasms 9590/3-9993/3

Use Only When Modules 1-8 are Not Applicable

Rule PH30: Rules PH1-PH29 do not apply

1. Use the Heme DB to determine the primary site and histology when rules PH1-PH29 do **not** apply.
2. For primary site, use the information under Primary Site(s) in the Heme DB **and/or** the Abstractor Notes as instructed in the introduction of this manual.

Rule PH31: Coding numerically higher ICD-O-code

1. Code the histology to the numerically higher ICD-O code when the histology code cannot be determined using the Heme DB.
2. This rule should rarely be used.

This is the end of the rules for coding primary site and histology.

Appendix A
History of Hematopoietic and Lymphoid Neoplasm Coding

***Note*: The 2024 release of the Hematopoietic Manual and Database is based on the** *World Health Organization Classification of Tumours of Haematopoietic and Lymphoid Tissues*. 5th Edition, World Health Organization, 2024.

The Hematolymphoid Tumors 5th edition, WHO Blue Book (2024)

Excerpt from the introduction to the 5th edition

"Evidence-based classification of disease is fundamental for the treatment of individual patients; for monitoring of global disease incidence; and for investigating all aspects of disease causation, prevention, and therapy. The World Health Organization (WHO) classification of haematolymphoid tumours has provided a global reference since its third edition was published in 2001. The definitions laid down in the successive WHO classifications have not only been adopted for use by pathologists, clinicians, and basic and translational research scientists, but they have also been incorporated into the International Classification of Diseases (ICD) and have thus served as a global reference for epidemiological monitoring across national and international health policy organizations."

"The fifth edition of the WHO classification of haematolymphoid tumours (WHO-HAEM5) is the first major update to the classification since the publication of the fourth edition in 2008, which was followed by a revision in 2017. While this classification builds on prior editions, it incorporates several fundamental structural and content updates that reflect scientific developments and clinical advances that occurred in the years following the publication of the fourth edition. The current edition has enhanced the hierarchical organization of the classification, improved the clarity and practicability of disease categories, and incorporated for the first time a clinical advisory component within the fabric of the team that wrote and edited this volume. At a fundamental level, the classification aims to strike a balance between incorporating scientific advances and retaining clinical pertinence and worldwide applicability."

Hematopoietic and Lymphoid Tissues, 4th edition (2008)

The World Health Organization Classification of Tumors of Hematopoietic and Lymphoid Tissues was published in 2008. The 4th Edition of this world-renowned reference describes the current standard classification system for tumors of the hematopoietic and lymphoid systems. The 2008 classification continues to be based on the principles originally outlined in the REAL classification system (grouping by phenotype). These principles have now been applied to the classification of myeloid, lymphoid, mast cell, and histiocytic/dendritic neoplasms. Additionally, when specialized testing demonstrates one or more diseases specific or disease-defining characteristics using immunophenotyping and/or genetic testing, these characteristics have been incorporated into the WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, 4th Edition classification system. Occasionally, a diagnosis may be based primarily on characteristic histologic features alone or in combination with clinical characteristics of the disease such as the presence or absence of a virus. Therefore, any combination of disease-specific characteristics may be described microscopically (histology/morphology), or may be identified by immunohistocytochemistry test, or identified by a specific immunophenotype or genetic abnormality. Part or all of these descriptive characteristics may be included in a new or updated hematopoietic or lymphoid neoplasm term or description (preferred term or synonym) or even in the disease classification (group) to which a specific disease entity may be assigned.

Hematopoietic and Lymphoid Tissues, 3rd edition (2001)

The World Health Organization Classification of Tumors of Hematopoietic and Lymphoid Tissues, 3rd Edition, published in 2001, was based on principles defined in the Revised European-American Classification of Lymphoid Neoplasms (REAL), originally published by the International Lymphoma Study Group in 1994. Both the REAL and current classifications group borderline and malignant tumors into broad categories by hematologic lineage: myeloid, lymphoid,

histiocytic/dendritic, and mast cell. Within these broad categories or phenotypes, tumors may present in solid or circulating phases. Solid phase is the presence of malignant cells in tissue, such as lymph nodes, soft tissues, or organs; generally, these have historically been called lymphomas. The circulating phase is characterized by the presence of malignant cells in the circulating blood or bone marrow; historically these have been called leukemias. According to the introduction to the WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, 4th Edition, the "…distinction between them (lymphomas and leukemias) is artificial. Thus B-cell chronic lymphocytic leukemia and B-cell small lymphocytic lymphoma are simply different manifestations of the same neoplasm, as are lymphoblastic lymphomas and lymphoblastic leukemias and Burkitt lymphoma and Burkitt leukemia" (2001 WHO Classification, page 13).

History of Coding Lymphoid Tissue and Hematopoietic System Neoplasms
Historically, diseases of lymphoid tissues and the hematopoietic system were believed to be separate entities, and the coding structure of the International Classification of Diseases was developed with this in mind. Prior to the early 1990s, the classification systems for lymphomas described malignant cells by their morphologic characteristics; for example, the size and shape of the tumor cell and its pattern of tumor growth and spread. The *International Classification of Diseases for Oncology,* Third Edition says this about the historic classifications:

Over the past 50 years many classifications of leukemia and lymphoma have been proposed. Some of these had a major impact on clinical practice while others are now largely forgotten. For most of this period, however, the distinction between lymphoma and leukemia has been regarded as of fundamental importance and classifications have tended to evolve separately (p. 13).

Compatibility with ICD-10 In order to ensure compatibility with ICD-O-3, there are a number of ways in which the Third Edition of ICD-O differs from the structure of the WHO classification of hematologic malignancies. Separate codes have been allocated to B-cell chronic lymphocytic leukemia and B-cell small lymphocytic lymphoma. These are now recognized to be exactly the same entity, and for presentation of data these categories may therefore be combined. The same argument applies to lymphoblastic lymphoma and acute lymphoblastic leukemia, which are now regarded as the same disease, but for which separate codes are provided. The existence of dual codes for the same WHO classification entities is further discussed in the first errata for ICD-O-3 (5-22-2001):

Resources used
World Health Organization Classification of Haematolymphoid Tumors, 5th edition, World Health Organization, 2024
International Classification of Disease for Oncology, Third Edition, Version 3.2. World Health Organization, 2020.

World Health Organization Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th Edition, World Health Organization, 2008.
World Health Organization Classification of Tumours of Haematopoietic and Lymphoid Tissues. 3rd Edition, World Health Organization, 2001.
International Classification of Diseases for Oncology, Third Edition. World Health Organization, 2000.
Essential Haematology, Fifth edition. Hoffbrand AV, Moss PAH and Pettit JE. Blackwell Publishing, 2006.
Abstracting and Coding Guide for the Hematopoietic Diseases. National Cancer Institute, 2002.

Appendix B
WHO Classification of Haematolymphoid Tumors
Histology Lineage
Updated based on the 5th edition of the WHO Classification of Haematolymphoid Tumors, Parts A and B, 2024.

Use the Hematopoietic Database to identify synonyms that correspond to the WHO Preferred Term.

Table B1: Myeloid precursor lesions

WHO Preferred Term	ICD-O
Clonal hematopoiesis	
Clonal hematopoiesis (CH)	9860/0
Clonal hematopoiesis of indeterminate potential (CHIP)	9860/0
VEXAS syndrome	9860/0
Clonal cytopenia of undetermined significance (CCUS)	9980/1

Table B2: Myeloproliferative neoplasms (MPNs)

WHO Preferred Term	ICD-O
Chronic myeloid leukemia (CML)	9875/3
Chronic neutrophilic leukemia (CNL)	9963/3
Chronic eosinophilic leukemia (CEL)	9964/3
Polycythemia vera (PV)	9950/3
Essential thrombocythemia (ET)	9962/3
Primary myelofibrosis (PMF) • Primary myelofibrosis, prefibrotic • Primary myelofibrosis, fibrotic	9961/3 9961/3 9961/3
Juvenile myelomonocytic leukemia	9946/3
Myeloproliferative neoplasm, NOS (unclassifiable) (See also Table B5: Myelodysplastic/myeloproliferative (MDS/MPN)	9975/3

Table B3: Mastocytosis

WHO Preferred Term	ICD-O
Cutaneous mastocytosis	9740/1
• Maculopapular cutaneous mastocytosis	9740/1
• Diffuse cutaneous mastocytosis	9740/1
• Mastocytoma	9740/1
Systemic mastocytosis	9741/1
• Indolent systemic mastocytosis	9741/1
• Bone marrow mastocytosis	9741/1
• Smoldering systemic mastocytosis	9741/1
Aggressive systemic mastocytosis	9741/3
Systemic mastocytosis with an associated hematological neoplasm	9741/3
Mast cell leukemia	9742/3
Mast cell sarcoma	9740/3

Table B4: Myelodysplastic neoplasms

WHO Preferred Term	ICD-O
Myelodysplastic neoplasms with defining genetic abnormalities	
Myelodysplastic neoplasm with low blasts and 5q deletion	9986/3
Myelodysplastic neoplasm with low blasts and *SF3B1* mutation	9982/3
Myelodysplastic neoplasm with biallelic *TP53* inactivation	9985/3
Myelodysplastic neoplasms defined morphologically	
Myelodysplastic neoplasm with low blasts	9985/3
• Myelodysplastic neoplasm with low blasts and single-lineage dysplasia	9980/3
• Myelodysplastic neoplasm with low blasts and multilineage dysplasia[†]	9985/3
Myelodysplastic neoplasm, hypoplastic	9985/3
Myelodysplastic neoplasm with increased blasts	9983/3
• Myelodysplastic neoplasm with increased blasts-1	9983/3
• Myelodysplastic neoplasm with increased blasts-2	9983/3
• Myelodysplastic neoplasm with increased blasts and fibrosis	9983/3
Myelodysplastic neoplasms of childhood	
Childhood myelodysplastic neoplasm with low blasts	9985/3
• Childhood myelodysplastic neoplasm with low blasts, hypocellular	
Childhood myelodysplastic neoplasm with increased blasts	9985/3

WHO Preferred Term	ICD-O
Other	
Myelodysplastic neoplasm with ring sideroblasts and multilineage dysplasia (MDS-RD-MLD) *(Note: This term is not included in the WHO 5th edition)*	9993/3
Myelodysplastic syndrome, NOS *(Note: This term is not included in the WHO 5th edition)*	9989/3

Table B5: Myelodysplastic/myeloproliferative (MDS/MPN)

WHO Preferred Term	ICD-O
Chronic myelomonocytic leukemia • Myelodysplastic chronic myelomonocytic leukemia • Myeloproliferative chronic myelomonocytic leukemia	9945/3
Myelodysplastic/myeloproliferative neoplasm with neutrophilia	9876/3
Myelodysplastic/myeloproliferative neoplasm with *SF3B1* mutation and thrombocytosis (See also Table B4: Myelodysplastic neoplasms)	9982/3
Myelodysplastic/myeloproliferative neoplasm, NOS (unclassifiable) (See also Table B2: Myeloproliferative neoplasms (MPNs)	9975/3

Table B6: Acute myeloid leukemia

WHO Preferred Term	ICD-O
Acute myeloid leukemia, NOS	9861/3
Acute myeloid leukemia with defining genetic abnormalities	
Acute promyelocytic leukemia with *PML*::*RARA* fusion • Acute promyelocytic leukemia with a variant *RARA* translocation	9866/3
Acute myeloid leukemia with *RUNX1*::*RUNX1T1* fusion	9896/3
Acute myeloid leukemia with *CBFB*::*MYH11* fusion	9871/3
Acute myeloid leukemia with *DEK*::*NUP214* fusion	9865/3
Acute myeloid leukemia with *RBM15*::*MRTFA* fusion	9911/3
Acute myeloid leukemia with *BCR*::*ABL1* fusion	9912/3
Acute myeloid leukemia with *KMT2A* rearrangement	9897/3
Acute myeloid leukemia with *MECOM* rearrangement	9869/3
Acute myeloid leukemia with *NUP98* rearrangement	9861/3
Acute myeloid leukemia with *NPM1* mutation	9877/3
Acute myeloid leukemia with *CEBPA* mutation	9878/3
Acute myeloid leukemia, myelodysplasia-related	9895/3
Acute myeloid leukemia with other defined genetic alterations	9861/3

WHO Preferred Term	ICD-O
• Acute myeloid leukemia with *CBFA2T3*::*GLIS2* fusion • Acute myeloid leukemia with *KAT6A*::*CREBBP* fusion • Acute myeloid leukemia with *FUS*::*ERG* fusion • Acute myeloid leukemia with *MNX1*::*ETV6* fusion • Acute myeloid leukemia with *NPM1*::*MLF1* fusion	9861/3 9861/3 9861/3 9861/3 9861/3
Acute myeloid leukemia with mutated RUNX1 *(Note: This histology is not included in the WHO 5th edition)*	9879/3
Acute myeloid leukemia defined by differentiation	
Acute myeloid leukemia with minimal differentiation	9872/3
Acute myeloid leukemia without maturation	9873/3
Acute myeloid leukemia with maturation	9874/3
Acute basophilic leukemia	9870/3
Acute myelomonocytic leukemia	9867/3
Acute monocytic leukemia	9891/3
Acute erythroid leukemia	9840/3
Acute megakaryoblastic leukemia	9910/3
Acute panmyelosis with myelofibrosis *(Note: This term is not included in the WHO 5th edition)*	9931/3
Myeloid Sarcoma	
Myeloid Sarcoma	9930/3

Table B7: Secondary myeloid neoplasms

WHO Preferred Term	ICD-O
Myeloid neoplasms and proliferations associated with antecedent or predisposing condition	
Myeloid neoplasm post cytotoxic therapy • Myelodysplastic neoplasm post cytotoxic therapy • Myelodysplastic/myeloproliferative neoplasm post cytotoxic therapy • Acute myeloid leukemia post cytotoxic therapy	9920/3
Myeloid neoplasms associated with germline predisposition (code as condition)	
Myeloid leukemia associated with Down syndrome	9898/3
Transient abnormal myelopoiesis	9898/1

Table B8: Myeloid/lymphoid neoplasms

WHO Preferred Term	ICD-O
Myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions	
Myeloid/lymphoid neoplasm with *PDGFRA* rearrangement	9965/3
Myeloid/lymphoid neoplasm with *PDGFRB* rearrangement	9966/3
Myeloid/lymphoid neoplasm with *FGFR1* rearrangement	9967/3
Myeloid/lymphoid neoplasm with *JAK2* rearrangement	9968/3
Myeloid/lymphoid neoplasm with *FLT3* rearrangement	9968/3
Myeloid/lymphoid neoplasm with *ETV6*::*ABL1* fusion	9968/3
Myeloid/lymphoid neoplasms with other tyrosine kinase fusion genes	9968/3

Table B9: Acute leukemias of mixed or ambiguous lineage

WHO Preferred Term	ICD-O
Acute leukemia of ambiguous lineage with defining genetic abnormalities	
Mixed-phenotype acute leukemia with *BCR*::*ABL1* fusion	9806/3
Mixed-phenotype acute leukemia with *KMT2A* rearrangement	9807/3
Acute leukemia of ambiguous lineage with other defined genetic alteration • Mixed-phenotype acute leukemia with *ZNF384* rearrangement • Acute leukemia of ambiguous lineage with *BCL11B* rearrangement	9805/3
Acute leukemia of ambiguous lineage defined immunophenotypically	
Mixed-phenotype acute leukemia, B/myeloid	9808/3
Mixed-phenotype acute leukemia, T/myeloid	9809/3
Mixed-phenotype acute leukemia, rare types	
Mixed-phenotype acute leukemia, B/T Mixed-phenotype acute leukemia, B/T/myeloid Mixed-phenotype acute leukemia, T/megakaryocytic	9805/3 9805/3 9805/3
Acute leukemia of ambiguous lineage, NOS[†]	9805/3
Acute undifferentiated leukemia	9801/3

Table B10: Plasmacytoid dendritic cell neoplasms

WHO Preferred Term	ICD-O
Mature plasmacytoid dendritic cell proliferation associated with myeloid neoplasm	9727/1
Blastic plasmacytoid dendritic cell neoplasm	9727/3

Table B11: Langerhans cell and other dendritic cell neoplasms

WHO Preferred Term	ICD-O
Langerhans cell neoplasms	
Langerhans cell histiocytosis	9751/1
Langerhans cell histiocytosis, disseminated	9751/3
Langerhans cell sarcoma • Primary Langerhans cell sarcoma • Secondary Langerhans cell sarcoma (following or associated with another hematological neoplasm)	9756/3
Other dendritic cell neoplasms	
Indeterminate dendritic cell tumor	9757/3
Interdigitating dendritic cell tumor	9757/3

Table B12: Histiocyte/macrophage neoplasms

WHO Preferred Term	ICD-O
Histiocytic neoplasms	
Juvenile xanthogranuloma (JXG)	9749/1
Erdheim-Chester disease (ECD)	9749/3
Rosai-Dorfman disease (RDD)	9749/3
ALK-positive histiocytosis	9750/3
Histiocytic sarcoma (HS)	9755/3

Table B13: Tumor like lesion with B-cell predominance

WHO Preferred Term	ICD-O
Reactive B-cell–rich lymphoid proliferations that can mimic lymphoma	
IgG4 -related disease (See also Table B17: Plasma cell neoplasms and other diseases with paraproteins)	9760/1
Unicentric Castleman disease	None
Idiopathic multicentric Castleman disease	None
SHV/HHV8-associated multicentric Castleman disease	None

Table B14: Precursor B-cell neoplasms

WHO Preferred Term	ICD-O
B-lymphoblastic leukemias/lymphomas	
B-lymphoblastic leukemia/lymphoma, NOS	9811/3
B-lymphoblastic leukemia/lymphoma with high hyperdiploidy	9815/3

WHO Preferred Term	ICD-O
B-lymphoblastic leukemia/lymphoma with hypodiploidy • B-lymphoblastic leukemia/lymphoma with hypodiploidy, near-haploid • B-lymphoblastic leukemia/lymphoma with hypodiploidy, low hypodiploid • B-lymphoblastic leukemia/lymphoma with hypodiploidy, high hypodiploid	9816/3 9816/3 9816/3 9816/3
B-lymphoblastic leukemia/lymphoma with iAMP21	9811/3
B-lymphoblastic leukemia/lymphoma with *BCR*::*ABL1* fusion	9812/3
B-lymphoblastic leukemia/lymphoma with *BCR*::*ABL1*-like features	9819/3
B-lymphoblastic leukemia/lymphoma with *KMT2A* rearrangement	9813/3
B-lymphoblastic leukemia/lymphoma with *ETV6*::*RUNX1* fusion	9814/3
B-lymphoblastic leukemia/lymphoma with *ETV6*::*RUNX1*-like features	9814/3
B-lymphoblastic leukemia/lymphoma with *TCF3*::*PBX1* fusion	9818/3
B-lymphoblastic leukemia/lymphoma with IGH::*IL3* fusion	9817/3
B-lymphoblastic leukemia/lymphoma with *TCF3*::*HLF* fusion	9818/3
B-lymphoblastic leukemia/lymphoma with other defined genetic alterations • B-lymphoblastic leukemia with *MEF2D* rearrangement • B-lymphoblastic leukemia with *ZNF384* rearrangement • B-lymphoblastic leukemia with *PAX5*alt • B-lymphoblastic leukemia with *PAX5* p.P80R • B-lymphoblastic leukemia with *NUTM1* rearrangement • B-lymphoblastic leukemia with *MYC* rearrangement • B-lymphoblastic leukemia with *DUX4* rearrangement • B-lymphoblastic leukemia/lymphoma, NOS	9811/3 9811/3 9811/3 9811/3 9811/3 9811/3 9811/3 9811/3 9811/3 9811/3

Table B15: Mature B-cell neoplasms

WHO Preferred Term	ICD-O
Preneoplastic and neoplastic small lymphocytic proliferations	
Monoclonal B-cell lymphocytosis, chronic lymphocytic leukemia type • Monoclonal B-cell lymphocytosis, low count or clonal B-cell expansion (chronic lymphocytic leukemia / small lymphocytic lymphoma type)	9823/1
Monoclonal B-cell lymphocytosis, non–chronic lymphocytic leukemia type	9591/1
Chronic lymphocytic leukemia / small lymphocytic lymphoma	9823/1
Splenic B-cell lymphomas and leukemias	
Hairy cell leukemia	9940/3
Splenic marginal zone lymphoma	9689/3

WHO Preferred Term	ICD-O
Splenic diffuse red pulp small B-cell lymphoma	9591/3
Splenic B-cell lymphoma/leukemia with prominent nucleoli	9591/3
Lymphoplasmacytic lymphoma	
Lymphoplasmacytic lymphoma • IgM-type lymphoplasmacytic lymphoma / Waldenström macroglobulinemia • Non–IgM-type lymphoplasmacytic lymphoma / Waldenström macroglobulinemia	9671/3 9761/3 9761/3
Marginal zone lymphoma	
Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue	9699/3
Immunoproliferative small intestinal disease (alpha heavy chain disease) (See also Table B17: Plasma cell neoplasms and other diseases with paraproteins)	9762/3
Primary cutaneous marginal zone lymphoma • Primary cutaneous marginal zone lymphoma, heavy chain class-switched form (Ig G+, IgA+, or IgE+) • Primary cutaneous marginal zone lymphoma, non–class-switched form (IgM+)	9699/3 9699/3 9699/3
Nodal marginal zone lymphoma	9699/3
Paediatric nodal marginal zone lymphoma	9699/3
Follicular lymphoma	
In situ follicular B-cell neoplasm	9695/1
Follicular lymphoma, NOS • Follicular large B-cell lymphoma • Follicular lymphoma with uncommon features	9690/3 9698/3 9690/3
Follicular lymphoma, grade 2 *(Note: This term is not included in the WHO 5th edition)*	9691/3
Follicular lymphoma, grade 1 *(Note: This term is not included in the WHO 5th edition)*	9695/3
Paediatric-type follicular lymphoma	9690/3
Duodenal-type follicular lymphoma	9695/3
Cutaneous follicle centre lymphoma	
Primary cutaneous follicle centre lymphoma	9597/3
Mantle cell lymphoma	
In situ mantle cell neoplasm	9673/1
Mantle cell lymphoma • Cyclin D1–positive mantle cell lymphoma • Cyclin D1–negative mantle cell lymphoma	9673/3 9673/3 9673/3
Leukemic non-nodal mantle cell lymphoma	9673/3

WHO Preferred Term	ICD-O
Large B-cell lymphomas	
Diffuse large B-cell lymphoma, NOS	9680/3
Diffuse large B-cell lymphoma, centroblastic subtype	9680/3
Diffuse large B-cell lymphoma, immunoblastic subtype	9680/3
Diffuse large B-cell lymphoma, anaplastic subtype	9680/3
Diffuse large B-cell lymphoma, germinal-centre B-cell subtype	9680/3
Diffuse large B-cell lymphoma, activated B-cell subtype	9680/3
Diffuse large B-cell lymphoma with *MYC* and *BCL6* rearrangements	9680/3
T-cell/histiocyte–rich large B-cell lymphoma	9688/3
• T-cell/histiocyte–rich large B-cell lymphoma, de novo[†]	9688/3
• T-cell/histiocyte–rich large B-cell lymphoma, progressed from nodular lymphocyte-predominant Hodgkin lymphoma	9688/3
Diffuse large B-cell lymphoma / high-grade B-cell lymphoma with *MYC* and *BCL2* rearrangements (DLBCL/HGBL-*MYC*/*BCL2*)	9680/3
• DLBCL/HGBL-*MYC*/*BCL2* without *BCL6* rearrangement	9680/3
• DLBCL/HGBL-*MYC*/*BCL2* with *BCL6* rearrangement	9680/3
• DLBCL/HGBL-*MYC*/*BCL2* (with or without *BCL6* rearrangement) with TdT expression	9680/3
ALK-positive large B-cell lymphoma	9737/3
Large B-cell lymphoma with *IRF4* rearrangement	9698/3
High-grade B-cell lymphoma with 11q aberration	9687/3
Lymphomatoid granulomatosis, NOS	9766/1
• Lymphomatoid granulomatosis, grade 1	9766/1
• Lymphomatoid granulomatosis, grade 2	9766/1
• Lymphomatoid granulomatosis, grade 3	9766/3
EBV-positive diffuse large B-cell lymphoma	9680/3
Diffuse large B-cell lymphoma associated with chronic inflammation	9680/3
Fibrin-associated large B-cell lymphoma	9678/3
Fluid overload–associated large B-cell lymphoma	9678/3
Plasmablastic lymphoma	9735/3
Primary large B-cell lymphoma of immune-privileged sites	9680/3
• Primary large B-cell lymphoma of the CNS	9680/3
• Primary large B-cell lymphoma of the vitreoretina	9680/3
• Primary large B-cell lymphoma of the testis	9680/3
Primary cutaneous diffuse large B-cell lymphoma, leg type	9680/3
Intravascular large B-cell lymphoma	9712/3

WHO Preferred Term	ICD-O
Mediastinal large B-cell lymphoma	9679/3
Mediastinal grey zone lymphoma	9596/3
High-grade B-cell lymphoma, NOS • High-grade B-cell lymphoma, NOS, with *MYC* and *BCL6* rearrangements	9680/3 9680/3
Burkitt lymphoma	
Burkitt lymphoma • Endemic Burkitt lymphoma • Sporadic Burkitt lymphoma • Immunodeficiency-associated Burkitt lymphoma	9687/3 9687/3 9687/3 9687/3
EBV-associated Burkitt lymphoma	9687/3
EBV-negative Burkitt lymphoma	9687/3
KSHV/HHV8-associated B-cell lymphoid proliferations and lymphomas	
Primary effusion lymphoma • Extracavitary primary effusion lymphoma†	9678/3 9678/3
KSHV/HHV8-positive diffuse large B-cell lymphoma† • KSHV/HHV8-positive germinotropic lymphoproliferative disorder	9738/3 None
Lymphoid proliferations and lymphomas associated with immune deficiency and dysregulation	
Hyperplasia's arising in immune deficiency/dysregulation	None
Polymorphic lymphoproliferative disorders arising in immune deficiency/dysregulation *(Note: WHO has this as a /1 for 5th edition; however, for 2025+, this is a /3 for the US and Canada)*	9971/3
EBV-positive mucocutaneous ulcer	9680/1
Lymphomas arising in immune deficiency/dysregulation (code as type of lymphoma)Inborn error of immunity–associated lymphoid proliferations and lymphomas (code as type of lymphoma)	None

Table B16: Hodgkin lymphoma

WHO Preferred Term	ICD-O
Classic Hodgkin lymphoma, NOS • Classic Hodgkin lymphoma, nodular sclerosis • Classic Hodgkin lymphoma, mixed cellularity • Classic Hodgkin lymphoma, lymphocyte-rich • Classic Hodgkin lymphoma, lymphocyte-depleted • Hodgkin lymphoma, lymphocyte depletion, reticular (*Note: This term is not included in the WHO 5th edition)*	9650/3 9663/3 9652/3 9651/3 9653/3 9655/3

WHO Preferred Term	ICD-O
Nodular lymphocyte-predominant Hodgkin lymphoma	9659/3

Table B17: Plasma cell neoplasms and other diseases with paraproteins

WHO Preferred Term	ICD-O
Monoclonal gammopathies	
Cold agglutinin disease (See also Table B13: Tumor like lesion with B-cell predominance)	9760/1
IgM monoclonal gammopathy of undetermined significance	9761/1
Non-IgM monoclonal gammopathy of undetermined significance • IgG monoclonal gammopathy of undetermined significance • IgA monoclonal gammopathy of undetermined significance • IgD monoclonal gammopathy of undetermined significance • IgE monoclonal gammopathy of undetermined significance • Light chain monoclonal gammopathy of undetermined significance	9765/1 9765/1 9765/1 9765/1 9765/1 9765/1
Monoclonal gammopathy of renal significance	9765/1
Diseases with monoclonal immunoglobulin deposition	
Immunoglobulin-related amyloidosis (AL amyloidosis) • Systemic AL amyloidosis • Localized AL amyloidosis • Heavy chain AL amyloidosis	9769/1 9769/1 9769/1 9769/1
Monoclonal immunoglobulin deposition disease • Light chain deposition disease • Light and heavy chain deposition disease • Heavy chain deposition disease *Heavy chain diseases*	9769/1 9769/1 9769/1 9769/1
Mu heavy chain disease Gamma heavy chain disease Alpha heavy chain disease (See also Table B15: Mature B-cell neoplasms)	9762/3 9762/3 9762/3
Plasma cell neoplasms	
Plasmacytoma • Solitary plasmacytoma of bone • Extramedullary plasmacytoma	 9731/3 9734/3

WHO Preferred Term	ICD-O
Plasma cell myeloma	9732/3
• Smoldering (asymptomatic) myeloma	9732/3
• Non-secretory myeloma	9732/3
• Plasma cell leukemia	9732/3
Plasma cell neoplasms with associated paraneoplastic syndrome (code as tumor type)	None
• Paraneoplastic syndrome (including AESOP)	
• POEMS syndrome	
• TEMPI syndrome	

Table B18: Tumor-like lesions with T-cell predominance

WHO Preferred Term	ICD-O
Kikuchi–Fujimoto disease	None
Autoimmune lymphoproliferative syndrome (ALPS)	None
• ALPS with germline homozygous or heterozygous *FAS* mutation	None
• ALPS with somatic *FAS* mutation	None
• ALPS with other specified FAS-pathway germline mutation (*FASLG*, *CASP10*, *CASP8*, *FADD*)	None
• ALPS with unknown underlying mutation	None
Indolent T-lymphoblastic proliferation	None

Table B19: Precursor T-cell neoplasms

WHO Preferred Term	ICD-O
T-lymphoblastic leukemia/lymphoma	
T-lymphoblastic leukemia/lymphoma, NOS	9837/3
Early T-precursor lymphoblastic leukemia/lymphoma	9837/3

Table B20: Mature T-cell and NK-cell neoplasms

WHO Preferred Term	ICD-O
Mature T-cell and NK-cell leukemias	
T-prolymphocytic leukemia	9834/3
T-large granular lymphocytic leukemia	9831/3
NK-large granular lymphocytic leukemia	9831/3

WHO Preferred Term	ICD-O
Adult T-cell leukemia/lymphoma • Smoldering adult T-cell leukemia/lymphoma • Chronic adult T-cell leukemia/lymphoma • Lymphoma adult T-cell leukemia/lymphoma • Acute adult T-cell leukemia/lymphoma	9827/3
Sezary syndrome	9701/3
Aggressive NK-cell leukemia	9948/3
Primary cutaneous T-cell lymphoid proliferations and lymphomas	
Primary cutaneous CD4-positive small or medium T-cell lymphoproliferative disorder	9709/1
Primary cutaneous acral CD8-positive T-cell lymphoproliferative disorder	9709/1
Mycosis Fungoides • Folliculotropic mycosis fungoides • Pagetoid reticulosis • Granulomatous slack skin disease	9700/3
Primary cutaneous CD30-positive T-cell lymphoproliferative disorder, lymphomatoid papulosis • Primary mucosal CD30-positive T-cell lymphoproliferative disorder • Lymphomatoid papulosis subtypes A, B, C, D, E • Lymphomatoid papulosis with *DUSP22* locus rearrangement	9718/1
Primary cutaneous CD30-positive T-cell lymphoproliferative disorder, primary cutaneous anaplastic large cell lymphoma	9718/3
Subcutaneous panniculitis-like T-cell lymphoma	9708/3
Primary cutaneous gamma-delta T-cell lymphoma	9726/3
Primary cutaneous CD8-positive aggressive epidermotropic cytotoxic T-cell lymphoma	9709/3
Primary cutaneous peripheral T-cell lymphoma, NOS	9709/3
Intestinal T-cell and NK-cell lymphoid proliferations and lymphomas	
Indolent T-cell lymphoma of the gastrointestinal tract	9702/1
Indolent NK-cell lymphoproliferative disorder of the gastrointestinal tract	9702/1
Enteropathy-associated T-cell lymphoma	9717/3
Monomorphic epitheliotropic intestinal T-cell lymphoma	9717/3
Intestinal T-cell lymphoma, NOS	9717/3
T-gamma lymphoproliferative disorder *(Note: This term is not included in the WHO 5th edition)*	9768/1
Hepatosplenic T-cell lymphoma	
Hepatosplenic T-cell lymphoma	9716/3
Anaplastic large cell lymphoma	
ALK-positive anaplastic large cell lymphoma	9714/3

WHO Preferred Term	ICD-O
ALK-negative anaplastic large cell lymphoma	9715/3
Breast implant–associated anaplastic large cell lymphoma	9715/3
Nodal T follicular helper cell lymphoma	
Nodal T follicular helper cell lymphoma, angioimmunoblastic type	9705/3
Nodal T follicular helper cell lymphoma, follicular type	9702/3
Nodal T follicular helper cell lymphoma, NOS	9702/3
Other peripheral T-cell lymphomas	
Peripheral T-cell lymphoma, NOS	9702/3
EBV-positive T-cell and NK-cell lymphomas	
EBV-positive nodal T- and NK-cell lymphoma	9702/3
Extranodal NK/T-cell lymphoma	9719/3
EBV-positive T-cell and NK-cell lymphoid proliferations and lymphomas of childhood	
Severe mosquito bite allergy	None
Hydroa vacciniforme lymphoproliferative disorder	9725/1
Systemic chronic active EBV-positive disease	9725/1
Systemic EBV-positive T-cell lymphoma of childhood	9724/3

Table B21: Mesenchymal dendritic cell neoplasms

WHO Preferred Term	ICD-O
Follicular dendritic cell neoplasms	
Follicular dendritic cell sarcoma	9758/3
EBV-positive inflammatory follicular dendritic cell sarcoma	9758/3
Fibroblastic reticular cell tumour	9759/3

Table B22: Genetic tumour syndromes associated with haematolymphoid tumours

WHO Preferred Term	ICD-O
Fanconi Anemia	
Bloom Syndrome	
Ataxia-telangiectasia	

Table B23: Other histologies

ICD-O-3.2 Preferred Term	ICD-O
Malignant lymphoma, NOS	9590/3
Leukemia, NOS	9800/3
Myeloid leukemia, NOS	9860/3
Lymphoid leukemia, NOS	9820/3
Chronic myeloid leukemia, NOS	9863/3
Prolymphocytic leukemia, NOS	9832/3
Lymphoproliferative disorder	9970/1

Appendix C
Lymph Node/Lymph Node Chain Reference Table

Use this table with the Primary Site and Histology Rules to determine whether involved lymph nodes are in a single ICD-O lymph node region or in multiple ICD-O lymph node regions.
This table contains the names of lymph nodes that have the capsule and sinus structure of true lymph nodes. Lymphoid tissue such as that in the GI tract, tonsils, etc., is not represented in this table.

Note: Pathology reports may identify lymph nodes within most organs, the most common being breast, parotid gland, lung, and pancreas. The lymph nodes in these organs are called intra- (organ name) lymph nodes such as intramammary lymph nodes. We have included the most common intra-organ lymph nodes on this table. For an intra-organ lymph node not listed on the table, code to the ICD-O topography code for that organ's regional lymph node chain(s).

***The right and left are separate regions per AJCC**

Lymph Node/Lymph Node Chain	Use for Multiple Primaries in Heme	ICD-O Lymph Node Region(s)	TNM Staging
Abdominal	C772	Intra-abdominal	Mesenteric
Anorectal (pararectal)	C775	Pelvic	Pelvic, right and left*
Anterior axillary (pectoral)	C773	Axilla or arm	Axillary, right and left*
Anterior cecal (prececal)	C772	Intra-abdominal	Mesenteric
Anterior deep cervical (laterotracheal, recurrent laryngeal, recurrent pharyngeal)	C770	Head, face and neck	Cervical, right and left*
Anterior jugular	C770	Head, face and neck	Cervical, right and left*
Anterior mediastinal	C771	Intrathoracic	Mediastinal
Aortic (ascending, subaortic, NOS)	C771	Intrathoracic	Mediastinal
Aortic (lateral and lumbar)	C772	Intra-abdominal	Para-aortic
Aortico-pulmonary window (subaortic)	C772	Intra-abdominal	Para-aortic
Apical (subclavian)	C770	Head, face and neck	Cervical, right and left*
Appendiceal	C772	Intra-abdominal	Mesenteric
Apical axillary (deep axillary, Level III axillary)	C773	Axilla or arm	Axillary, right and left*
Aselli's glands (nodes near pancreas)	C772	Intra-abdominal	Para-aortic
Auricular (infraauricular, postauricular, preauricalar, retroauricular, NOS)	C770	Head, face and neck	Cervical, right and left*
Axillary (anterior, brachial, deep, lateral, superficial, NOS)	C773	Axilla or arm	Axillary, right and left*
Axillary (Level I [low axillary, superficial axillary], Level II, Level III [apical, deep)	C773	Axilla or arm	Infraclavicular, right and left*
Azygos (lower paratracheal)	C771	Intrathoracic	Mediastinal
Brachial (lateral axillary)	C773	Axilla or arm	Axillary, right and left*
Brachiocephalic	C773	Axilla or arm	Axillary, right and left*

Lymph Node/Lymph Node Chain	Use for Multiple Primaries in Heme	ICD-O Lymph Node Region(s)	TNM Staging
Bronchial	C771	Intrathoracic	Hilar
Bronchopulmonary (hilar) (proximal lobar) (pulmonary root)	C771	Intrathoracic	Hilar
Buccal (buccinator)	C770	Head, face and neck	Cervical, right and left*
Calot's node (cystic, cysto-hepatic triangle or hepato-biliary triangle)	C772	Intra-abdominal	Para-aortic
Cardiac (cardial)	C771	Intrathoracic	Mediastinal
Cardioesophageal (tracheobronchial, tracheal bifurcation)	C771	Intrathoracic	Mediastinal
Carinal (tracheal bifurcation, tracheobronchial)	C771	Intrathoracic	Mediastinal
Caval (para-)	C772	Intra-abdominal	Para-aortic
Cecal (anterior, posterior, prececal, retrocecal, NOS)	C772	Intra-abdominal	Mesenteric
Celiac	C772	Intra-abdominal	Para-aortic
Central compartment (paralaryngeal, prelaryngeal [Delphian]) adjacent to thyroid gland	C770	Head, face and neck	Cervical, right and left*
Cervical, NOS	C770	Head, face and neck	Cervical, right and left*
Cervical paratracheal	C770	Head, face and neck	Cervical, right and left*
Cervical periesophageal	C770	Head, face and neck	Cervical, right and left*
Cloquet's node (inguinal)	C774	Inguinal region or leg	Inguino-femoral, right and left*
Colic (ileocolic, left, mesocolic, middle, right, NOS)	C772	Intra-abdominal	Mesenteric
Common bile duct(pericholedochal)	C772	Intra-abdominal	Para-aortic
Common hepatic	C771	Intrathoracic	Mediastinal
Common iliac	C775	Pelvic	Pelvic, right and left*
Cubital	C773	Axilla or arm	Axillary, right and left*
Cystic (Calot's node, cysto-hepatic triangle or hepato-biliary triangle)	C772	Intra-abdominal	Para-aortic
Cystic duct	C772	Intra-abdominal	Para-aortic
Deep axillary	C773	Axilla or arm	Axillary, right and left*
Deep cervical (lower, middle, upper, NOS)	C771	Intrathoracic	Cervical, right and left*
Delphian node (precricoid)	C770	Head, face and neck	Cervical, right and left*
Deltopectoral	C773	Axilla or arm	Axillary, right and left*
Diaphragmatic, sub	C771	Intrathoracic	Mediastinal
Duodenal	C772	Intra-abdominal	Para-aortic
Epicolic (Foramen of Winslow, omental)	C772	Intra-abdominal	Mesenteric
Epitrochlear	C773	Axilla or arm	Axillary, right and left*
Esophageal (para-, peri-)	C771	Intrathoracic	Mediastinal
Esophageal groove	C770	Head, face and neck	Cervical, right and left*

Lymph Node/Lymph Node Chain	Use for Multiple Primaries in Heme	ICD-O Lymph Node Region(s)	TNM Staging
External iliac	C775	Pelvic	Pelvic, right and left*
Facial (buccal, buccinator, nasolabial)	C770	Head, face and neck	Cervical, right and left*
Femoral (superficial inguinal)	C774	Inguinal region or leg	Inguino-femoral, right and left*
Foramen of Winslow (epicolic, omental)	C772	Intra-abdominal	Mesenteric
Gastric (inferior, left, right, superior, NOS)	C772	Intra-abdominal	Mesenteric
Gastrocolic	C772	Intra-abdominal	Mesenteric
Gastroduodenal	C772	Intra-abdominal	Mesenteric
Gastroepiploic (gastro-omental)	C772	Intra-abdominal	Mesenteric
Gastrohepatic	C772	Intra-abdominal	Mesenteric
Gastropancreatic	C772	Intra-abdominal	Mesenteric
Gerota's node (promontorial, middle sacral)	C775	Pelvic	Para-aortic
Greater curvature	C772	Intra-abdominal	Mesenteric
Greater omentum (greater omental)	C772	Intra-abdominal	Mesenteric
Groin	C774	Inguinal region or leg	Inguino-femoral, right and left*
Hemorrhoidal (inferior, middle, superior, NOS)	C775	Pelvic	Pelvic, right and left*
Hepatic (hepatic artery, hepatic pedicle, inferior vena cava, lienal, porta hepatis [hilar], NOS)	C772	Intra-abdominal	Para-aortic
Hepatic artery	C772	Intra-abdominal	Para-aortic
Hepatic pedicle	C772	Intra-abdominal	Para-aortic
Hepatoduodenal ligament (hilar)	C772	Intra-abdominal	Para-aortic
Highest deep inguinal (Rosenmuller or Node of Cloquet)	C774	Inguinal region or leg	Inguino-femoral, right and left*
Hilar ([in hilus of liver], hepatoduodenal ligament, porta hepatis, portal, splenic, NOS)	C772	Intra-abdominal	Mesenteric
Hilar (bronchial, bronchopulmonary, proximal lobar, pulmonary root)	C771	Intrathoracic	Hilar, right and left*
Hypogastric (internal iliac)	C775	Pelvic	Pelvic, right and left*
Ileocolic	C772	Intra-abdominal	Mesenteric
Iliac (common, external, internal [hypogastric, obturator])	C775	Pelvic	Pelvic, right and left*
Inferior deep cervical (scalene)	C770	Head, face and neck	Cervical, right and left*
Inferior gastric (right, NOS)	C772	Intra-abdominal	Mesenteric
Inferior hemorrhoidal	C775	Pelvic	Pelvic, right and left*
Inferior (deep) jugular	C770	Head, face and neck	Cervical, right and left*
Inferior mesenteric	C772	Intra-abdominal	Mesenteric
Inferior rectal (hemorrhoidal)	C775	Pelvic	Pelvic, right and left*

Lymph Node/Lymph Node Chain	Use for Multiple Primaries in Heme	ICD-O Lymph Node Region(s)	TNM Staging
Inferior phrenic vein	C771	Intra-thoracic	Mediastinal
Inferior vena cava	C772	Intra-abdominal	Para-aortic
Infraauricular	C770	Head, face and neck	Cervical, right and left*
Infraclavicular (subclavicular)	C773	Axilla or arm	Infraclavicular, right and left*
Infrapyloric	C772	Intra-abdominal	Para-aortic
Infundibulopelvic (utero-ovarian)	C775	Pelvic	Pelvic, right and left*
Inguinal (deep, sublingual, superficial, NOS)	C774	Inguinal region or leg	Inguino-femoral, right and left*
Interaortocaval	C772	Intra-abdominal	Para-aortic
Intercostal	C771	Intrathoracic	Mediastinal
Interlobar (within the lung) (intrapulmonary)	C771	Intrathoracic	Mediastinal
Internal iliac (hypogastric, obturator)	C775	Pelvic	Pelvic, right and left*
Internal jugular (upper deep cervical)	C770	Head, face, and neck	Cervical, right and left*
Internal mammary (parasternal)	C771	Intrathoracic	Mediastinal
Interpectoral (Rotter's node)	C773	Axilla or arm	Axillary, right and left*
Intestinal	C772	Intra-abdominal	Mesenteric
Intra-abdominal	C772	Intra-abdominal	Mesenteric
Intrabronchial, NOS	C771	Intrathoracic	Hilar
Intramammary	C773	Axilla or arm	Axillary, right and left*
Intrapancreatic	C772	Intra-abdominal	Para-aortic
Intraparotid	C770	Head, face and neck	Cervical, right and left*
Intrapelvic	C775	Pelvic	Pelvic, right and left*
Intrapulmonary (segmental, subsegmental)	C771	Intrathoracic	Mediastinal
Jugular (anterior, inferior [deep], internal, lateral, lower, mid, superior, NOS)	C770	Head, face and neck	Cervical, right and left*
Jugulodigastric (subdigastric)	C770	Head, face and neck	Cervical, right and left*
Jugulo-omohyoid (supraomohyoid)	C770	Head, face and neck	Cervical, right and left*
Lateral aortic	C772	Intra-abdominal	Para-aortic
Lateral axillary (brachial)	C773	Axilla or arm	Axillary, right and left*
Lateral compartment (jugular, mid and lower; supraclavicular; upper deep jugular; spinal accessory; retropharyngeal; submandibular; submental)	C770	Head, face and neck	Cervical, right and left*
Lateral jugular	C770	Head, face and neck	Cervical, right and left*
Laterosacral (lateral sacral)	C775	Pelvic	Pelvic, right and left*
Laterotracheal (anterior deep cervical)	C771	Intrathoracic	Cervical, right and left*

Lymph Node/Lymph Node Chain	Use for Multiple Primaries in Heme	ICD-O Lymph Node Region(s)	TNM Staging
Left colic	C772	Intra-abdominal	Mesenteric
Left gastric (superior gastric)	C772	Intra-abdominal	Mesenteric
Left gastrocolic (superior gastrocolic)	C772	Intra-abdominal	Mesenteric
Left supraclavicular (Virchow's node, Trosier's node)	C770	Head, face, and neck	Cervical, right and left*
Leg/Lower limb	C774	Inguinal region or leg	Inguino-femoral, right and left*
Lesser curvature	C772	Intra-abdominal	Mesenteric
Lesser omentum (lesser omental)	C772	Intra-abdominal	Mesenteric
Level I axillary (low axillary) (superficial axillary)	C773	Axilla or arm	Infraclavicular, right and left*
Level II axillary	C773	Axilla or arm	Infraclavicular, right and left*
Level III axillary (deep axillary, high axillary)	C773	Axilla or arm	Infraclavicular, right and left*
Lienal (splenic)	C772	Intra-abdominal	Mesenteric
Lobar (intrapulmonary)	C771	Intrathoracic	Hilar
Lobar (proximal, pulmonary)	C771	Intrathoracic	Hilar
Low axillary (Level I axillary)	C773	Axilla or arm	Infraclavicular, right and left*
Lower deep cervical	C771	Intrathoracic	Cervical, right and left*
Lower jugular	C770	Head, face and neck	Cervical, right and left*
Lower paratracheal (azygos)	C771	Intrathoracic	Mediastinal
Lower periesophageal (intrathoracic esophagus)	C771	Intrathoracic	Mediastinal
Lower peritracheal	C771	Intrathoracic	Mediastinal
Lower thoracic paraesophageal	C771	Intrathoracic	Mediastinal
Lumbar aortic	C772	Intra-abdominal	Para-aortic
Mandibular	C770	Head, face and neck	Cervical, right and left*
Mastoid (postauricular, retroauricular, NOS)	C770	Head, face and neck	Cervical, right and left*
Mediastinal (anterior, posterior, superior, NOS)	C771	Intrathoracic	Mediastinal
Mesenteric (inferior, sigmoid [sigmoidal], superior, NOS)	C772	Intra-abdominal	Mesenteric
Mesocolic	C772	Intra-abdominal	Mesenteric
Mid jugular	C770	Head, face and neck	Cervical, right and left*
Midcolic	C772	Intra-abdominal	Pelvic, right and left*
Middle deep cervical	C771	Intrathoracic	Cervical, right and left*
Middle (right) colic	C772	Intra-abdominal	Mesenteric
Middle hemorrhoidal	C775	Pelvic	Pelvic, right and left*
Middle sacral (Gerota's node, promontorial)	C775	Pelvic	Pelvic, right and left*
Middle thoracic paraesophageal	C771	Intrathoracic	Mediastinal

Lymph Node/Lymph Node Chain	Use for Multiple Primaries in Heme	ICD-O Lymph Node Region(s)	TNM Staging
Nasolabial (facial)	C770	Head, face and neck	Cervical, right and left*
Node of Cloquet's or Rosenmuller (highest deep inguinal)	C774	Inguinal region or leg	Inguino-femoral, right and left*
Obturator (internal iliac)	C775	Pelvic	Pelvic, right and left*
Occipital (suboccipital)	C770	Head, face and neck	Cervical, right and left*
Pancreatic (Aselli's glands [nodes near pancreas], parapancreatic; peripancreatic, NOS)	C772	Intra-abdominal	Para-aortic
Pancreaticoduodenal (anterior, posterior, NOS)	C772	Intra-abdominal	Para-aortic
Pancreaticosplenic (pancreaticolineal)	C772	Intra-abdominal	Mesenteric
Para-aortic	C772	Intra-abdominal	Para-aortic
Parabronchial (peribronchial)	C771	Intrathoracic	Mediastinal
Paracardial	C772	Intra-abdominal	Mesenteric
Paracaval	C772	Intra-abdominal	Para-aortic
Paracervical	C775	Pelvic	Pelvic, right and left*
Paracolic (pericolic)	C772	Intra-abdominal	Para-aortic
Paraesophageal	C771	Intrathoracic	Mediastinal
Paralaryngeal	C770	Head, face and neck	Cervical, right and left*
Parametrial	C775	Pelvic	Pelvic, right and left*
Parapancreatic	C772	Intra-abdominal	Para-aortic
Parapharyngeal	C770	Head, face and neck	Cervical, right and left*
Pararectal (anorectal)	C775	Pelvic	Pelvic, right and left*
Parasternal (internal mammary)	C771	Intrathoracic	Mediastinal
Paratracheal (lower, NOS)	C771	Intrathoracic	Mediastinal
Parotid (peri-, NOS)	C770	Head, face and neck	Cervical, right and left*
Pectoral (anterior axillary)	C773	Axilla or arm	Axillary, right and left*
Pelvic, NOS	C775	Pelvic	Pelvic, right and left*
Peri-aortic	C772	Intra-abdominal	Para-aortic
Peri-parotid	C770	Head, face and neck	Cervical, right and left*
Peri-thymic	C770	Head, face and neck	Cervical, right and left*
Peribronchial (parabronchial)	C771	Intrathoracic	Mediastinal
Pericardial (pericardiac)	C771	Intrathoracic	Mediastinal
Pericaval	C772	Intra-abdominal	Para-aortic
Pericholedochal (common bile duct)	C772	Intra-abdominal	Para-aortic
Pericolic (paracolic)	C772	Intra-abdominal	Mesenteric

Lymph Node/Lymph Node Chain	Use for Multiple Primaries in Heme	ICD-O Lymph Node Region(s)	TNM Staging
Periduodenal	C772	Intra-abdominal	Para-aortic
Periesophageal	C771	Intrathoracic	Mediastinal
Perigastric (except cardiac)	C772	Intra-abdominal	Mesenteric
Peripancreatic	C772	Intra-abdominal	Para-aortic
Periportal	C772	Intra-abdominal	Pelvic, right and left*
Periprostatic	C775	Pelvic	Pelvic, right and left*
Perirectal	C775	Pelvic	Pelvic, right and left*
Periparotid	C770	Head, face and neck	Cervical, right and left*
Perithyroidal	C771	Intrathoracic	Mediastinal
Peritracheal (lower)	C771	Intrathoracic	Mediastinal
Periureteral	C772	Intra-abdominal	Para-aortic
Perivesical	C775	Pelvic	Pelvic, right and left*
Pharyngeal (Delphian node, prepharyngeal, retropharyngeal, NOS)	C770	Head, face and neck	Cervical, right and left*
Phrenic vein (inferior, superior, NOS)	C771	Intra-thoracic	Mediastinal
Popliteal	C774	Inguinal region or leg	Inguino-femoral, right and left*
Porta hepatis [in hilus of liver]	C772	Intra-abdominal	Para-aortic
Portal (portal vein)	C772	Intra-abdominal	Para-aortic
Postauricular (mastoid, retroauricular)	C770	Head, face and neck	Cervical, right and left*
Posterior axillary (subscapular)	C773	Axilla or arm	Axillary, right and left*
Posterior cecal (retrocecal)	C772	Intra-abdominal	Para-aortic
Posterior cervical (spinal accessory)	C770	Head, face and neck	Cervical, right and left*
Posterior mediastinal (tracheoesophageal)	C771	Intrathoracic	Mediastinal
Postglandular	C770	Head, face and neck	Cervical, right and left*
Posterior triangle	C770	Head, face and neck	Cervical, right and left*
Postvascular	C770	Head, face and neck	Cervical, right and left*
Preaortic	C772	Intra-abdominal	Para-aortic
Preauricular	C770	Head, face and neck	Cervical, right and left*
Precarinal	C771	Intrathoracic	Mediastinal
Prececal (anterior cecal)	C772	Intra-abdominal	Mesenteric
Precricoid (Delphian node)	C770	Head, face and neck	Cervical, right and left*
Preglandular	C770	Head, face and neck	Cervical, right and left*
Prepharyngeal (Delphian node), adjacent to thyroid gland; anterior to thyroid isthmus	C770	Head, face and neck	Cervical, right and left*

Lymph Node/Lymph Node Chain	Use for Multiple Primaries in Heme	ICD-O Lymph Node Region(s)	TNM Staging
Presacral	C775	Pelvic	Pelvic, right and left*
Presymphseal	C775	Pelvic	Pelvic, right and left*
Pretracheal	C770	Head, face and neck	Cervical, right and left*
Prevascular	C770	Head, face and neck	Cervical, right and left*
Promontorial (Gerota's node, middle sacral)	C775	Pelvic	Para-aortic
Proximal lobar (bronchopulmonary, hilar, pulmonary root)	C771	Intrathoracic	Hilar
Proximal mesentery	C772	Intra-abdominal	Mesenteric
Pulmonary ligament	C771	Intrathoracic	Mediastinal
Pulmonary (pulmonary root, NOS)	C771	Intrathoracic	Hilar
Pyloric (infrapyloric, subpyloric, suprapyloric)	C772	Intra-abdominal	Para-aortic
Rectal (superior, NOS)	C775	Pelvic	Pelvic, right and left*
Recurrent laryngeal (anterior deep cervical, laterotracheal)	C770	Head, face and neck	Cervical, right and left*
Recurrent pharyngeal (anterior deep cervical)	C770	Head, face and neck	Cervical, right and left*
Renal artery	C772	Intra-abdominal	Para-aortic
Renal hilar	C772	Intra-abdominal	Para-aortic
Retroaortic	C772	Intra-abdominal	Para-aortic
Retro-auricular (mastoid, postauricular)	C770	Head, face and neck	Cervical, right and left*
Retrocaval	C772	Intra-abdominal	Para-aortic
Retrocecal (posterior cecal)	C772	Intra-abdominal	Para-aortic
Retrocrural	C771	Intra-thoracic	Mediastinal
Retropancreatic	C772	Intra-abdominal	Para-aortic
Retroperitoneal	C772	Intra-abdominal	Para-aortic
Retropharyngeal	C770	Head, face and neck	Cervical, right and left*
Retrotracheal (tracheal)	C771	Intrathoracic	Mediastinal
Right colic	C772	Intra-abdominal	Mesenteric
Right gastric	C772	Intra-abdominal	Mesenteric
Rosenmuller or Node of Cloquet (highest deep inguinal)	C774	Inguinal region or leg	Inguino-femoral, right and left*
Rotter's nodes (interpectoral between major and minor pectoralis)	C773	Axilla or arm	Axillary, right and left*
Rouviere's node (retropharyngeal)	C770	Head, face and neck	Cervical, right and left*
Sacral (lateral sacral, laterosacral, middle sacral, presacral, NOS)	C775	Pelvic	Pelvic, right and left*
Sacral (uterosacral)	C774	Pelvic	Pelvic, right and left*
Scalene (inferior deep cervical)	C770	Head, face and neck	Cervical, right and left*
Segmental (intrapulmonary, subsegmental)	C771	Intrathoracic	Mediastinal

Lymph Node/Lymph Node Chain	Use for Multiple Primaries in Heme	ICD-O Lymph Node Region(s)	TNM Staging
Sigmoid (sigmoidal mesenteric, NOS)	C772	Intra-abdominal	Mesenteric
Sister Mary Joseph	C772	Intra-abdominal	Mesenteric
Spermatic vein	C774	Inguinal region or leg	Inguino-femoral, right and left*
Spinal accessory (posterior cervical)	C770	Head, face and neck	Cervical, right and left*
Splenic (hilar, lienal)	C772	Intra-abdominal	Mesenteric
Subaortic	C771	Intrathoracic	Para-aortic
Subcapsular (posterior axillary)	C773	Axilla or arm	Axillary, right and left*
Subcarinal	C771	Intrathoracic	Mediastinal
Subclavian (apical)	C770	Head, face and neck	Cervical, right and left*
Subclavicular (infraclavicular)	C773	Axilla or arm	Infraclavicular, right and left*
Subdigastric (jugulodigastric)	C770	Head, face and neck	Cervical, right and left*
Subinguinal (superficial inguinal)	C774	Inguinal region or leg	Inguino-femoral, right and left*
Sublingual	C770	Head, face and neck	Cervical, right and left*
Submandibular (submaxillary)	C770	Head, face and neck	Cervical, right and left*
Submaxillary (submandibular)	C770	Head, face and neck	Cervical, right and left*
Submental	C770	Head, face and neck	Cervical, right and left*
Suboccipital (occipital)	C770	Head, face and neck	Cervical, right and left*
Subpleural (in the periphery of the lung)	C771	Intrathoracic	Mediastinal
Subpyloric	C772	Intra-abdominal	Para-aortic
Subsegmental (intrapulmonary, segmental)	C771	Intrathoracic	Mediastinal
Substernal	C771	Intrathoracic	Mediastinal
Superficial axillary (Level I axillary)	C773	Axilla or arm	Infraclavicular, right and left*
Superficial inguinal (femoral, subinguinal)	C774	Inguinal region or leg	Inguino-femoral, right and left*
Superior gastric (left gastric)	C772	Intra-abdominal	Mesenteric
Superior gastrocolic (left gastrocolic)	C772	Intra-abdominal	Mesenteric
Superior hemorrhoidal	C775	Pelvic	Pelvic, right and left*
Superior hilum	C772	Intra-abdominal	Pelvic, right and left*
Superior jugular	C770	Head, face and neck	Cervical, right and left*
Superior mediastinal	C771	Intrathoracic	Mediastinal
Superior mesenteric	C772	Intra-abdominal	Pelvic, right and left*
Superior phrenic vein	C771	Intra-thoracic	Mediastinal
Superior rectal (hemorrhoidal)	C775	Pelvic	Pelvic, right and left*
Supraclavicular (transverse cervical)	C770	Head, face and neck	Cervical, right and left*

Lymph Node/Lymph Node Chain	Use for Multiple Primaries in Heme	ICD-O Lymph Node Region(s)	TNM Staging
Supraomohyoid (jugulo-omohyoid)	C770	Head, face and neck	Cervical, right and left*
Suprapancreatic	C772	Intra-abdominal	Para-aortic
Suprapyloric	C772	Intra-abdominal	Para-aortic
Thoracic	C771	Intrathoracic	Mediastinal
Thyroid	C770	Head, face and neck	Cervical, right and left*
Tibial	C774	Inguinal region or leg	Inguino-femoral, right and left*
Tracheal (retrotracheal, NOS)	C771	Intrathoracic	Mediastinal
Tracheal bifurcation (carinal, tracheobronchial)	C771	Intrathoracic	Mediastinal
Tracheobronchial (carinal, tracheal bifurcation)	C771	Intrathoracic	Mediastinal
Tracheoesophageal (posterior mediastinal)	C771	Intrathoracic	Mediastinal
Transverse cervical (supraclavicular)	C770	Head, face, and neck	Cervical, right and left*
Trosier's node (left supraclavicular)	C770	Head, face, and neck	Cervical, right and left*
Upper deep cervical (internal jugular)	C770	Head, face, and neck	Cervical, right and left*
Upper thoracic paraesophageal	C771	Intrathoracic	Mediastinal
Utero-ovarian (infundibulopelvic)	C775	Pelvic	Pelvic, right and left*
Uterosacral	C774	Pelvic	Pelvic, right and left*
Virchow's node (left supraclavicular)	C770	Head, face, and neck	Cervical, right and left*

***The right and left are separate regions per AJCC**

Appendix D: Introduction to Genetic Nomenclature

The information included in Appendix D has been graciously provided by SEER*Educate.

Making sense of all the genetic abnormalities, mutations, and rearrangements involving the hematopoietic and lymphoid neoplasms is challenging. The following information is provided as a brief introduction to some of the nomenclature, genetic alterations and molecular information needed to successfully code hematopoietic histologies. This document is not intended to be inclusive of all terminology you will encounter, but is intended to be an introduction to this subject matter.

Chromosomes

1. Human somatic cells are diploid, meaning they contain 46 chromosomes (2 copies of 23 chromosomes (or 23 pairs))
   - Chromosomes are numbered 1 through 22 and the sex chromosomes are labeled X or Y.
   - Only gametes (egg or sperm cells) are haploid, meaning they have 23 chromosomes each.
2. Hyperdiploid cells have greater than 46 chromosomes (more than the usual number).
3. Hypodiploid cells have less than 46 chromosomes (less than the usual number).
4. Chromosomes are comprised of a **short arm**, labeled "p," and a **long arm**, labeled "q."
   - The location of genetic abnormalities may be further clarified by the arm on which it occurs:
     - ***Example***: A deletion of 5q (del(5q)) indicates there is a deletion on the long arm ("q") of chromosome 5.

How to Translate a Cytogenetic Location

Different genes are in different chromosomes, which are in the nucleus of a cell. Genes are given a genomic address (or a cytogenetic location). Mutations and chromosomal abnormalities may also be described using the cytogenetic location(s) of the mutation/abnormality.

The **cytogenetic location** is comprised of the following:

Chromosome + Arm + Region + Band +/- Sub-band

A mnemonic can help you remember how to interpret the position of gene abnormalities/mutations described: **CARBS** (**C**hromosome + **A**rm + **R**egion + **B**and +/- **S**ub-band)

Notes:

1. The cytogenetic location may, or may not, be given down to the location of the sub-band. When the sub-band is noted, it follows a decimal point (e.g., ".1").

2. The region, band and/or sub-band may be combined and called the "position."

   Example: In describing the TCF3 gene, the cytogenetic report (pathology report, chart note, etc.) may refer to it as: 19p13.3 (instead of TCF3). The term "19p13.3" is the cytogenetic location of that gene and it is broken down as follows:

19	=	Chromosome number 19	**C**
p	=	Short arm (of chromosome 19)	**A**
1	=	Region	**R**
3	=	Band	**B**
.3	=	Sub-band	**S**

Selected Types of Abnormalities/Mutations

Mutation Type	Abbreviation(s)	Description	Nomenclature Example(s)
Insertion *	ins	Addition of DNA into a gene.	ins(18;5)(q21.1;q31.2)
Deletion	del	Removal of DNA; may occur in one or more base pairs, entire gene(s), or chromosome arm (p or q).	del(5q); del(6q21)
Duplication *	dup	DNA abnormally copied one or more times.	dup(21); FLT3-ITD (Where ITD = internal tandem duplication)
Inversion	inv	Rearrangement within a single chromosome in which a chromosome segment undergoes breakage and rearrangement within itself.	inv(16); inv(3); inv(16)(p13.1;q22); inv(3)(q21;q26.2) (Sometimes described as a translocation between a single chromosome: t(16;16)(p13.1;q22))
Translocation	t(x;x) **	Rearrangement between two chromosomes in which a chromosome segment breaks off and attaches to a different chromosome.	t(9;22); t(8;21); t(9;22)(q34;q11.2); t(8;21)(q22;q22)
Trisomy	(XY, +x) **	An extra copy (three total copies) of the specified chromosome.	47(XY,+8); Trisomy 21; Gain of chromosome 9 (Sometimes these are referred to as just "Trisomy" or "Gain of" abnormalities without abbreviation or specific karyotype notation.)
Monosomy	(XY,-x) **	The presence of only one chromosome from the specified chromosome pair.	45(XY,-16); Monosomy 7; Loss of chromosome 5 (Sometimes these are referred to as just "Monosomy" or "Loss of" abnormalities without abbreviation or specific karyotype notation.)

***** Uncommon as a sole genetic/molecular abnormality documented in heme/lymphoid neoplasms.

****** Where lowercase "x" represents the chromosome number involved.

Important Reminders

1. Sometimes the pathology report will not provide the full position of the abnormality/rearrangement, but will only describe the chromosome(s) involved in the rearrangement (e.g., inversion or translocation), or will only describe the genes involved in the rearrangement. Just because the pathologist/clinician did not provide the full position of that rearrangement does not always mean the more specific histology cannot be coded. Keep in mind there are many variations in how pathologists/physicians refer to the same thing.

   Examples
   a. BCR-ABL1 = BCR-ABL fusion protein = Philadelphia (Ph) chromosome = t(9;22)(q34.1;q11.2) = t(9;22)(q34;q11) = t(9;22) = ABL1 at 9q34.1 = BCR at 22q11.2 = BCR-ABL1 major p210 = p210 transcript = BCR-ABL1 minor p190, etc.
   b. CBFB-MYH11 = CBF-beta/MYH11 = inv(16)(p13q22) = inv(16)(p13.1q22) = inv(16)(p13;q22) = t(16;16)(p13.1;q22), etc.

2. Some specified translocations or abnormalities occur between variable chromosomes. That is, only one specific chromosome is identified in the Heme DB and the other is identified by a "v," where "v" stands for variable.

   Example
   a. The translocation "t(v;11q23.3)" is identified in specific types of leukemia/lymphoma. This is a translocation between any chromosome (represented by "v") and 11q23.3. A number of different chromosomes may be substituted for "v."

3. Some heme/lymphoid neoplasms may be associated with multiple genetic abnormalities; not all of them are listed in the Heme DB. For example, acute myeloid leukemia with myelodysplasia-related changes (AML-MRC) does have multiple genetic abnormalities listed in the Heme DB. If a diagnosis of AML-MRC was made, but not all the genetic abnormalities listed match, it does not disprove this diagnosis. AML-MRC is frequently associated with other genetic abnormalities (like monosomies and trisomies) not listed in the Heme DB. Additional information can be found in online resources (see link below).

Additional Online Resources

- https://ghr.nlm.nih.gov/primer#howgeneswork
- http://atlasgeneticsoncology.org

Appendix E: Terms added to the Hematopoietic Database from the WHO 5th edition of Hematolymphoid Tumors

ICD-O Code	Term
9591/3	Splenic B-cell lymphoma/leukemia with prominent nuclei
9673/1	In situ mantle cell neoplasm
9673/3	Cyclin D1-negative MCL Cyclin D1-positive MCL Leukemic non-nodal mantle cell lymphoma
9678/3	Fluid overload-associated large B-cell lymphoma Fluid-overload effusion lymphoma KSHV/HHV8-negative effusion-based lymphoma
9680/3	AIDS-related diffuse large B-cell lymphoma DLBCL/HGBL-MYC/BCL2 with BCL6 rearrangement DLBCL/HGBL-MYC/BCL2 (with or without BCL6 rearrangement) with TdT expression DLBCL/HGBL-MYC/BCL2 without BCL6 rearrangement High grade B-cell lymphoma with MYC and BCL6 rearrangement Immunodeficiency-associated lymphoproliferative disorders Primary large B-cell lymphoma of immune privileged sites Primary large B-cell lymphoma of the testis
9687/3	Burkitt lymphoma, EBV-associated Burkitt lymphoma, EBV-negative
9690/3	BCL2-R-negative CD23-positive follicle centre lymphoma Classic Follicular Lymphoma (cFL) Follicular lymphoma with a predominantly diffuse growth pattern (dFL) Follicular lymphoma with uncommon features Follicular lymphoma with unusual cytological features (uFL) Pediatric follicular lymphoma
9698/3	Follicular large B-cell lymphoma
9699/3	Primary cutaneous marginal zone lymphoma (PCMZL) Primary cutaneous marginal zone lymphoma, heavy chain class-switched form (IgG+, IgA+, or IgE+) Primary cutaneous marginal zone lymphoma, non-class-switched form (IgM+) Primary cutaneous marginal zone lymphoproliferative disorder
9700/3	Hypopigmented mycosis fungoides

ICD-O Code	Term
9702/1	Atypical NK-cell proliferation of the gastrointestinal tract Indolent clonal T-cell lymphoproliferative disorder of the gastrointestinal tract Indolent NK-cell lymphoproliferative disorder of the gastrointestinal tract Lymphomatoid gastropathy NK-cell enteropathy
9702/3	EBV-positive nodal T- and NK-cell lymphoma Nodal EBV+ cytotoxic T-cell lymphoma Nodal peripheral T-cell lymphoma, EBV+ positive Nodal T follicular helper cell lymphoma, follicular type (nTFHL-F) Nodal T follicular helper cell lymphoma, NOS (nTFHL) Primary nodal EBV-positive T/NK-cell lymphoma
9705/3	Nodal T follicular helper cell lymphoma, angioimmunoblastic type (nTFHL-AL)
9709/3	Primary cutaneous peripheral T-cell lymphoma, unspecified
9712/3	Classic intravascular (large) B-cell lymphoma (Classic IVLBCL) Intravascular large B-cell lymphoma, classic Intravascular large B-cell lymphoma, cutaneous Intravascular large B-cell lymphoma, hemophagocytic
9714/3	ALK-positive anaplastic large cell lymphoma, common ALK positive anaplastic large cell lymphoma, Composite ALK positive anaplastic large cell lymphoma, Hodgkin like ALK positive anaplastic large cell lymphoma, lymphohistiocytic ALK positive anaplastic large cell lymphoma, small cell
9717/3	Enteropathy-associated T-cell lymphoma, type 1 Enteropathy-associated T-cell lymphoma, type 2
9718/1	Lymphomatoid papulosis type A Lymphomatoid papulosis type B Lymphomatoid papulosis type C Lymphomatoid papulosis type D Lymphomatoid papulosis type E Lymphomatoid papulosis with DUSP22 locus rearrangement Primary mucosal CD30+ T-cell lymphoproliferative disorder
9718/3	Ocular adnexal T-cell lymphoma Primary mucosal CD30 positive large T-cell lymphoma
9719/3	EBV-positive extranodal NK/T-cell lymphoma NK-lymphoblastic Leukemia/lymphoma

ICD-O Code	Term
9725/1	Hydroa vacciniforme lymphoproliferative disorder, classic Hydroa vacciniforme lymphoproliferative disorder, systemic Systemic chronic active EBV-positive disease
9727/1	Mature plasmacytoid dendritic cell proliferation Mature plasmacytoid dendritic cell proliferation associated with myeloid neoplasm
9738/1	KSHV/HHV8-positive germinotropic lymphoproliferative disorder (GLPD)
9738/3	KSHV/HHV8-positive diffuse large B-cell lymphoma
9750/3	ALK-positive histiocytosis ALK-rearranged histiocytosis ALK-related histiocytosis
9756/3	Langerhans cell sarcoma, Primary Langerhans cell sarcoma, Secondary Malignant histiocytosis of Langerhans phenotype
9757/3	Indeterminate dendritic cell histiocytosis
9758/3	EBV-positive inflammatory follicular dendritic cell sarcoma
9759/3	Fibroblastic reticular cell sarcoma
9760/1	IgG4-related disease Cold agglutinin disease
9761/3	IgM LPL/Waldenstrom Macroglobulinemia type IgM-type lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia Non-IgM-type lymphoplasmacytic lymphoma/Waldenstrom macroglobulinemia Non-IgM LPL/Waldenstrom Macroglobulinemia type
9765/1	IgA MGUS IgD MGUS IgE MGUS IgG MGUS Light chain MGUS Monoclonal gammopathy of renal significance
9766/3	EBV-positive diffuse large B-cell lymphoma
9769/1	Heavy chain AL amyloidosis Immunoglobulin-related amyloidosis (AL amyloidosis), NOS Localized AL amyloidosis

ICD-O Code	Term
9805/3	Acute leukemia of ambiguous lineage with BCL11B rearrangement Acute leukemia of ambiguous lineage with other defined genetic abnormalities Mixed-phenotype acute leukemia B/T Mixed-phenotype acute leukemia B/T/Myeloid Mixed-phenotype acute leukemia, T/megakaryocytic Mixed-phenotype acute leukemia (MPAL) with ZNF384 rearrangement
9806/3	Mixed-phenotype acute leukemia with *BCR::ABL1*
9807/3	Mixed-phenotype acute leukemia with *KMT2A* rearrangement
9811/3	B-lymphoblastic leukemia/lymphoma with DUX4 rearrangement B-lymphoblastic leukemia/lymphoma with MEF2D rearrangement B-lymphoblastic leukemia/lymphoma with MYC rearrangement B-lymphoblastic leukemia/lymphoma NUTM1 rearrangement B-lymphoblastic leukemia/lymphoma with other defined genetic alterations B-lymphoblastic leukemia/lymphoma with PAX5 alt B-lymphoblastic leukemia/lymphoma with PAX5p.P80R B-lymphoblastic leukemia/lymphoma with ZNF384 rearrangement
9812/3	B-(acute) lymphoblastic leukemia/lymphoma (B-ALL) with BCR::ABL1 fusion
9813/3	B-lymphoblastic leukemia/lymphoma with *KMT2A* rearrangement
9814/3	B-lymphoblastic leukemia/lymphoma with ETV6:RUNX1 fusion
9816/3	B-ALL with high hypodiploidy B-ALL with low hypodiploidy B-ALL with near-haploidy
9817/3	B-lymphoblastic leukemia/lymphoma with *IGH::IL3* fusion
9818/3	B-lymphoblastic leukemia/lymphoma with TCF3::PBX1
9819/3	Philadelphia-like (Ph-like) B-ALL *BCR::ABL1*-like B-ALL/LBL
9823/1	MBL, low count or clonal B-cell expansion (CLL/SLL) type
9827/3	Cutaneous adult T-cell leukemia/lymphoma
9860/0	Clonal hematopoiesis (CH) Clonal hematopoiesis, age related (ARCH) Clonal hematopoiesis of indeterminate potential (CHIP) VEXAS syndrome

ICD-O Code	Term
9861/3	Acute myeloid leukemia with CBFA2T3::GLIS2 fusion Acute myeloid leukemia with KAT6A::CREBBP fusion Acute myeloid leukemia with DEK::NUP214 fusion Acute myeloid leukemia with FUS::ERG fusion Acute myeloid leukemia with MNX1::ETV6 fusion Acute myeloid leukemia with NPM1::MLF1 fusion Acute myeloid leukemia with NUP98 rearrangement Acute myeloid leukemia with other defined genetic alterations Acute myeloid leukemia with RUNX1T3 (CBFA2T3):: GLIS2
9871/3	Acute myeloid leukemia with CBFB rearrangement
9876/3	Myelodysplastic/myeloproliferative neoplasm with neutrophilia
9895/3	Acute myeloid leukemia post myelodysplastic-myeloproliferative neoplasm
9897/3	Acute myeloid leukemia with KMT2A rearrangement Acute myeloid leukemia with KMT2A::MLLT3 or other exact fusion Acute myeloid leukemia with t(9;11)(p21.3; q23.3) or other exact balanced translocation
9912/3	Acute myeloid leukemia with t(9;22)(q34;q11.2)
9920/3	Acute myeloid leukemia post cytotoxic therapy Myeloid neoplasm post cytotoxic therapy Myelodysplastic/myeloproliferative neoplasm post cytotoxic therapy
9945/3	Myelodysplastic chronic myelomonocytic leukemia Myeloproliferative chronic myelomonocytic leukemia
9946/3	JMML in children with CBL syndrome JMML in neurofibromatosis type 1 (NF1) JMML-like disorders in children with Noonan syndrome (NS) KRAS-mutated JMML NRAS-mutated JMML PTPN11-mutated JMML
9966/3	Chronic myelomonocytic leukemia with eosinophilia associated with t(5;12) Myeloid neoplasms associated with *PDGFRB* rearrangement
9968/3	Myeloid/lymphoid neoplasm with ETV6::ABL1 fusion Myeloid/lymphoid neoplasm with FLT3 rearrangement Myeloid/lymphoid neoplasm with other tyrosine kinase fusion genes

ICD-O Code	Term
9982/3	MDS with low blasts and ring sideroblasts Myelodysplastic neoplasm with low blasts and SF3B1 mutation Myelodysplastic neoplasm with low blast count and SF3B1 Myelodysplastic/myeloproliferative neoplasm with SF3B1 mutation and thrombocytosis
9983/3	Childhood myelodysplastic neoplasm with excess blasts Myelodysplastic neoplasm with increased blasts and fibrosis
9985/3	Myelodysplastic neoplasm, hypoplastic Myelodysplastic neoplasm with low blasts, NOS Myelodysplastic neoplasm with low blasts and multilineage dysplasia Myelodysplastic neoplasm with multi-hit *TP53* inactivation
9986/3	Myelodysplastic syndrome with low blasts and 5q deletion