ONCOLOGY: CYTOGENETIC TESTING

OVERVIEW

Cytogenetic analysis of solid tumors and hematologic malignancies aims to both classify the type of tumor or cancer present and also to identify somatic oncogenic mutations in cancer. These mutations, often called “driver” mutations, are becoming increasingly useful for targeted therapy selection, and may give insight into prognosis and treatment response in a subset of cancers. In addition, molecular analysis of solid tumors and hematologic malignancies, in particular, can also aid in making a diagnosis of a specific type of malignancy. For solid tumors, molecular analysis can be performed via direct testing of the tumor (which is addressed in this policy) or via circulating tumor DNA or circulating tumor cells (CTCs) (see Other Related Policies). For hematologic malignancies, molecular analysis can be performed on blood samples or bone marrow biopsy samples (skin or buccal cells/saliva is occasionally used in patients who have received a hematopoietic stem cell transplant).

POLICY REFERENCE TABLE

Below is a list of higher volume tests and the associated laboratories for each coverage criteria section. This list is not all inclusive.

Coverage Criteria Sections	Example Tests (Labs)	Common CPT Codes	Common ICD Codes	Ref
ALK Rearrangement Analysis	ALK Rearrangement, FISH	88271, 88274, 88275, 88291	C34, C73	1, 4, 5
BCR/ABL Rearrangement Analysis	BCR-ABL FISH	88271, 88274, 88275, 88291	C91.00-C91.02, D45, D47.1, D47.3	8, 9, 10, 11, 12
Bladder Cancer Diagnostic and Recurrence FISH Tests	UroVysion®, Abbott Molecular	88120, 88121	C67.0-C67.9, D09.0, D49.4, R31.9, Z85.51	17, 20, 21

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) FISH Panel Analysis	FISH CLL Panel, Blood (Johns Hopkins Medical Institutions - Pathology Laboratory) Chronic Lymphocytic Leukemia (CLL) Profile, FISH (LabCorp) Chronic Lymphocytic Leukemia (CLL) Prognostic Panel, Comprehensive (Quest Diagnostics)	88271, 88274, 88275, 88291	C91, C94, C95, Z85.6	13
ERBB2 (*HER2*) Amplification Analysis	ERBB2 FISH (or CISH) Analysis	88341, 88342, 88360, 88361	C08, C15, C16, C18, C19, C20, C50	2, 6, 7, 14, 15
Multiple Myeloma FISH Panel Analysis	Myeloma, FISH, Fixed Cells (Mayo Medical Laboratories) Multiple Myeloma (MM) Profile, FISH (LabCorp) Multiple Myeloma Panel by FISH (ARUP Laboratories) FISH Profile Multiple Myeloma, Blood (Johns Hopkins Medical Institutions - Pathology Laboratory)	88271, 88274, 88275, 88291	C90	16, 19
NTRK Fusion Analysis	NTRK1/2/3 FISH Analysis	88271, 88274, 88275, 88291, 88341, 88342, 88360, 88361 88373, 88374, 88377	C00-D49	2, 3, 5, 6, 7, 12, 14, 18, 22, 23, 24
PD-L1 Protein Expression Analysis	PD-L1 IHC Analysis	88341, 88342, 88360, 88361	C00-D49	1, 3, 6, 7, 14, 15, 17, 18
PML/RARA Rearrangement Analysis	PML/RARA Rearrangement Analysis	88271, 88274, 88275, 88291	C91-C95	8
ROS1 Rearrangement Analysis	ROS1 FISH Analysis	88271, 88274, 88275, 88291, 88373, 88374,	C34	1, 4

		88377		

OTHER RELATED POLICIES

This policy document provides coverage criteria for ONCOLOGY: CYTOGENETIC TESTING. Please refer to:

- ***Oncology: Molecular Analysis of Solid Tumors and Hematologic Malignancies*** for criteria related to DNA testing of a solid tumor or a blood cancer.
- ***Genetic Testing: Hereditary Cancer Susceptibility Syndromes*** for coverage criteria related to genetic testing for hereditary cancer predisposition syndromes.
- ***Oncology: Cancer Screening*** for coverage criteria related to the use of non-invasive fecal, urine, or blood tests for screening for cancer.
- ***Oncology: Circulating Tumor DNA and Circulating Tumor Cells (Liquid Biopsy)*** for criteria related to circulating tumor DNA (ctDNA) or circulating tumor cell testing performed on peripheral blood for cancer diagnosis, management and surveillance.
- ***Oncology: Algorithmic Testing*** for coverage criteria related to gene expression profiling and tumor biomarker tests with algorithmic analyses.
- ***Genetic Testing: Exome and Genome Sequencing for the Diagnosis of Genetic Disorders*** for coverage criteria related to whole genome and whole exome sequencing in rare genetic syndromes.
- ***Genetic Testing: General Approach to Genetic Testing*** for coverage criteria related to cytogenetic testing in oncology that is not specifically discussed in this or another non-general policy.

COVERAGE CRITERIA

ALK Rearrangement Analysis

I. Somatic ALK rearrangement analysis (88271, 88274, 88275, 88291) in solid tumors is considered medically necessary when:

   A. The member has a diagnosis of or is in the initial work up stage for:

      1. Advanced or metastatic lung adenocarcinoma, **OR**
      2. Advanced or metastatic large cell lung carcinoma, **OR**
      3. Advanced or metastatic squamous cell lung carcinoma, **OR**
      4. Advanced or metastatic non-small cell lung cancer (NSCLC) not otherwise specified (NOS), **OR**
      5. Anaplastic thyroid carcinoma.

back to top

BCR/ABL Rearrangement Analysis

I. Somatic *BCR/ABL1* rearrangement analysis via fluorescent in situ hybridization (FISH) (88271, 88274, 88275, 88291) in peripheral blood or bone marrow is considered **medically necessary** when:

   A. The member is suspected to have a myeloproliferative neoplasm (i.e., polycythemia vera, essential thrombocythemia, primary myelofibrosis, chronic myeloid leukemia), **OR**

   B. The member is undergoing diagnostic workup for:

      1. Acute lymphoblastic leukemia (ALL), **OR**
      2. Acute myeloid leukemia (AML), **OR**
      3. Chronic myelogenous leukemia (CML), **OR**
      4. Lymphoblastic leukemia, **OR**

5. Gastrointestinal stromal tumor (GIST).

back to top

Bladder Cancer Diagnostic and Recurrence FISH Tests

I. Bladder cancer diagnostic and recurrence FISH tests (e.g., Urovysion) (88120, 88121) for the screening, diagnosis of, and monitoring for bladder cancer are considered **investigational**.

back to top

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) FISH Panel Analysis

I. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) FISH panel analysis (88271, 88274, 88275, 88291) in peripheral blood or bone marrow is considered **medically necessary** when:

   A. The panel includes analysis for +12, del(11q), del(13q), and del(17p), **AND**

   B. The member is undergoing initial diagnostic workup for chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).

back to top

ERBB2 (HER2) Amplification Analysis

I. Somatic ERBB2 (HER2) amplification analysis via in situ hybridization (ISH) (i.e., FISH or CISH) (88341, 88342, 88360, 88361) in solid tumors is considered medically necessary when:

   A. The member has any of the following:

      1. Recurrent or newly diagnosed stage I-IV invasive breast cancer, **OR**

      2. Suspected or proven metastatic gastric cancer, **OR**

3. Suspected or proven metastatic, synchronous or metachronous colorectal cancer or documented metachronous metastases by CT, MRI and/or biopsy, **OR**

4. Suspected or proven metastatic esophageal and/or esophagogastric junction adenocarcinoma, **OR**

5. Metastatic salivary gland tumors with distant metastases.

back to top

Multiple Myeloma FISH Panel Analysis

I. Multiple myeloma FISH panel analysis (88271, 88274, 88275, 88291) in bone marrow is considered medically necessary when:

   A. The panel includes analysis for del(13), del(17p13), t(4;14), t(11;14), t(14;16), t(14;20), 1q21 gain/amplification, del(1p), **AND**

   B. The member is undergoing initial diagnostic workup for multiple myeloma.

back to top

NTRK Fusion Analysis

I. Somatic NTRK 1/2/3 fusion analysis (88271, 88274, 88275, 88291, 88341, 88342, 88360, 88361 88373, 88374, 88377) via fluorescent in situ hybridization (FISH) or immunohistochemistry (IHC) in solid tumors is considered medically necessary when:

   A. The member is undergoing initial diagnostic workup for or has a diagnosis of:

      1. Advanced or metastatic lung adenocarcinoma, **OR**

      2. Advanced or metastatic large cell lung carcinoma, **OR**

      3. Advanced or metastatic squamous cell lung carcinoma, **OR**

4. Advanced or metastatic non-small cell lung cancer (NSCLC) not otherwise specified (NOS), **OR**
5. Unknown primary cancers, **OR**
6. Advanced or metastatic colorectal cancer, **OR**
7. Recurrent, progressive or metastatic cervical cancer, **OR**
8. Recurrent, progressive or metastatic vulvar cancer, **OR**
9. Recurrent or metastatic uterine cancer or a diagnosis of uterine sarcoma, **OR**
10. Recurrent or stage IV invasive breast cancer, **OR**
11. Locally advanced, recurrent or metastatic gastric cancer, **OR**
12. Locally advanced, recurrent or metastatic esophageal cancer, **OR**
13. Anaplastic thyroid carcinoma or locally recurrent, advanced and/or metastatic papillary, follicular or Hurthle cell thyroid carcinoma, **OR**
14. Pediatric acute lymphoblastic leukemia (ALL), **OR**
15. Soft tissue sarcoma, **AND**
    a) Previous tumor testing was negative for *KIT* and *PDGFRA* somatic mutations.

back to top

PD-L1 Protein Expression Analysis

I. PD-L1 protein expression analysis via immunohistochemistry (IHC) (88341, 88342, 88360, 88361) in solid tumors is considered medically necessary when:

A. The member has a diagnosis of or is in the initial work up stage for:

1. Advanced or metastatic lung adenocarcinoma, **OR**
2. Advanced or metastatic large cell lung carcinoma, **OR**

3. Advanced or metastatic squamous cell lung carcinoma, **OR**
4. Advanced or metastatic non-small cell lung cancer (NSCLC) not otherwise specified (NOS), **OR**
5. Locally advanced or metastatic bladder cancer, **OR**
6. Recurrent, progressive, or metastatic cervical cancer, **OR**
7. Recurrent or stage IV triple negative breast cancer, **OR**
8. Suspected or proven metastatic esophageal and/or esophagogastric junction adenocarcinoma, **OR**
9. Suspected or proven metastatic gastric cancer, **OR**
10. Recurrent, unresectable, or metastatic nasopharyngeal cancer, **OR**
11. Recurrent, progressive or metastatic vulvar cancer.

Note: PD-L1 protein expression analysis via IHC is often performed as an adjunct component of comprehensive molecular profiling panels for solid tumors

back to top

PML/RARA Rearrangement Analysis

I. PML/RARA rearrangement analysis via fluorescent in situ hybridization (FISH) (88271, 88274, 88275, 88291) in peripheral blood or bone marrow is considered medically necessary when:

   A. The member is undergoing initial diagnostic work up for acute leukemia.

back to top

ROS1 Rearrangement Analysis

I. Somatic ROS1 rearrangement analysis via fluorescent in situ hybridization (FISH) (88271, 88274, 88275, 88291, 88373, 88374, 88377) in solid tumors is considered medically necessary when:

A. The member has a diagnosis of:

1. Advanced or metastatic lung adenocarcinoma, **OR**
2. Advanced or metastatic large cell lung carcinoma, **OR**
3. Advanced or metastatic squamous cell lung carcinoma, **OR**
4. Advanced or metastatic non-small cell lung cancer (NSCLC) not otherwise specified (NOS).

back to top

NOTES AND DEFINITIONS

Advanced cancer is cancer that is unlikely to be cured or controlled with treatment. The cancer may have spread from where it first started to nearby tissue, lymph nodes, or distant parts of the body. Treatment may be given to help shrink the tumor, slow the growth of cancer cells, or relieve symptoms.

BACKGROUND AND RATIONALE

Practice Guidelines and Position Statements

American Society of Clinical Oncology (ASCO)

Lung Cancer

The American Society of Clinical Oncology (2018) endorsed the College of American Pathologists/International Association for the Study of Lung cancer/Association of Molecular Pathology Clinical Practice Guideline Update for Molecular Testing for the Selection of Patients with Lung Cancer for Treatment with Targeted Tyrosine Kinase Inhibitors which recommends that physicians should use molecular testing for the appropriate genetic targets on either primary or metastatic lung lesions to guide initial therapy selection. They further recommend that multiplexed genetic sequencing panels are preferred where available over multiple single gene tests to identify other treatment options beyond *EGFR, ALK, BRAF,* and *ROS1*.

The panel recommends that *EGFR, ALK, ROS1* and *BRAF* testing should be performed on all patients with advanced lung adenocarcinoma. They went on to state that *RET, HER2, KRAS,* and *MET* molecular testing are not indicated as stand alone tests but are appropriate to include as part of a larger testing panel

Multiple Myeloma

ASCO and Cancer Care Ontario (CCO) published a joint clinical practice guideline for the treatment of multiple myeloma (2019) that included the following:

- Recommendation 3.5. There is insufficient evidence to make modifications to maintenance therapy based on depth of response, including minimal residual disease (MRD) status (Type: informal consensus/evidence based; Evidence quality: low/intermediate, benefit outweighs harm; Strength of recommendation: moderate).
- Recommendation 4.2. The goal of initial therapy for transplant-eligible patients should be achievement of the best depth of remission. MRD-negative status has been associated with improved outcomes, but it should not be used to guide treatment goals outside the context of a clinical trial (Type: evidence based; Evidence quality: high, benefit outweighs harm; Strength of recommendation: moderate).
- Recommendation 8.2. Repeat risk assessment at the time of relapse should be performed and should include bone marrow with fluorescence in situ hybridization for myeloma abnormalities seen with progression, including 17p and 1q abnormalities. Fluorescence in situ hybridization for primary abnormalities (translocations and trisomies), if seen in the initial diagnostic marrow, does not need to be repeated (Type: evidence based; Evidence quality: high, benefit outweighs harm; Strength of recommendation: strong).

<u>National Comprehensive Cancer Network (NCCN):</u>

ALK Rearrangement Analysis

The NCCN (1.2021) guidelines on thyroid carcinoma recommend molecular diagnostic testing for evaluating FNA results that are suspicious for follicular cell neoplasms or AUS/FLUS and somatic RET testing in all individuals with newly diagnosed medullary thyroid carcinoma. Additionally they comment that molecular testing has shown to be beneficial when making targeted therapy decisions. The guideline also comments that individuals with anaplastic thyroid cancer and/or metastatic disease should undergo

molecular testing including BRAF, NTRK, ALK, RET, MSI, dMMR, and tumor mutational burden if not previously done.

NCCN guidelines on non-small cell lung cancer (v.5.2021) recommend ALK rearrangement testing in patients with Advanced or metastatic disease: Adenocarcinoma, Large Cell, Squamous cell, and NSCLC not otherwise specified (NOS).

BCR/ABL Rearrangement Analysis

NCCN guidelines for acute lymphoblastic leukemia (v.1.2021) recommend BCR/ABL rearrangement analysis for patients for the diagnosis/workup of ALL.

NCCN guidelines for acute myeloid leukemia (v3.2021) recommend BCR/ABL rearrangement analysis for patients for the evaluation of acute leukemia.

NCCN guidelines for pediatric acute lymphoblastic leukemia (v.2.2021) recommend BCR/ABL rearrangement analysis for patients for the diagnosis/work-up of ALL.

NCCN guidelines for chronic myeloid leukemia (v.1.2022) recommend BCR/ABL rearrangement analysis for patients for the diagnosis/work-up of CML.

NCCN guidelines for myeloproliferative neoplasms (v.1.2021) recommend BCR/ABL rearrangement analysis for patients during the workup of suspected MPN.

Bladder Cancer Diagnostic and Recurrence FISH Tests

NCCN guidelines for bladder cancer (v.3.2021) do not currently recommend the use of bladder cancer diagnostic and recurrence FISH tests (e.g., Urovysion).

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) FISH Panel Analysis

NCCN guidelines for CLL/SLL (v.1.2022) recommend consideration of FISH testing for the rearrangements specified (at a minimum) during the diagnostic workup for CLL/SLL.

ERBB2 (HER2) Amplification Analysis

NCCN guidelines for esophageal and esophagogastric junction cancers (v.4.2021) recommend ERBB2 testing during the workup of documented or suspected metastatic adenocarcinoma.

NCCN guidelines for head and neck cancers (v.3.2021) recommend ERBB2 testing for therapeutic options for individuals diagnosed with recurrent, unresectable or metastatic salivary gland tumor.

NCCN guidelines for colon cancer (v.2.2021) recommend ERBB2 testing during the workup for suspected or proven metastatic, synchronous or metachronous colorectal cancer or documented metachronous metastases by CT, MRI and/or biopsy

NCCN guidelines for gastric cancer (v.3.2021) recommend ERBB2 testing during the workup of documented or suspected metastatic adenocarcinoma.

NCCN guidelines for breast cancer (v.5.2021) recommend ERBB2 testing during the workup of recurrent or newly diagnosed stage I-IV invasive breast cancer.

Multiple Myeloma FISH Panel Analysis

NCCN guidelines for multiple myeloma (v.1.2022) recommend FISH testing during the initial workup of multiple myeloma for prognostic purposes.

NTRK Fusion Analysis

The NCCN (1.2021) guidelines on thyroid carcinoma recommend molecular diagnostic testing for evaluating FNA results that are suspicious for follicular cell neoplasms or AUS/FLUS and somatic RET testing in all individuals with newly diagnosed medullary thyroid carcinoma. Additionally they comment that molecular testing has shown to be beneficial when making targeted therapy decisions. The guideline also comments that individuals with anaplastic thyroid cancer and/or metastatic disease should undergo molecular testing including BRAF, NTRK, ALK, RET, MSI, dMMR, and tumor mutational burden if not previously done.

The NCCN guideline for colon cancer (v.2.2021) recommends NTRK fusion analysis for patients with advanced or metastatic colorectal cancer.

The NCCN guideline for non-small cell lung cancer (v.5.2021) recommends NTRK fusion analysis for patients with Advanced or metastatic disease: Adenocarcinoma, Large Cell, Squamous cell, and NSCLC not otherwise specified (NOS)

The NCCN guideline for occult primary (v.1.2022) recommends NTRK fusion analysis for cancer of unknown primary.

The NCCN guideline for cervical cancer (v.1.2021) recommends NTRK fusion analysis for recurrent, progressive or metastatic cervical cancer.

The NCCN guideline for vulvar (v.3.2021) recommends NTRK fusion analysis for recurrent, progressive or metastatic vulvar cancer.

The NCCN guideline for uterine neoplasms (v.3.2021) recommends NTRK fusion analysis for recurrent or metastatic uterine cancer or a diagnosis of uterine sarcoma.

The NCCN guideline for breast cancer (v.5.2021) recommends NTRK fusion analysis for recurrent or stage IV invasive breast cancer.

The NCCN guideline for gastric cancer (v.3.2021) recommends NTRK fusion analysis for locally advanced, recurrent or metastatic gastric cancer.

The NCCN guideline for esophageal and esophagogastric junction cancer (v.4.2021) recommends NTRK fusion analysis for locally advanced, recurrent or metastatic esophageal cancer.

The NCCN guideline for pediatric acute lymphoblastic leukemia (v.2.2021) recommends NTRK fusion analysis for pediatric acute lymphoblastic leukemia (ALL).

The NCCN guideline for soft tissue sarcomas (v.2.2021) recommends NTRK fusion analysis for soft tissue sarcoma when previous tumor testing was negative for *KIT* and *PDGFRA* somatic mutations.

PD-L1 Protein Expression Analysis

The NCCN guideline for gastric cancer (v.3.2021) recommends PD-L1 testing during the workup for documented or suspected metastatic adenocarcinoma.

The NCCN guideline for head and neck cancers (v.3.2021) recommends PD-L1 testing during the workup phase for cancer of the nasopharynx.

NCCN guidelines for bladder cancer (v.3.2021) recommend PD-L1 testing in individuals with locally advanced or metastatic (stage IV) bladder cancer.

The NCCN guideline for vulvar cancer (v.3.2021) recommends PD-L1 testing for individuals with recurrent, progressive, or metastatic vulvar cancer.

The NCCN guideline for Esophageal and Esophagogastric Junction Cancers (v.4.2021) recommends PD-L1 testing for individuals during the workup phase for documented or suspected metastatic esophageal and esophagogastric junction cancers.

The NCCN guideline for cervical cancer (v.1.2021) recommends PD-L1 testing for individuals with recurrent, progressive, or metastatic cervical cancer.

NCCN guidelines for non-small cell lung cancer (v.5.2021) recommend PD-L1 testing in patients with Advanced or metastatic disease: Adenocarcinoma, Large Cell, Squamous cell, and NSCLC not otherwise specified (NOS).

The NCCN guideline for breast cancer (v.5.2021) recommends PD-L1 testing for individuals with recurrent or stage IV triple negative breast cancer.

PML/RARA Rearrangement Analysis

NCCN guidelines for acute lymphoblastic leukemia (v.1.2021) recommend PML/RARA rearrangement analysis for patients for the evaluation of acute leukemia.

ROS1 Rearrangement Analysis

NCCN guidelines on non-small cell lung cancer (v.5.2021) recommend ROS1 rearrangement testing in patients with Advanced or metastatic disease: Adenocarcinoma, Large Cell, Squamous cell, and NSCLC not otherwise specified (NOS).

The American Urological Association and Society of Urologic Oncology

The American Urological Association and Society of Urologic Oncology (2016) addressed the diagnosis and treatment of non-muscle-invasive bladder cancer, based on a systematic review and includes the following statements on the use of urine markers after the diagnosis of bladder cancer:

- “Urinary biomarker analysis should not replace cystoscopic evaluation in the surveillance of NMIBC.”
- “Urinary biomarker analysis or cytology should not routinely be used during surveillance In a patient with a history of low-risk cancer and a normal cystoscopy.”
- “Urinary biomarker analysis may be used to assess response to intravesical BCG (UroVysion® FISH) and adjudicate equivocal cytology (UroVysion® FISH and ImmunoCyt™) in a patient with NMIBC.”

back to top

REFERENCES

1. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. Version 5.2021. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf
2. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Colon Cancer. Version 2.2021. http://www.nccn.org/professionals/physician_gls/PDF/colon.pdf
3. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Cervical Cancer. Version 1.2021. https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf
4. Kalemkerian GP, Narula N, Kennedy EB, et al. Molecular Testing Guideline for the Selection of Patients With Lung Cancer for Treatment With Targeted Tyrosine Kinase Inhibitors: American Society of Clinical Oncology Endorsement of the College of American Pathologists/International Association for the Study of Lung Cancer/Association for Molecular Pathology Clinical Practice Guideline Update. J Clin Oncol. 2018;36(9):911-919. doi:10.1200/JCO.2017.76.7293
5. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Thyroid Carcinoma. Version 1.2021. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf
6. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Gastric Cancer. Version 4.2021. https://www.nccn.org/professionals/physician_gls/pdf/gastric.pdf
7. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Esophageal and Esophagogastric Junction Cancer. Version 4.2021. https://www.nccn.org/professionals/physician_gls/pdf/esophageal.pdf
8. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia. Version 3.2021. https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf
9. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. Version 1.2021. https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf

10. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Chronic Myeloid Leukemia. Version 1.2022. https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf
11. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Acute Lymphoblastic Leukemia. Version 1.2021. https://www.nccn.org/professionals/physician_gls/pdf/all.pdf
12. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Pediatric Acute Lymphoblastic Leukemia. Version 2.2021. https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf
13. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia. Version 1.2022. https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf
14. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 5.2021. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf
15. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Head and Neck Cancers. Version 3.2021. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf
16. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma. Version 1.2022. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf
17. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Bladder Cancer. Version 3.2021. https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf
18. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Vulvar Cancer (Squamous Cell Carcinoma). Version 3.2021. https://www.nccn.org/professionals/physician_gls/pdf/vulvar.pdf
19. Mikhael J, Ismaila N, Cheung MC, et al. Treatment of Multiple Myeloma: ASCO and CCO Joint Clinical Practice Guideline [published correction appears in J Clin Oncol. 2020 Jul 20;38(21):2469]. J Clin Oncol. 2019;37(14):1228-1263. doi:10.1200/JCO.18.02096
20. Chang SS, Boorjian SA, Chou R, et al. Diagnosis and treatment of non-muscle invasive bladder cancer: AUA/SUO Guideline. *J Urol.* 2016;196(4):1021-1029. doi:10.1016/j.juro.2016.06.049.

21. Chou R, Gore JL, Buckley D, et al. Urinary Biomarkers for Diagnosis of Bladder Cancer: A Systematic Review and Meta-analysis. *Ann Intern Med*. 2015;163(12):922-931. doi:10.7326/M15-0997.
22. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Occult Primary (Cancer of Unknown Primary [CUP]). Version 1.2022. https://www.nccn.org/professionals/physician_gls/pdf/occult.pdf
23. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasms. Version 3.2021. https://www.nccn.org/professionals/physician_gls/pdf/uterine.pdf
24. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Soft Tissue Sarcoma. Version 2.2021. https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf
25. National Cancer Institute. Dictionary of Cancer Terms. Accessed 3/24/2022. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/advanced-cancer

back to top