

Evolut Clinical Guideline 2046 for Positron Emission Tomography (PET) Scan, PET Scan with Computed Tomography (CT) for Attenuation

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STATEMENT

General Information

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

Purpose

Oncologic PET is generally indicated for biopsy-proven cancer or strongly suspected cancer based on other diagnostic testing. The appropriateness of an ordered PET/CT study is dependent on the type of cancer and which radiopharmaceutical will be used for the PET/CT.

Special Note

See legislative language for specific mandates in the State of Washington

See legislative language for specific mandates in the State of Arkansas

INDICATIONS

Bone Tumors & Sarcomas

Angiosarcoma ⁽¹⁾

Angiosarcoma is a rare and aggressive cancer that originates in the lining of blood vessels and lymph nodes. Most patients undergo both conventional imaging with CT or Magnetic Resonance Imaging (MRI) of the primary site of disease, CT Chest and MRI Brain, in addition to PET/CT to determine the extent of disease and response to treatment.

- Initial Staging, Restaging, Pre-surgical evaluation, Recurrence, Surveillance
 - Indicated

Chondrosarcoma ⁽²⁾

Most patients with this disease undergo conventional imaging with a CT or MRI of the primary disease site, with or without CT Chest. PET/CT is not used. Patients with metastatic chondrosarcoma undergo imaging with CT abdomen/pelvis in addition to other imaging. **De-differentiated chondrosarcoma is treated according to the osteosarcoma pathway. Mesenchymal chondrosarcoma is treated according to the Ewing sarcoma pathway.**

- Initial Staging, Restaging, Pre-surgical evaluation, Recurrence, Surveillance
 - NOT Indicated

Chordoma ⁽²⁾

Most patients with this disease undergo conventional imaging with a CT or MRI of the primary disease site, CT Chest, and CT Abdomen & Pelvis. PET/CT is used to supplement conventional imaging in the scenarios described below. Poorly differentiated or de-differentiated chordoma is treated according to the soft tissue sarcoma guideline.

- Initial Staging
- Indicated to clarify inconclusive conventional imaging
- Restaging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When initial staging PET demonstrated disease not seen on conventional imaging
- Pre-Surgical evaluation
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When initial staging PET demonstrated disease not seen on conventional imaging
- Recurrence
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When initial staging PET demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

Clear Cell Sarcoma, Epithelioid Sarcoma, Rhabdomyosarcoma ⁽¹⁾

Most patients undergo both conventional imaging with CT or MRI of the primary site of disease and CT Chest in addition to PET/CT to determine the extent of disease and response to treatment.

- Initial Staging
 - Indicated
- Restaging
 - Indicated

- Pre-surgical evaluation
 - Indicated
- Recurrence
 - Indicated
- Surveillance
 - **NOT** indicated

Ewing Sarcoma (includes extraosseous Ewing sarcoma, mesenchymal chondrosarcoma, and desmoplastic small round cell tumors ⁽²⁾

Most patients with this disease undergo imaging evaluation with a CT or MRI of the primary disease site, CT Chest, and a PET/CT. Given that treatment for the disease is intensive and multi-modal (chemotherapy, surgery and/or radiation therapy) and requires extensive coordination across medical specialties, multiple imaging studies are appropriate throughout the treatment course to facilitate appropriate and timely care delivery.

- Initial Staging
 - Indicated
- Restaging
 - Indicated
- Pre-surgical evaluation
 - Indicated
- Recurrence
 - Indicated
- Surveillance
 - For patients with a history of metastatic disease, indicated every 3 months for 2 years, then every 4 months up to year 3 post completion of treatment

Giant Cell Tumor of Bone ⁽²⁾

Most patients with this disease undergo conventional imaging with a CT or MRI of the primary disease site, with or without CT Chest. PET/CT is not used. Malignant transformation is treated according to the Osteosarcoma guideline.

- Initial Staging, Restaging, Pre-surgical evaluation, Recurrence, Surveillance
 - **NOT** Indicated

Malignant Peripheral Nerve Sheath Tumor (MPNST) ⁽¹⁾

MPNST is a rare and aggressive tumor that can occur either spontaneously or in individuals with NF1. PET/CT is used in confirmed MPNST in addition to conventional imaging with a CT or MRI of the primary disease site, with or without CT Chest. There are additional indications for PET when transformation of a neurofibroma to MPNST occurs as detailed below.

- Initial Staging - biopsy confirmed diagnosis (regardless of NF1 Status)
 - Indicated if considering neoadjuvant therapy **OR**
 - To clarify inconclusive conventional imaging
- Initial Staging - suspected diagnosis in setting of known Neurofibromatosis Type 1 (NF1)
 - Indicated if there is concern for malignant transformation of neurofibroma to MPNST based on **ANY ONE** of the following:
 - Change in conventional imaging (e.g. growth or change in characteristics of mass)
 - Change in texture on exam
 - Change in symptoms (new or worsening pain)
- Restaging (for confirmed MPNST, regardless of NF1 status)
 - Indicated if being treated with chemotherapy **OR**
 - To clarify inconclusive conventional imaging
- Pre-surgical evaluation
 - Indicated
- Recurrence
 - Indicated
- Surveillance
 - **NOT** indicated

Myxoid/Round Cell Liposarcoma ⁽¹⁾

Myxoid/round cell liposarcoma is a rare subtype of liposarcoma, a cancer that originates in fat cells. Most patients undergo both conventional imaging with CT or MRI of the primary site of disease, MRI Spine, in addition to PET/CT to determine the extent of disease and response to treatment.

- Initial Staging
 - Indicated
- Restaging
 - Indicated
- Pre-surgical evaluation

- Indicated
- Recurrence
 - Indicated
- Surveillance
 - **NOT** indicated

Osteosarcoma (including giant cell tumor of bone with malignant transformation) ⁽²⁾

Most patients with this disease undergo imaging evaluation with a CT or MRI of the primary disease site, CT Chest, and a PET/CT. Given that treatment for the disease is intensive and multi-modal (chemotherapy, surgery and/or radiation therapy) and requires extensive coordination across medical specialties, multiple imaging studies are appropriate throughout the treatment course to facilitate most appropriate and timely care delivery.

- Initial Staging
 - Indicated
- Restaging
 - Indicated
- Pre-surgical evaluation
 - Indicated
- Recurrence
 - Indicated
- Surveillance
 - Indicated for patients with a history of metastatic disease every 3 months for 2 years, every 6 months for 3 years (total 5 years off treatment)

Soft Tissue Sarcoma - All Other Histologies ⁽¹⁾

Soft tissue sarcomas are a group of rare cancers that develop in the soft tissues of the body (e.g. muscles, fat, blood vessels, nerves, tendons, and linings of joints). There are more than 50 types of soft tissue sarcomas that are treated with a combination of surgery, radiation therapy, and chemotherapy. For all soft tissue sarcoma sub-types not specifically mentioned, most patients undergo conventional imaging with CT or MRI of the primary site of disease, CT Chest, with or without CT Abdomen & Pelvis. PET/CT is used to supplement conventional imaging in the scenarios described below.

- Initial Staging
 - Indicated if considering neoadjuvant therapy **OR**
 - To clarify inconclusive conventional imaging
- Restaging

- Indicated if being treated with chemotherapy **OR**
- To clarify inconclusive conventional imaging **OR**
- When previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated if being treated with chemotherapy **OR**
 - To clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Recurrence
 - Indicated if being treated with chemotherapy **OR**
 - To clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

Breast Cancer ⁽³⁾

FDG PET

The need for and type of imaging evaluations for this disease vary depending on the stage of the disease. Most patients with stage I and II breast cancer (based on pathologic evaluation of the primary breast mass and axillary lymph nodes) do not undergo advanced imaging evaluations. CT scans of the chest, abdomen and pelvis are indicated for stage I and II breast cancer if there are specific signs or symptoms suggesting disease spread. In stage I and II patients, FDG PET/CT is rarely needed and can be considered on a case-by-case basis to supplement conventional imaging. In stage III and IV patients, conventional imaging with CT scans of the chest, abdomen and pelvis and bone scan to evaluate for metastatic disease are appropriate. FDG PET/CT is used to supplement conventional imaging in the scenarios described below.

- Initial Staging
 - Stage I, II:
 - If concern distant metastatic disease, indicated to clarify inconclusive findings on conventional imaging (CT chest, abdomen and pelvis and/or bone scan) **OR**
 - If abnormal finding on breast MRI, indicated to clarify inconclusive findings when finding will change stage and/or treatment approach (indeterminate findings in the infraclavicular, internal mammary, or supraclavicular lymph nodes)
 - Stage III, IV:
 - Indicated to clarify inconclusive findings on conventional imaging after full staging is complete (CT scans of the chest, abdomen and pelvis and bone scan)
- Restaging

- Indicated to clarify inconclusive findings on conventional imaging **OR**
- When initial staging PET demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated to clarify inconclusive findings on conventional imaging when results will impact the operative plan
- Recurrence
 - Local recurrence:
 - If abnormal finding on breast MRI, indicated to clarify inconclusive findings when finding will change stage and/or treatment approach (indeterminate findings in the infraclavicular, internal mammary, or supraclavicular lymph nodes)
 - Systemic recurrence:
 - Indicated to clarify inconclusive findings on conventional imaging after full staging is complete (CT scans of the chest, abdomen and pelvis and bone scan)
- Surveillance
 - **NOT** indicated

Special Tracer PET (FES/Cerianna)

FES PET/CT is indicated for use in select patients with a previous diagnosis of estrogen-receptor positive (ER+) breast cancer who experience recurrence or progression. Specific indications are detailed below.

- Initial Staging, Restaging, Pre-surgical evaluation, Surveillance
 - **NOT** Indicated
- Recurrence
 - **FES** (Fluoroestradiol F 18 or Cerianna®) is indicated for recurrent or metastatic breast cancer when **ALL** of the following are present:
 - Biopsy of recurrent or metastatic site is indeterminate for ER status **OR** unable to be performed **AND**
 - ER status is needed to make a treatment decision

CNS Cancers ⁽⁴⁾

All Histologies

When an oncologic PET using FDG (using CPT codes 78811 and 78814) is requested for a primary brain malignancy, it should be reordered as a Brain PET (CPT 78608).

When a tracer other than FDG is used (such as SSTR (dotatate) for meningioma), the CPT codes covered by this guideline (78811 and 78814) apply when medical necessity is met (see indications below) rather than the Brain PET code (CPT code 78608).

NOTE: See non-malignant disease section for amyloid/dementia

Meningioma

Most patients with this disease undergo imaging evaluation with MRI of the brain and possibly the spinal axis. SSTR (Dotatate) PET/CT is used to supplement conventional imaging in the scenarios described below.

- Special Tracer PET: **SSTR** (Dotatate) PET
 - Initial Staging:
 - Indicated if diagnosis in question after Brain MRI (**biopsy not needed**)
 - Restaging
 - Indicated if presence of residual disease in question after Brain MRI (**biopsy not needed**)
 - Pre-surgical evaluation
 - Indicated if extent of disease in question after Brain MRI (**biopsy not needed**)
 - Recurrence
 - Indicated if Brain MRI indeterminate for recurrence (**biopsy not needed**)
 - Surveillance
 - **NOT** indicated

NOTE: See above all histologies section regarding FDG

Primary CNS Lymphoma

This is a rare and aggressive lymphoma that originates in the central nervous system. PET/CT is used to determine the extent of disease and to monitor response to treatment. MRI of the brain and whole spine are appropriate in addition to PET/CT.

- Initial Staging:
 - Indicated
- Restaging:
 - Indicated
- Pre-surgical evaluation
 - N/A
- Recurrence
 - Indicated
- Surveillance
 - **NOT** indicated

Gastrointestinal Tract Cancers

Anal Carcinoma (including perianal carcinoma) ⁽⁵⁾

Most patients with this disease undergo conventional imaging with CT chest, abdomen and pelvis with or without MRI pelvis. PET/CT is used to supplement conventional imaging in the scenarios described below.

- Initial Staging
 - With prior indeterminate imaging **OR**
 - To verify staging before treatment after CT chest, abdomen and pelvis are complete and show localized disease
- Restaging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - N/A
- Recurrence
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

Colon Cancer and Appendiceal Adenocarcinoma ⁽⁶⁾

Most patients with this disease undergo conventional imaging with CT Chest and CT Abdomen & Pelvis. PET/CT is used to supplement conventional imaging in the scenarios described below. When there are known or suspected liver metastases at any stage in treatment, Abdomen MRI is indicated in addition to PET/CT.

- Initial Staging
 - Indicated to clarify inconclusive conventional imaging (including evaluation of peritoneal disease) **OR**
 - If conventional imaging demonstrates potentially surgically curable metastatic disease **OR**
 - In patients considered for image-guided liver-directed therapies
- Restaging
 - Indicated to clarify inconclusive conventional imaging (including evaluation of peritoneal disease) **OR**
 - In patients considered for image-guided liver-directed therapies **OR**

- With rising CEA and no evidence of disease on conventional imaging **OR**
- When previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated to clarify inconclusive conventional imaging (including evaluation of peritoneal disease) **OR**
 - If conventional imaging demonstrates potentially surgically curable metastatic disease **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Recurrence
 - Indicated to clarify inconclusive conventional imaging (including evaluation of peritoneal disease) **OR**
 - If conventional imaging demonstrates potentially surgically curable metastatic disease **OR**
 - With rising CEA and stable findings or no evidence of disease on conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

NOTE: Circulating tumor DNA (ctDNA) is not recommended in the surveillance setting to monitor for disease recurrence. Conventional imaging is appropriate with rising ctDNA testing. PET/CT is not supported to evaluate a patient with a positive ctDNA test who has negative conventional imaging.

Esophageal & EJ Junction Cancers (squamous cell carcinoma and adenocarcinoma) ⁽⁷⁾

Most patients with this disease undergo conventional imaging with CT Chest and CT abdomen with or without CT of the pelvis. CT is superior to PET/CT for evaluation of local and regional disease. For patients who do not have clear distant metastatic disease on initial CT evaluation, PET/CT has shown metastatic disease in a large percentage of cases, changing treatment plans and prognosis.

- Initial Staging
 - Stages I-III (based on initial CT scans)
 - Indicated
 - Stage IV (based on initial CT scans)
 - To clarify inconclusive conventional imaging when result will impact treatment plan
- Restaging

- Stages I-III:
 - Indicated
- Stage IV:
 - Indicated to clarify inconclusive imaging on conventional imaging when result will impact treatment plan **OR**
 - If previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated
 - **NOTE:** Following chemoradiation PET is indicated 5-8 weeks after completion of therapy
- Recurrence
 - Indicated if conventional imaging does not demonstrate distant metastases **OR**
 - To clarify inconclusive conventional imaging **OR**
 - If previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

Gastric Cancer ⁽⁸⁾

Most patients with this disease undergo conventional imaging with CT Chest and CT abdomen and pelvis. PET/CT is useful in patients with locally advanced or metastatic disease to further delineate the extent of disease.

- Initial Staging
 - Indicated for patients with locally advanced (T2 or higher, N1 or higher) or metastatic disease on conventional imaging **OR**
 - To clarify inconclusive conventional imaging
- Restaging
 - Indicated if the patient received neoadjuvant/perioperative treatment **OR**
 - To clarify inconclusive conventional imaging **OR**
 - If previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated if the patient received neoadjuvant/perioperative treatment **OR**
 - To clarify inconclusive conventional imaging **OR**
 - If previous PET/CT demonstrated disease not seen on conventional imaging
- Recurrence

- Indicated
- Surveillance
 - **NOT** indicated

Gastrointestinal Stromal Tumors ⁽⁹⁾

Gastrointestinal stromal tumors are rare cancers that originate in the digestive system, most often in the stomach and small intestine. Most patients with this disease undergo conventional imaging evaluation with CT scans of the chest, abdomen and pelvis. Surgical resection of the primary tumor is a mainstay of treatment. PET/CT is useful in select circumstances detailed below.

- Initial Staging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - In patients who are not candidates for up front surgical resection
- Restaging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - Once 2-4 weeks after initiation of TKI (tyrosine kinase inhibitor) therapy **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated to clarify inconclusive conventional imaging **OR**
 - If needed to determine surgical resectability **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Recurrence
 - Indicated to clarify inconclusive conventional imaging **OR**
 - In patients who are not candidates for up front surgical resection **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

Rectal Cancer ⁽¹⁰⁾

Most patients with this disease undergo conventional imaging with CT Chest, CT Abdomen & Pelvis, with or without MRI Pelvis. PET/CT is used to supplement conventional imaging in the scenarios described below. When there are known or suspected liver metastases, Abdomen MRI is indicated in addition to PET at any phase in treatment.

- Initial Staging
 - Indicated to clarify inconclusive conventional imaging **OR**

- If conventional imaging demonstrates potentially surgically curable metastatic disease **OR**
- In patients considered for image-guided liver-directed therapies
- Restaging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - If conventional imaging demonstrates potentially surgically curable metastatic disease **OR**
 - In patients considered for image-guided liver-directed therapies **OR**
 - With rising CEA and no evidence of disease on conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated to clarify inconclusive conventional imaging **OR**
 - If conventional imaging demonstrates potentially surgically curable metastatic disease **OR**
 - In patients considered for image-guided liver-directed therapies **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Recurrence
 - Indicated to clarify inconclusive conventional imaging **OR**
 - If conventional imaging demonstrates potentially surgically curable metastatic disease **OR**
 - With rising CEA and no evidence of disease on conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

NOTE: Circulating tumor DNA (ctDNA) is not recommended in the surveillance setting to monitor for disease recurrence. Conventional imaging is appropriate with rising ctDNA testing. PET/CT is not supported to evaluate a patient with a positive ctDNA test who has negative conventional imaging.

Small Bowel Adenocarcinoma ⁽¹¹⁾

Most patients with this disease undergo conventional imaging with CT Chest and CT Abdomen & Pelvis. MRCP is sometimes needed for duodenal malignancies. PET/CT is used to supplement conventional imaging in the scenarios described below.

- Initial Staging
 - Indicated to clarify inconclusive conventional imaging (including evaluation of peritoneal disease)

- Restaging
 - Indicated to clarify inconclusive conventional imaging (including evaluation of peritoneal disease) **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated to clarify inconclusive conventional imaging (including evaluation of peritoneal disease) **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Recurrence
 - Indicated to clarify inconclusive conventional imaging (including evaluation of peritoneal disease) **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

Genitourinary Cancers

Bladder Cancer ⁽¹²⁾

Most patients with this disease undergo conventional imaging with CT chest, abdomen and pelvis. PET/CT is used to supplement conventional imaging as PET/CT has demonstrated the ability to identify metastatic disease not seen on CT scans in a significant percentage of patients.

- Initial Staging
 - Non-muscle invasive bladder cancer (NMIBC):
 - **NOT** indicated
 - Muscle-invasive bladder cancer (MIBC):
 - Indicated to verify staging before treatment after CT chest, abdomen and pelvis are complete and show localized disease **OR**
 - To clarify inconclusive conventional imaging outside of the urinary tract
- Restaging
 - Non-muscle invasive bladder cancer (NMIBC):
 - **NOT** indicated
 - Muscle-invasive bladder cancer (MIBC):
 - Indicated to clarify indeterminate findings on conventional imaging outside of the kidney or bladder **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging

- Pre-surgical evaluation
 - Indicated prior to cystectomy to verify staging after pre-surgical restaging CT chest, abdomen and pelvis are complete
- Recurrence
 - Indicated to clarify inconclusive conventional imaging outside of the kidney or bladder **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging

Kidney Cancer ⁽¹³⁾

Most patients with this disease undergo conventional imaging with CT scans of the chest, abdomen and pelvis. PET/CT has several limitations in this disease. The FDG tracer is excreted through the kidneys, decreasing the contrast between renal lesions and kidney tissue potentially obscuring or masking results. Additionally, FDG is inconsistently taken up by renal cell carcinoma making the validity of the study questionable. PET/CT is not routinely used.

- Initial Staging, Restaging, Pre-surgical evaluation, Recurrence, Surveillance
 - **NOT** indicated

Prostate Cancer ⁽¹⁴⁾

Prostate cancer is typically diagnosed on biopsy. Localized disease may be treated with radiation, surgery or observed on an active surveillance protocol. Following definitive treatment to the prostate with surgery (radical prostatectomy (RP)), the PSA level should be undetectable after 3 months post-surgery. Following radiation to the prostate, the PSA may fluctuate. Following definitive treatment to the prostate (radiation or surgery), patients are monitored with PSA levels. When the PSA indicates a concern (see recurrence) this may be called a biochemical recurrence. Metastatic disease may be treated with systemic therapy (which may be continuous or intermittent) and is typically followed by monitoring PSA levels and conventional imaging. PSMA PET/CT is used to verify extent of disease at diagnosis for higher risk patients and to evaluate for recurrent disease when PSA is rising. PSMA PET/CT has several additional specific indications described below. Pelvis MRI is indicated in addition to PSMA PET/CT.

Neuroendocrine/small cell variant is typically followed with CT scans of the chest, abdomen and pelvis and bone scan. FDG PET/CT can be used in select circumstances.

- **FDG PET**
 - Initial Staging, Restaging, Pre-surgical evaluation, Recurrence, Surveillance:
 - Small cell variant:
 - Indicated to clarify inconclusive conventional imaging
 - All other patients:
 - **NOT** indicated
- **Special Tracer (PSMA) PET**

- Initial Staging (PSMA is the ONLY tracer appropriate for initial staging)
 - Indicated for **ANY** of the following:
 - Patients with very high risk, high risk, or unfavorable intermediate risk prostate cancer (see **background**) **OR**
 - With prior imaging that is indeterminate for either lymph node involvement or metastatic disease **AND** clarification of that finding will change treatment

NOTE: Not indicated for initial staging of known distant metastatic disease

NOTE: A biopsy typically confirms the diagnosis of prostate cancer prior to PSMA PET. If the PSA is > 50, there is no clinical concern for infection **AND** there is an intent to treat the patient for prostate cancer without biopsy confirmation, PSMA PET is indicated.

- Restaging (PSMA):
 - Known Metastatic Disease
 - With prior indeterminate imaging **OR**
 - Discordance between imaging and PSA (i.e. rising PSA with stable imaging or stable PSA with progression on imaging) **OR**
 - To verify presence of PSMA-positive lesions prior to administration of Lu-177/Pluvicto)
- Pre-surgical evaluation (radical prostatectomy)
 - Active Surveillance
 - Indicated when disease progresses to very high risk, high risk or unfavorable intermediate risk using the most recent Gleason score/biopsy result, clinical stage and PSA level
 - Post-radiation
 - Prior to salvage prostatectomy when PSMA PET has not been done to confirm localized disease (see **Recurrence section**)
 - Known metastatic disease
 - **NOT** indicated
- Recurrence (PSMA)
 - Post Radical Prostatectomy biochemical recurrence
 - Indicated for **ANY ONE** of the following:
 - ◆ PSA persistence defined as detectable PSA (0.1ng/mL or greater) at 3 months post-operatively (only one level required)
 - ◆ Rising PSA on two or more occasions
 - ◆ PSA rise to > 0.1ng/mL if PSA was previously undetectable
 - ◆ PSA has doubled since last negative PSMA PET (repeat level verifying doubling required if PSA is not progressively rising)

- Post Prostate Whole Gland Radiation biochemical recurrence
 - Indicated for **ANY ONE** of the following:
 - ◆ PSA increase of ≥ 2 ng/mL above the nadir when increase is verified on repeat level
 - ◆ Progressively rising PSA above the nadir (two separate levels above nadir required)
 - ◆ PSA has doubled since last negative PSMA PET (repeat level verifying doubling required if PSA is not progressively rising)
- Imaging Recurrence
 - Indicated with prior imaging that is indeterminate for either lymph node involvement or metastatic disease **AND** clarification of that finding will change treatment
- Surveillance
 - Active surveillance of localized disease
 - Indicated when disease progresses to very high risk, high risk or unfavorable intermediate risk using the most recent Gleason score/biopsy result, clinical stage and PSA level
 - Observation of metastatic disease
 - Indicated when there is discordance between imaging and PSA (i.e. rising PSA with stable imaging or stable PSA with progression on imaging)
 - Post-treatment
 - **NOT** indicated (see Recurrence section if concern for recurrent disease)

Penile Cancer ⁽¹⁵⁾

Most patients with this disease undergo conventional imaging with CT of the chest, abdomen and pelvis, with or without an MRI of the pelvis to evaluate nodal disease. PET/CT is used to supplement conventional imaging in the scenarios described below.

- Initial Staging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - With **ANY ONE** of the following
 - T1b or higher primary tumor
 - Palpable lymph nodes (any T stage)
 - Abnormal lymph nodes on imaging
 - Suspected metastatic disease
- Restaging
 - Indicated to clarify inconclusive conventional imaging **OR**

- To evaluate suspected inguinal lymph node positive disease (based on imaging or exam) **OR**
- When previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated to clarify inconclusive conventional imaging **OR**
 - To evaluate suspected inguinal lymph node positive disease (based on imaging or exam) **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Recurrence
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

Testicular Cancer ⁽¹⁶⁾

Testicular germ cell tumors are divided into two groups - seminomas and non-seminomas (embryonal carcinoma, yolk sac tumor, choriocarcinoma, teratoma). Most patients with this disease undergo conventional imaging with CT scans of the chest, abdomen and pelvis. PET/CT is used in rare circumstances to supplement conventional imaging when needed to determine a treatment plan.

- Initial Staging
 - **NOT** indicated
- Restaging
 - Non-seminoma:
 - **NOT** indicated
 - Pure seminoma:
 - With a residual mass > 3cm following chemotherapy **AND** it has been at least 6 weeks since completion of chemotherapy

NOTE: If this PET is equivocal or borderline for residual disease, an additional repeat PET >6 weeks later is appropriate to identify patients that can be safely observed without additional surgery. If a persistently FDG-avid mass is present on the second PET, resection or biopsy is recommended.

- Pre-surgical evaluation
 - **NOT** indicated
- Recurrence
 - **NOT** indicated

- Surveillance
 - **NOT** indicated

Gynecological Cancers

Cervical Cancer (squamous cell carcinoma, adenocarcinoma, and small cell neuroendocrine carcinoma of the cervix (NECC)) and Vaginal Cancer ⁽¹⁷⁾

For most patients, PET/CT is used to determine the extent of disease, monitor response to treatment, and in high-risk patients monitor for recurrence after treatment. Brain MRI is indicated in addition to PET for patients with NECC.

- Initial Staging
 - Indicated
 - Pelvis MRI is indicated in addition to PET
- Restaging
 - Indicated
- Pre-surgical evaluation
 - Indicated
- Recurrence
 - Indicated
- Surveillance
 - Surveillance imaging in the absence of signs or symptoms of recurrent disease in the first two years following treatment is appropriate for some higher stage patients. PET/CT for surveillance is at the discretion of the ordering provider.

Uterine Neoplasms (Endometrial carcinoma and uterine Sarcoma) ⁽¹⁷⁾

Most patients with this disease undergo conventional imaging with CT Chest and CT Abdomen & Pelvis, with or without MRI pelvis. PET/CT is used to supplement conventional imaging in the scenarios described below.

- Initial Staging
 - All histologic subtypes:
 - Indicated to clarify inconclusive conventional imaging
 - High-grade carcinoma (poorly differentiated, serous clear cell, undifferentiated carcinoma, carcinosarcoma)
 - Indicated
- Restaging

- All histologic subtypes:
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging **OR**
- High-grade carcinoma (poorly differentiated, serous clear cell, undifferentiated carcinoma, carcinosarcoma)
 - Indicated
- Pre-surgical evaluation
 - All histologic subtypes:
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging **OR**
 - High-grade carcinoma (poorly differentiated, serous clear cell, undifferentiated carcinoma, carcinosarcoma)
 - Indicated
- Recurrence
 - All histologic subtypes:
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging **OR**
 - High-grade carcinoma (poorly differentiated, serous clear cell, undifferentiated carcinoma, carcinosarcoma)
 - Indicated
- Surveillance
 - **NOT** indicated

Gestational Trophoblastic Neoplasia ⁽¹⁸⁾

Gestational trophoblastic neoplasia (invasive moles, choriocarcinomas, placental-site trophoblastic tumors, epithelioid trophoblastic tumors) arise from abnormal growth of trophoblastic cells (cells that normally develop into the placenta during pregnancy). Treatment is often multimodal (chemotherapy, surgery, and/or radiation therapy). Most patients with this disease undergo conventional imaging evaluation with CT chest, abdomen and pelvis with or without MRI Pelvis. PET/CT is useful in select circumstances detailed below.

- Initial Staging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - To evaluate for potentially surgically curable metastatic disease

- Restaging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - To evaluate for potentially surgically curable metastatic disease **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated
- Recurrence
 - Indicated to clarify inconclusive conventional imaging **OR**
 - To evaluate for potentially surgically curable metastatic disease **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - Indicated for patients when hCG is an unreliable tumor marker, at the end of treatment then every 6-12 months for up to 3 years

Ovarian, Fallopian Tube, and Primary Peritoneal Cancer ⁽¹⁹⁾

Most patients with this disease undergo conventional imaging with CT chest, abdomen and pelvis, with or without MRI pelvis. PET/CT is also commonly used to determine the extent of disease and monitor response to treatment.

- Initial Staging
 - Indicated
- Restaging
 - Indicated
- Pre-surgical evaluation
 - Indicated
- Recurrence
 - Indicated
- Surveillance
 - Indicated when tumor markers are unreliable, the physical exam is unreliable, and/or there is a high risk of recurrence at the discretion of the ordering provider

Vulvar Cancer (squamous cell carcinoma and adenocarcinoma) ⁽²⁰⁾

Most patients with this disease undergo conventional imaging with MRI Pelvis, and CT scans of the chest, abdomen and pelvis if there is a clinical concern for metastatic disease. PET/CT is used to supplement conventional imaging in the scenarios described below. Vulvar and vulvovaginal melanoma follow the cutaneous melanoma guideline.

- Initial Staging
 - If clinical stage II or higher (extension beyond vulva/perineum) **OR**
 - For patients with positive sentinel lymph node biopsy to evaluate for undissected nodal disease in the groin/pelvis **OR**
 - Indicated to clarify inconclusive conventional imaging
- Restaging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging **OR**
 - Once 3-6 months after completion of primary therapy **OR**
- Pre-surgical evaluation
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Recurrence
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

Head & Neck Cancer (including cancers of the oral cavity, nasopharynx, oropharynx, hypopharynx, larynx (glottic and supraglottic), paranasal sinuses, salivary glands, and mucosal melanoma) ⁽²¹⁾

Most patients with this disease undergo conventional imaging with CT or MRI of the primary site of disease and the neck as well as PET/CT. Most patients receive surgery and/or radiation therapy. PET/CT is useful after completion of treatment in the scenarios detailed below.

- Initial Staging
 - Indicated
 - **NOTE:** For Initial staging requests where there is concern for H&N cancer based on symptoms, exam, or pathology (e.g. positive biopsy of lymph nodes within the neck) without a confirmed primary tumor site - patients should undergo conventional imaging. If conventional imaging does not reveal an obvious primary, PET/CT should be ordered before exam under anesthesia, biopsies and tonsillectomy to help identify potential primary sites before any intervention occurs.

- Restaging
 - Indicated
 - **NOTE:** Given the overlapping time intervals for primary site imaging and end of treatment FDG PET/CT imaging, both primary site and PET/CT imaging can be performed at the same time without being considered overlapping imaging. If the end of therapy PET demonstrates possible residual disease, one additional PET is appropriate ≥ 6 weeks after end-of-therapy PET as it may help identify those patients who can be safely observed without additional cancer-directed treatment
- Pre-surgical evaluation
 - Indicated
- Recurrence
 - Indicated
- Surveillance
 - **NOT** indicated

Leukemias & Lymphomas

Acute Lymphoblastic Leukemia (ALL) (Pediatric and Adult) ^(22,23)

Most patients with this disease do not require routine imaging evaluations to determine and/or monitor the extent of disease (bone marrow evaluation is used to monitor disease response). For patients with physical exam findings or imaging findings (Xray, ultrasound or CT scan) suggestive of lymphomatous involvement, PET/CT is the preferred imaging modality.

- Initial Staging
 - Indicated with physical exam findings of lymphomatous involvement **OR**
 - If other imaging (x-ray, ultrasound, or CT scan) demonstrates possible lymphomatous involvement
- Restaging
 - If lymphomatous involvement was present at diagnosis **OR**
 - With new signs or symptoms of disease progression during treatment
- Pre-surgical evaluation
 - N/A
- Recurrence
 - Indicated with physical exam findings of lymphomatous involvement **OR**
 - If other imaging (x-ray, ultrasound, or CT scan) demonstrates possible lymphomatous involvement

- Surveillance
 - **NOT** indicated

Acute Myeloid Leukemia (AML) (Pediatric and Adult) ⁽²⁴⁾

Most patients with this disease do not require routine imaging evaluations to determine and/or monitor the extent of disease (bone marrow evaluation is used to monitor disease response). For patients with clinical suspicion for extramedullary disease (e.g. lymph nodes, spleen liver, skin, gingiva, CNS), conventional imaging with CT scans or PET/CT are used.

- Initial Staging
 - Indicated with clinical suspicion for extramedullary disease (myeloid sarcoma) (on exam or prior imaging)
- Restaging
 - Indicated if extramedullary disease was present at diagnosis **OR**
 - If there is clinical suspicion for progression during treatment
- Pre-surgical evaluation
 - N/A
- Recurrence
 - Indicated with clinical suspicion for extramedullary disease (myeloid sarcoma) (on exam or prior imaging)
- Surveillance
 - **NOT** indicated

B-Cell Lymphomas – Adult (Follicular lymphoma, marginal zone lymphoma, primary mediastinal large B-cell lymphoma, mantle cell lymphoma, diffuse large B cell lymphoma, Burkitt lymphoma, B-lymphoblastic lymphoma, all others) ⁽²⁵⁾

B cell lymphomas represent several different specific cancer types. PET/CT is commonly used to determine the extent of disease and monitor response to treatment.

- Initial Staging
 - Indicated
- Restaging
 - Indicated
- Pre-surgical evaluation
 - N/A
- Recurrence

- Indicated
- Surveillance
 - Follicular lymphoma, primary mediastinal large B-cell lymphoma, diffuse large B cell lymphoma:
 - Indicated in rare situations where disease was only visible on PET/CT (e.g. without anatomic correlate, extensive bone disease that would be difficult to follow with conventional imaging every 6 months for 2 years)
 - All other histologies
 - **NOT** indicated

Pediatric Aggressive Mature B-Cell Lymphomas (includes Burkitt lymphoma, diffuse large B-cell lymphoma, primary mediastinal large B-cell lymphoma, large C-bell lymphoma with IRF4 rearrangement, large B-cell lymphoma with 11q aberration/High grade B-cell lymphoma with 11q aberrations, high grade B-cell lymphoma with MYC and BCL2 or BCL6 rearrangements, B-Lymphoblastic Lymphoma) ⁽²⁶⁾

Most patients with these diseases undergo BOTH conventional imaging with CT scans of the neck, chest, abdomen and pelvis and PET/CT to determine the extent of disease and to monitor response to treatment.

- Initial Staging
 - Indicated
- Restaging
 - Indicated
- Pre-surgical evaluation
 - N/A
- Recurrence
 - Indicated
- Surveillance
 - **NOT** indicated

NOTE: This portion of the guideline should be applied to patients treated at a pediatric institution on a pediatric protocol which can include young adults into their 20's.

Castleman's Disease ⁽²⁷⁾

This is a rare disorder affecting the lymph nodes and immune system. PET/CT is used to determine the extent of disease and to monitor response to treatment.

- Initial Staging
 - Indicated
- Restaging
 - Indicated
- Pre-surgical evaluation
 - N/A
- Recurrence
 - Indicated
- Surveillance
 - **NOT** indicated

Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL) ⁽²⁸⁾

Most patients with this disease do not require routine imaging evaluations to determine and/or monitor the extent of disease (blood tests and bone marrow evaluation are used to monitor disease response). CT scans may be appropriate for the evaluation of symptoms of bulky disease or for assessment of risk of tumor lysis syndrome prior to initiation of therapy. PET/CT is useful to direct nodal biopsy if histologic transformation is suspected (if disease is suspected of evolving from indolent disease into a high-grade lymphoma). Histologic transformation may be evaluated with progressive lymphadenopathy, B symptoms, LDH elevation, or electrolyte disturbances.

- Initial Staging
 - Indicated to direct nodal biopsy if histologic transformation is suspected
- Restaging
 - Indicated to direct nodal biopsy if histologic transformation is suspected **OR**
 - With accelerated CLL (significant increase in lymphocyte count, worsening symptoms)
- Pre-surgical evaluation
 - N/A
- Recurrence
 - Indicated to direct nodal biopsy if histologic transformation is suspected
- Surveillance
 - **NOT** indicated

Chronic Myeloid Leukemia (CML) ⁽²⁹⁾

Most patients with this disease do not require routine imaging evaluations to determine and/or monitor the extent of disease (blood tests and bone marrow evaluation are used to monitor disease response).

- Initial Staging, Restaging, Pre-surgical evaluation, Recurrence, Surveillance
 - **NOT** Indicated

Hodgkin Lymphoma (Pediatric and Adult) ^(30,31)

Most patients with disease undergo BOTH conventional imaging with CT scans and pelvis and PET/CT to determine the extent of disease and to monitor response to treatment. Specific indications for CT and PET/CT are detailed in the scenarios below.

- Initial Staging
 - Indicated
 - **NOTE:** Imaging should be performed no more than 4 weeks before starting therapy. In a situation where care has been delayed, repeat initial staging imaging is appropriate.
- Restaging
 - Indicated
 - One repeat PET is appropriate if the end of treatment PET was positive (Deauville Score 4-5)
- Pre-surgical evaluation
 - N/A
- Recurrence
 - Indicated
- Surveillance
 - **NOT** indicated
 - **NOTE:** Imaging studies are only recommended when relapse is suspected or when required based on clinical trial participation, because most patients will clinically declare themselves and there is no survival advantage in pre-emptive imaging. FDG PET/CT is not advised due to risk of false positives in the absence of signs, symptoms, or imaging findings concerning for recurrent disease.

Kaposi Sarcoma ⁽³²⁾

Kaposi sarcoma forms in the lining of the blood and lymph vessels. It typically presents as lesions on the skin and may also affect internal organs such as the digestive tract and lungs. Many patients with this disease do not require routine imaging evaluations to determine and/or monitor the extent of disease. PET/CT is occasionally used to supplement conventional imaging in the scenarios described below.

- Initial Staging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - If there are concerns for coexisting Kaposi sarcoma-associated herpesvirus (KSHV) associated inflammatory cytokine syndrome (KICS), multicentric Castleman disease, or KSHV+ lymphoma
- Restaging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging **OR**
 - If there are concerns for coexisting Kaposi sarcoma-associated herpesvirus (KSHV) associated inflammatory cytokine syndrome (KICS), multicentric Castleman disease, or KSHV+ lymphoma
- Pre-surgical evaluation
 - N/A
- Recurrence
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging **OR**
 - If there are concerns for coexisting Kaposi sarcoma-associated herpesvirus (KSHV) associated inflammatory cytokine syndrome (KICS), multicentric Castleman disease, or KSHV+ lymphoma
- Surveillance
 - **NOT** indicated

Post-Transplant Lymphoproliferative Disease ⁽²⁵⁾

Post-transplant lymphoproliferative disease (PTLD) is a rare but serious complication that can occur after organ or stem cell transplantation. It involves the uncontrolled proliferation of B cells, which can lead to lymphoma. Risk factors for development of PTLD are immunosuppression (higher immunosuppression increases the risk), EBV serostatus (EBV-negative before transplant at higher risk), and the type of transplant (higher risk in lung, heart). Treatment ranges from decreasing immunosuppression to aggressive chemotherapy. For patients who have risk factors for PTLD, PET/CT is an appropriate imaging modality to evaluate for disease, monitor response to treatment, and screen for recurrence given the significantly increased medical complexity in patients who have received previous transplants.

- Initial Staging
 - Indicated for biopsy prove or suspicion of PTLD
- Restaging
 - Indicated
- Pre-surgical evaluation

- N/A
- Recurrence
 - Indicated
- Surveillance
 - Indicated

T Cell Lymphomas ⁽³³⁾

Most patients with disease undergo PET/CT to determine the extent of disease and to monitor response to treatment.

- Initial Staging
 - Indicated
- Restaging
 - Indicated
- Pre-surgical evaluation
 - N/A
- Recurrence
 - Indicated
- Surveillance
 - Peripheral T-cell lymphomas
 - Indicated every 6 months for 2 years then annually for 5 years
 - Other histologies
 - **NOT** indicated

Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma ⁽³⁴⁾

This is a rare cancer that is classified as non-Hodgkin lymphoma. Most patients with this disease are followed with imaging studies, using either CT scans or PET/CT at the discretion of the treating provider.

- Initial Staging
 - Indicated
- Restaging
 - Indicated
- Pre-surgical evaluation
 - N/A
- Recurrence

- Indicated
- Surveillance
 - **NOT** indicated

Liver & Hepatobiliary Cancers

Ampullary Adenocarcinoma ⁽³⁵⁾

Most patients with this disease undergo conventional imaging with CT chest and abdomen with or without CT pelvis. PET/CT is used to supplement conventional imaging in the scenarios described below.

- Initial Staging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - In patients without clear evidence of distant metastatic disease on conventional imaging who demonstrate high risk features (e.g. borderline resectable disease, presence of regional adenopathy, suspicion of peritoneal metastases, markedly elevated CA 19-9).
- Restaging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated to clarify inconclusive conventional imaging **OR**
 - To confirm localized disease before proceeding to surgery after completion of CT chest and CT abdomen
- Recurrence
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

Biliary Tract Cancers ⁽³⁶⁾

Most patients with these diseases undergo conventional imaging with CT Chest and CT Abdomen with or without CT Pelvis. PET/CT is used to supplement conventional imaging in the scenarios described below.

- Initial Staging
 - Indicated to clarify inconclusive conventional imaging
- Restaging

- Indicated to clarify inconclusive conventional imaging **OR**
- When previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated to clarify inconclusive conventional imaging
- Recurrence
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

Hepatocellular Carcinoma ⁽³⁷⁾

The diagnosis of this disease can be made on imaging alone or via biopsy. Curative intent treatment for this disease requires surgical resection of sites of disease. For patients who are not candidates for up front surgical resection, liver transplantation is potentially curative. Imaging requests for patients who are receiving systemic therapy, local/regional therapies to control disease, and those awaiting transplant should be reviewed under the 'restaging' indication. Most patients with this disease undergo conventional imaging with multiphase CT or MRI of the liver (ordered as abdomen), CT chest and CT abdomen and pelvis. PET/CT is used to supplement conventional imaging in the scenarios described below.

- Initial Staging
 - Indicated to clarify inconclusive conventional imaging
- Restaging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Recurrence
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

NOTE: Follow Restaging indications for patients with known disease who are not receiving active treatment. Use surveillance indications for patients who have completed treatment and have no known active disease.

YTTRIUM-90 (Y90)

Y90 PET SCAN: Indicated when performed immediately after treatment of liver malignancy (primary or metastatic). The Y90 treatment is also the tracer for this and PET is performed within 24 hours of treatment (while Y90 is still detectable) to confirm the final distribution of the Y90.

Lung Cancers

Non-Small Cell Lung Cancer ⁽³⁸⁾

NSCLC is the most common type of lung cancer and includes multiple histologies (adenocarcinoma, squamous cell carcinoma, large cell carcinoma). Treatment depends largely on the stage of disease and is typically multimodal, including chemotherapy, surgery, radiation therapy, and immunotherapy. Most patients with disease undergo both conventional imaging with CT of the chest and MRI of the brain as well as PET/CT to determine the extent of treatment and to monitor for response to treatment. PET/CT is used to supplement conventional imaging in the scenarios described below.

- Initial Staging
 - Indicated
- Restaging
 - Indicated for **ANY** of the following:
 - Pre- and post-radiation evaluation **OR**
 - Evaluation prior to starting maintenance immunotherapy **OR**
 - To clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging **OR**
 - End of treatment evaluation (prior to transitioning to surveillance)
- Pre-surgical evaluation
 - Indicated
 - Chest CT is indicated in addition to PET
- Recurrence
 - Indicated
 - Brain MRI is indicated in addition to PET
- Surveillance
 - **NOT** indicated

Small Cell Lung Cancer ⁽³⁹⁾

SCLC is the less common type of lung cancer and is aggressive, tending to spread quickly to lymph nodes, bones, brain, and liver. Treatment depends largely on the stage of disease (limited stage, cancer confined to one side of the chest; extensive stage - cancer has spread to the other lung and/or other parts of the body) and is typically multimodal, including chemotherapy, radiation therapy, and immunotherapy. Most patients with this disease undergo conventional imaging with CT Chest, CT Abdomen & Pelvis, and MRI of the brain. PET/CT has been shown to upstage many patients. PET/CT is used to supplement conventional imaging in the scenarios described below.

- Initial staging (all patients)
 - Indicated if conventional imaging does not obviously demonstrate extensive stage disease **OR**
 - To clarify inconclusive conventional imaging that would clarify limited versus extensive stage disease and/or change the treatment plan
- Restaging
 - Indicated for limited stage disease **OR**
 - Prior to chest radiation **OR**
 - To clarify inconclusive conventional imaging
- Pre-surgical evaluation
 - Indicated for limited stage disease **OR**
 - To clarify inconclusive conventional imaging
- Recurrence
 - Indicated if conventional imaging does not obviously demonstrate extensive stage disease **OR**
 - To clarify inconclusive conventional imaging
- Surveillance
 - **NOT** indicated

Lung Nodules ⁽⁴⁰⁾

When a lung nodule is seen on low dose CT (or standard Chest CT without known malignancy), PET is indicated for **ANY** of the following:

- If the solid component of the dominant nodule (either solitary or clearly dominant) is \geq 8mm **OR**
- If there is a part solid/mixed nodule with the solid component 6 mm or larger **OR**
- If there is a mixed nodule (i.e., ground glass and solid nodule) with the solid component of the nodule \geq 4mm on LDCT when there has been **EITHER**

- Interval growth of the solid component of at least 1.5mm **OR**
- Interval development of a new mixed nodule with the solid nodule component \geq 4mm

Neuroendocrine & Adrenal Tumors ⁽⁴¹⁾

Adrenocortical Carcinoma

Adrenocortical Carcinoma (ACC) is a rare, aggressive cancer that is often characterized by excessive hormone production leading to symptoms such as hypertension, weight gain, and virilization. ACC is often diagnosed on imaging rather than biopsy. Features of an adrenal mass on conventional imaging in a patient with no history of another primary malignancy that are suspicious for adrenocortical carcinoma include: size $>$ 4 cm and a homogenous mass with irregular margins and/or local invasion. Most patients with this disease undergo conventional imaging with CT scans of the chest, abdomen and pelvis. PET/CT is used to supplement conventional imaging in the scenarios described below.

- **FDG PET**
 - Adrenal (other than pheochromocytoma/paraganglioma)
 - **Initial Staging:**
 - Indicated (biopsy confirmed and suspected based on imaging)
 - **Restaging:**
 - Localized resectable disease
 - ◆ Indicated to clarify inconclusive conventional imaging
 - Locoregional unresectable or metastatic disease
 - ◆ Indicated
 - **Pre-surgical evaluation**
 - Indicated
 - **Recurrence**
 - Completely resected disease
 - ◆ With symptoms, laboratory or imaging findings of recurrence
 - Unresected disease:
 - ◆ Indicated
 - **Surveillance**
 - Completely resected disease:
 - ◆ NOT indicated (followed with conventional imaging)
 - Unresectable or metastatic disease:
 - ◆ Indicated every 3-6 months for up to 5 years

Paraganglioma and Pheochromocytoma

These are neuroendocrine tumors that require both conventional imaging with CT or MRI of areas of disease and functional imaging with FDG or SSTR PET/CT. Abdomen MRI (to evaluate the liver) is appropriate in addition to PET/CT at all time points. Treatment typically involves surgical resection of the tumor with pre-operative medical preparation to manage hormone levels. Both SSTR (Dotatate) PET and FDG PET are used in rare circumstances and can be considered on a case-by-case basis.

- **FDG PET or Special Tracer SSTR (Dotatate) PET**
 - Initial Staging
 - Indicated when there is a high clinical suspicion based on imaging and biochemical evaluation prior to biopsy **OR**
 - For biopsy proven disease
 - Restaging
 - Completely resected disease:
 - Indicated to clarify inconclusive conventional imaging
 - Unresected disease:
 - Indicated
 - Pre-surgical evaluation
 - Indicated
 - Recurrence
 - Completely resected disease
 - With symptoms, laboratory or imaging findings of recurrence
 - Unresected disease:
 - Indicated
 - Surveillance
 - Completely resected disease:
 - **NOT** indicated (followed with conventional imaging)
 - Unresectable disease:
 - Indicated every 3-6 months

Well-Differentiated Neuroendocrine Tumors (NET)

Surgical resection of primary and metastatic sites of disease is a mainstay of treatment for well-differentiated NETs. Conventional imaging of primary sites of disease in addition to functional imaging with SSTR PET/CT is used for all patients to determine the extent of disease. SSTR PET/CT is used more extensively throughout treatment for individuals with unresected or metastatic disease. FDG PET/CT is used in select patients. SSTR (Dotatate) PET plus FDG

PET are used in rare circumstances and can be considered on a case-by-case basis. SSTR PET/CT to evaluate for possible NET based on labs and/or symptoms can be considered on a case-by-case basis.

Special Tracer SSTR (Dotatate) PET

- Initial Staging:
 - Indicated
 - Abdomen MRI (liver) is indicated in addition to PET
- Restaging:
 - Completely resected disease:
 - Indicated to clarify inconclusive conventional imaging
 - Unresected disease:
 - Indicated
- Pre-surgical evaluation:
 - Indicated
 - Abdomen MRI (liver) is indicated in addition to PET
- Recurrence:
 - Completely resected disease
 - With symptoms, laboratory or imaging findings of recurrence
 - Unresected disease:
 - Indicated
- Surveillance:
 - Completely resected disease:
 - **NOT** indicated (followed with conventional imaging)
 - Unresectable disease:
 - Indicated every 3-6 months

FDG PET

- Initial Staging:
 - Indicated for high-grade well-differentiated NET **AND**
 - With a high Ki67 ($\geq 55\%$) **AND**
 - Negative initial staging SSTR PET
- Restaging:
 - Indicated with
 - Recent negative SSTR PET **OR**

- Prior positive FDG PET
- Pre-surgical evaluation
 - Indicated with
 - Recent negative SSTR PET **OR**
 - Prior positive FDG PET
- Recurrence
 - Indicated with
 - Recent negative SSTR PET **OR**
 - Prior positive FDG PET
- Surveillance
 - Completely resected disease:
 - **NOT** indicated (followed with conventional imaging)
 - Unresectable disease:
 - Indicated every 3-6 months

Poorly Differentiated Neuroendocrine Tumors

Poorly differentiated neuroendocrine tumors (NECs) are aggressive, high-grade malignancies characterized by rapid growth and a tendency to metastasize. Most patients undergo conventional imaging to assess the primary site of disease and FDG PET/CT to determine the extent of disease and response to treatment. Treatment often includes a combination of chemotherapy, targeted therapy, and emerging options like immunotherapy and peptide receptor radionuclide therapy (PRRT). Both SSTR (Dotatate) PET and FDG PET are used in rare circumstances and can be considered on a case-by-case basis.

This portion of the guideline addresses extrapulmonary poorly differentiated (large or small cell carcinoma/mixed neuroendocrine-non-neuroendocrine neoplasms, large cell neuroendocrine carcinoma of the lung, mixed neuroendocrine tumors, extra-pulmonary small cell carcinoma (i.e. primary site of disease is not in the lung)). See **small cell lung cancer** for primary site of disease in the lung. See **cervical cancer** for primary site of disease in the cervix. See **prostate cancer** for primary site of disease in the prostate.

- **FDG PET**
 - Initial Staging
 - Indicated
 - Restaging
 - With prior indeterminate imaging **OR**
 - With symptoms, laboratory or imaging findings of progression
 - Pre-surgical evaluation

- Indicated
- Recurrence
 - Indicated
- Surveillance
 - **NOT** indicated
- **Special Tracer SSTR (Dotatate) PET**
 - Initial Staging, Restaging, Pre-surgical evaluation, Recurrence, Surveillance
 - **NOT** Indicated

Non-Malignant Disease

Dementia (42–44)

- Special Tracer PET
 - Amyloid PET for evaluation for mild cognitive impairment or dementia in the following situations:
 - Detection of early Alzheimer's disease **OR**
 - Differentiation between Alzheimer's, dementia with Lewy body disease (DLB) and frontotemporal lobar degeneration (FTD) **OR**
 - Assessment for the presence of beta amyloid plaque in Alzheimer's disease when being considered for treatments that target beta-amyloid plaque

AND ALL the following criteria are met (criteria apply to **ANY** of the above 3 indications):

- Brain MRI is insufficient or indeterminant **AND**
- Objective measures demonstrate objective impairment (MMSE/MoCA < 26 or mild cognitive impairment on neuropsychological testing) **AND**
- Full lab evaluation (thyroid function tests, CBC, CMP including LFTs and B12) has been completed and if abnormal, have been treated and cognitive difficulty persists **AND**
- Medication side effects ⁽⁴⁴⁾ and medical causes, such as vascular or traumatic or inflammatory etiologies have been excluded

NOTE: Brain CT is an alternative to brain MRI when MRI is contraindicated or cannot be performed for detection and differentiation but **NOT** for treatment planning as MRI is a prerequisite to beta-amyloid targeted treatment

Sarcoidosis (45,46)

- Known sarcoidosis:
 - **ONLY** if conventional testing (CXR, CT and inflammatory serology) are indeterminate for known sarcoid to determine:

- If treatment might be helpful **OR**
- Extent of disease, if it will potentially change management **OR**
- Response to treatment
- Suspected sarcoidosis:
 - To determine most suitable site to biopsy

Vasculitis

- In limited circumstances for patients with known vasculitis, PET is indicated after conventional imaging (MRA/CTA/MR/CT) is insufficient to determine treatment ⁽⁴⁷⁾

Other Malignancies

Histiocytic Neoplasms ⁽⁴⁸⁾

Histiocytic neoplasms are rare hematologic disorders characterized by the accumulation of neoplastic histiocytes. These disorders vary widely in their clinical presentation and prognosis, ranging from localized and mild to disseminated and potentially fatal. PET/CT is used to determine the extent of disease, to monitor response to treatment and to evaluate for recurrent disease after completion of treatment. CT or MRI of the primary site(s) of disease are sometimes used in addition to or in place of PET/CT.

- Langerhan's cell histiocytosis, Erdheim Chester disease, Rosai-Dorfman disease
 - Initial Staging
 - Indicated
 - Restaging
 - Indicated
 - Pre-surgical evaluation
 - Indicated
 - Recurrence
 - Indicated
 - Surveillance
 - Every 3-6 months for 2 years then annually

Melanoma: Uveal ⁽⁴⁹⁾

Uveal melanoma is a rare type of melanoma that originates in the uvea (iris, ciliary body, choroid). Most patients with this disease undergo conventional imaging evaluation with MRI of the orbit and CT or MRI of the chest, abdomen and pelvis (The primary sites of metastases are liver and lung). PET/CT is occasionally used to supplement conventional imaging in the scenarios described below.

- Initial Staging

- Indicated to clarify indeterminate conventional imaging
- Restaging
 - Indicated to clarify indeterminate conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated to clarify indeterminate conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Recurrence
 - Indicated to clarify indeterminate conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

Merkel Cell Carcinoma ⁽⁵⁰⁾

Merkel cell carcinoma is a rare and aggressive type of skin cancer that originates in the epidermis. Imaging is encouraged for staging of most cases as occult metastases result in upstaging in a significant number of patients. PET/CT is used to determine the extent of disease and to monitor response to treatment.

- Initial Staging
 - Indicated
- Restaging
 - Indicated
- Pre-surgical evaluation
 - Indicated
- Recurrence
 - Indicated
- Surveillance
 - Surveillance imaging is typically performed using CT scans. PET/CT can be used to evaluate for in-transit metastases if the primary lesion is on the extremity at the discretion of the ordering provider.

Mesothelioma: Peritoneal ⁽⁵¹⁾

Peritoneal mesothelioma is a rare and aggressive cancer that develops in the peritoneum. It is primarily caused by exposure to asbestos fibers. PET/CT is used to determine the extent of disease and to monitor response to treatment.

- Initial Staging
 - Indicated
- Restaging
 - Indicated
- Pre-surgical evaluation
 - Indicated
- Recurrence
 - Indicated
- Surveillance
 - **NOT** indicated

Mesothelioma: Pleural ⁽⁵²⁾

Pleural mesothelioma is a rare and aggressive cancer that develops in the pleura. It is primarily caused by exposure to asbestos fibers. PET/CT is used to determine the extent of disease and to monitor response to treatment. Chest CT is appropriate in addition to PET/CT. The evaluation of recurrent pleural effusion and/or pleural thickening includes CT chest, thoracentesis and pleural biopsy. The diagnostic sensitivity of this investigation is 70-75%. If the first biopsy is non-diagnostic, there is a higher chance that subsequent biopsies will be non-diagnostic, thus a PET to guide subsequent biopsy is reasonable in this situation.

- Initial Staging
 - Indicated
- Restaging
 - Indicated
- Pre-surgical evaluation
 - Indicated
- Recurrence
 - Indicated
- Surveillance
 - **NOT** indicated

Neuroblastoma ⁽⁵³⁾

Neuroblastoma is a rare cancer that develops from neuroblasts and is seen primarily in young children. Primary tumors are commonly found in the adrenal glands, abdomen, chest, neck, and pelvis. Metastatic disease is commonly seen in the bone marrow, bones, liver, lymph nodes, skin and brain. Patients with this disease undergo many imaging studies to define primary and metastatic sites of disease as even patients with widely metastatic disease are treated with

curative intent. Routine imaging studies include CT or MRI of the primary tumor site, chest, abdomen and pelvis, and brain. These tumors often encase vasculature, necessitating CTA or MRA in addition to the above imaging. These tumors also invade neural foramina, necessitating dedicated spine imaging. Functional imaging with Iodine 123 (123I-MIBG) is routinely used given the high specificity and sensitivity to identify metastatic disease. When tumors are not MIBG avid, or when MIBG imaging and anatomic imaging do not correlate, FDG PET/CT is appropriate. Treatment is multimodal including chemotherapy, surgery, radiation, autologous stem cell transplant and immunotherapy. Treatment decisions are sometimes made at the granular level of individual metastatic disease sites, warranting explicit characterization of all sites of disease. Due to the complexity of these tumors, the intensity and complexity of treatment, and the young age of patients requiring sedation for imaging, multiple overlapping imaging studies and modalities are often necessary.

- Initial Staging
 - Indicated when any disease is not avid on MIBG scan, **OR**
 - If there are discordant findings between MIBG scan and anatomic imaging (e.g. concerning area of disease on MIBG scan without anatomic correlate on conventional imaging, or concerning area of disease on conventional imaging without anatomic correlate on MIBG scan).
- Restaging
 - Indicated when FDG PET was used for initial staging **OR**
 - When any disease is not avid on MIBG scan, **OR**
 - If there are discordant findings between MIBG scan and anatomic imaging (e.g. concerning area of disease on MIBG scan without anatomic correlate on conventional imaging, or concerning area of disease on conventional imaging without anatomic correlate on MIBG scan) **OR**
 - If MIBG has become indeterminate or discordant
- Pre-surgical evaluation
 - Indicated when FDG PET was used for initial staging **OR**
 - When any disease is not avid on MIBG scan, **OR**
 - If there are discordant findings between MIBG scan and anatomic imaging (e.g. concerning area of disease on MIBG scan without anatomic correlate on conventional imaging or concerning area of disease on conventional imaging without anatomic correlate on MIBG scan) **OR**
 - If MIBG has become indeterminate or discordant
- Recurrence
 - Indicated when FDG PET was used for initial staging **OR**
 - When any disease is not avid on MIBG scan, **OR**
 - If there are discordant findings between MIBG scan and anatomic imaging (e.g. concerning area of disease on MIBG scan without anatomic correlate on

conventional imaging or concerning area of disease on conventional imaging without anatomic correlate on MIBG scan) **OR**

- If MIBG has become indeterminate or discordant
- Surveillance
 - If PET is used for functional imaging evaluation in place of MIBG during treatment, surveillance PET is appropriate every 3-6 months for 1 year, then every 6 months for 1 year, then annually

Occult Primary ⁽⁵⁴⁾

An occult primary tumor is a type of cancer where the primary tumor site cannot be identified. Metastatic cancer cells have been identified somewhere in the body, however the location where the cancer started remains unknown. The workup in this situation requires biopsy to determine histology (e.g. adenocarcinoma vs squamous cell carcinoma) of the occult primary and some combination of conventional imaging studies and diagnostic procedures (e.g. CT scans of the chest, abdomen and pelvis, mammogram, colonoscopy). PET/CT is occasionally used following biopsy and initial workup to supplement conventional imaging in the scenarios described below.

- Initial Staging
 - Indicated to clarify inconclusive conventional imaging
 - **NOTE:** See **Head and Neck Cancer** section for occult primary in the lymph nodes of the neck
- Restaging
 - Follow indications based on how cancer is being treated (e.g. if treating as head and neck, defer to head and neck cancer guidance for all future requests).
- Pre-surgical evaluation
 - Follow indications based on how cancer is being treated (e.g. if treating as head and neck, defer to head and neck cancer guidance for all future requests).
- Recurrence
 - Follow indications based on how cancer is being treated (e.g. if treating as head and neck, defer to head and neck cancer guidance for all future requests).
- Surveillance
 - **NOT** indicated

Thymomas & Thymic Carcinomas ⁽⁵⁵⁾

Most patients with these diseases undergo imaging with CT scan of the chest and PET/CT to determine the extent of disease and response to treatment.

- Initial Staging:
 - Indicated (biopsy not needed, can approve based on suspicion of this diagnosis on

chest CT)

- Restaging:
 - Indicated
- Pre-surgical evaluation:
 - Indicated
- Recurrence
 - Indicated
- Surveillance
 - **NOT** indicated

Thyroid Carcinoma ⁽⁵⁶⁾

Papillary, Follicular, Oncocytic and Poorly Differentiated:

Differentiated thyroid carcinomas (papillary, follicular, oncocytic thyroid carcinomas (poorly differentiated and differentiated)) can concentrate iodine, express TSH receptors and produce thyroglobulin (Tg). Most patients with this disease undergo whole body iodine imaging (I-123 or I-131) when there is a suspicion of disease or confirmed disease. PET/CT has limited uses in these types of thyroid cancer unless the disease is non-iodine avid or has a high likelihood of not being iodine avid, PET/CT is used to supplement other imaging in the scenarios described below:

- Initial Staging:
 - **NOT** Indicated
- Restaging Following Total/Completion Thyroidectomy and/or Radioiodine Ablation (RAI) for **ANY ONE** of the following:
 - With known or suspected metastases (based on laboratory or imaging findings) **AND** I-123/131 is negative
 - With rising or new Tg Antibody
 - **Oncocytic** thyroid cancer following thyroidectomy if **ANY** of the following are present:
 - Tumor > 2 cm
 - ≥ 1 focus of vascular invasion
 - Any positive lymph node (≥ cN1)
 - Positive margin
 - Gross residual disease (including extension outside the thyroid)
 - Postop Tg ≥ 1 ng/mL
- Pre-surgical evaluation

- **NOT** indicated
- Recurrence:
 - Indicated when recurrence is suspected based on laboratory or imaging findings **AND**
 - I-123/131 is negative (or was previously negative in the setting of known disease)
- Surveillance
 - **NOT** indicated

Anaplastic or De-Differentiated:

Anaplastic thyroid cancer (ATC) is a highly aggressive form of thyroid malignancy, characterized by rapid growth and a high propensity for metastasis. These tumors are not typically iodine avid. Most patients with this disease undergo conventional imaging and PET/CT to define the extent of disease and to monitor response to treatment

- Initial Staging:
 - Indicated
- Restaging:
 - Indicated
- Pre-surgical evaluation:
 - Indicated
- Recurrence:
 - Indicated
- Surveillance:
 - Indicated 3-6 months after initial therapy

Medullary:

Medullary Thyroid Carcinoma (MTC) arises from the neuroendocrine parafollicular C cells of the thyroid and is often associated with elevated calcitonin levels. This type of thyroid cancer can be sporadic or linked with multiple endocrine neoplasia type 2 (MEN2). Most patients with this disease undergo imaging with ultrasound of the neck. SSTR PET/CT is used to supplement conventional imaging in the situations described below:

- **Special Tracer SSTR (dotatate) PET:**
 - Initial Staging:
 - Indicated
 - Restaging:
 - Indicated when tumor markers (calcitonin and/or CEA) are rising **AND**

- Conventional imaging is negative
- Pre-surgical evaluation:
 - Indicated
- Recurrence:
 - Indicated when tumor markers (calcitonin and/or CEA) are rising **AND**
 - Conventional imaging is negative
- Surveillance:
 - **NOT** indicated
- FDG PET
 - Initial Staging:
 - **NOT** indicated
 - Restaging:
 - **NOT** indicated
 - Pre-surgical evaluation
 - **NOT** indicated
 - Recurrence
 - Indicated when tumor markers (calcitonin and/or CEA) are rising **AND**
 - Conventional imaging is negative
 - Surveillance
 - **NOT** indicated

Wilms Tumor ⁽⁵⁷⁾

Wilms tumor (nephroblastoma) is a rare kidney cancer that primarily affects children. Most patients with this disease undergo conventional imaging with CT scans of the chest, abdomen and pelvis. PET/CT is occasionally used to supplement conventional imaging in the scenarios described below.

- Initial Staging:
 - Indicated to clarify inconclusive conventional imaging
- Restaging:
 - Indicated to clarify inconclusive conventional imaging
- Pre-surgical evaluation
 - Indicated to clarify inconclusive conventional imaging
- Recurrence
 - Indicated to clarify inconclusive conventional imaging

- Surveillance
 - **NOT** indicated

Pancreatic Cancer ⁽⁵⁸⁾

Most patients with this disease undergo conventional imaging with CT chest, abdomen and pelvis, and CT or MRI of the pancreas with a dedicated pancreatic protocol. PET/CT is used to supplement conventional imaging in the scenarios described below.

- Initial Staging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - In patients without clear evidence of distant metastatic disease on conventional imaging who demonstrate high risk features (e.g. borderline resectable disease, presence of regional adenopathy, suspicion of peritoneal metastases, markedly elevated CA 19-9). The purpose of the PET/CT is to detect extra-pancreatic metastases that would change management strategy.
- Restaging
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Pre-surgical evaluation
 - Indicated
- Recurrence
 - Indicated to clarify inconclusive conventional imaging **OR**
 - When previous PET/CT demonstrated disease not seen on conventional imaging
- Surveillance
 - **NOT** indicated

Plasma Cell Dyscrasias

Plasma Cell Dyscrasias

Plasma cell dyscrasias are a group of disorders characterized by the abnormal proliferation of plasma cells, which are a type of white blood cell responsible for producing antibodies. The M-protein is an abnormal immunoglobulin produced by a single clone of plasma cells and can be detected in the blood or urine via protein electrophoresis (SPEP or UPEP). Monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM), and multiple myeloma are stages in the spectrum of plasma cell disorders. MGUS is characterized by <10% clonal plasma cells in the bone marrow and is observed without treatment. Smoldering multiple myeloma is characterized by 10-60% clonal plasma cells in the bone marrow and has a higher risk of progression to multiple myeloma. Multiple myeloma is characterized by >10% clonal plasma cells in the bone marrow with myeloma-defining events. Myeloma-defining events are any of the following: 1. $\geq 60\%$ clonal plasma cells in the bone marrow; 2. serum

involved/uninvolved free light chain ratio of 100 or greater; 3. more than one focal lesion on MRI that is at least 5mm in size; 4. Hypercalcemia; 5. renal insufficiency; 6. Anemia; or 7. bone lesions.

MGUS ⁽⁵⁹⁾

- Initial Staging, Restaging, Pre-surgical evaluation, Recurrence, Surveillance
 - **NOT** Indicated

NOTE: Whole Body Low Dose CT (CPT 76497) is used rather than PET - see Evolent Clinical Guideline 2061 for Unlisted Studies under Unlisted CT

Multiple Myeloma ⁽⁵⁹⁾

Treatment for multiple myeloma is divided into two phases: active and maintenance treatment. Active treatment is given at the onset of disease or during relapse and is more aggressive. The primary goal of active treatment is to reduce tumor burden and induce remission using chemotherapy, stem cell transplant, radiation therapy, and immunotherapy. Maintenance treatment is given after achieving remission, is less intensive, and is long term. The goal of maintenance therapy is to prolong remission. PET/CT is used during active treatment to evaluate the extent of disease at diagnosis and to monitor response to treatment. It is used less frequently in maintenance treatment. Nuanced scenarios are detailed below.

- Initial Staging:
 - Indicated
- Restaging
 - Active treatment
 - Indicated every 2-3 cycles of therapy, during evaluation for stem cell transplantation or CAR-T therapy, and at 1, 3, 6 and 12 months post-transplant or CAR-T
 - Maintenance treatment:
 - Indicated annually (including for patients who do not have measurable levels of M protein or free light chains)
- Pre-surgical evaluation
 - N/A
- Recurrence
 - Indicated at any phase in treatment or surveillance with signs, symptoms, lab or imaging studies concerning for recurrence
- Surveillance:
 - Indicated annually (including for patients who do not have measurable levels of M protein or free light chains)

Smoldering Myeloma (suspected or confirmed) ⁽⁵⁹⁾

Patients with suspected or confirmed smoldering myeloma based on bone marrow evaluation should undergo imaging evaluation to look for lesions that would meet criteria for the diagnosis of multiple myeloma. PET/CT is a commonly used modality to evaluate for bone lesions at diagnosis and annually to monitor for progression to active myeloma.

- Initial Staging:
 - Indicated
- Restaging:
 - N/A
- Pre-surgical evaluation:
 - N/A
- Recurrence
 - Indicated with signs, symptoms or lab values suggestive of progression to multiple myeloma
- Surveillance
 - Indicated annually due to risk of progression to multiple myeloma

Solitary Plasmacytoma ⁽⁵⁹⁾

There are two types of plasmacytoma - solitary plasmacytoma of bone (SPB) and extramedullary plasmacytoma (EMP). Both have a risk of progression to multiple myeloma (50% for SPB, 15% for EMP). PET/CT is used to evaluate the disease at diagnosis. Treatment is often with radiation and less frequently surgery. Even after successful treatment, there remains a significant risk of progression to multiple myeloma warranting PET/CT in the surveillance setting.

- Initial Staging:
 - Indicated
- Restaging:
 - Indicated
- Pre-surgical evaluation:
 - Indicated
- Restaging:
 - Indicated with signs, symptoms, or lab values suggestive of progression to multiple myeloma
- Surveillance:
 - Indicated once within 3-12 months post-treatment then annually for 5 years

Systemic Light Chain Amyloidosis ⁽⁶⁰⁾

This disease (also known as AL amyloidosis or primary amyloidosis) is a rare and serious condition where light chains accumulate in various organs and tissues. Patients with this disease may undergo conventional imaging to determine organ involvement (e.g. heart, chest). FDG PET/CT is used to determine the extent of disease in some patients and can be used following biopsy confirmation of disease or with high clinical suspicion based on labs, symptoms and other imaging findings.

- Initial Staging:
 - Indicated
- Restaging:
 - Indicated
- Pre-surgical evaluation
 - N/A
- Recurrence
 - Indicated
- Surveillance
 - **NOT** indicated

Skin Cancers

Basal Cell Skin Cancer ⁽⁶¹⁾

Most patients with this disease do not undergo imaging evaluations. Conventional imaging is indicated for high risk locally advanced disease, regional disease, or metastatic disease at the discretion of the treating provider. PET/CT is used in rare circumstances to supplement conventional imaging when needed to determine a treatment plan.

- Initial Staging
 - Indicated to clarify inconclusive conventional imaging when needed to direct treatment
- Restaging
 - Indicated to clarify inconclusive conventional imaging when needed to direct treatment
- Pre-surgical evaluation
 - Indicated to clarify inconclusive conventional imaging when needed to direct treatment
- Recurrence
 - Indicated to clarify inconclusive conventional imaging when needed to direct treatment

- Surveillance
 - **NOT** indicated

Melanoma: Cutaneous ⁽⁶²⁾

The need for and type of imaging evaluations for this disease vary depending on the stage of the disease. Most patients with stage I and II melanoma (based on pathologic evaluation of the biopsy) do not undergo advanced imaging evaluations. Conventional imaging with CT or MRI of the affected area is indicated for stage I and II melanoma when needed for surgical planning. CT scans of the chest, abdomen and pelvis are indicated if there are specific signs or symptoms suggesting disease spread. In stage I and II patients, PET/CT is not used. It can be considered on a case-by-case basis to supplement conventional imaging. In stage III (Any T, N1 or higher) and stage IV patients, systemic imaging to determine the extent of disease and to monitor response to treatment is appropriate. PET/CT is widely used in patients with stage III and IV melanoma to determine the extent of disease and monitor response to systemic treatment. PET/CT has additional nuanced indications described in the scenarios detailed below.

- Initial Staging
 - Stage I
 - **NOT** indicated
 - Stage II
 - Indicated to clarify inconclusive conventional imaging
 - Stage III/IV
 - Indicated
- Restaging
 - Stage I
 - **NOT** indicated
 - Stage II
 - Indicated to clarify inconclusive conventional imaging
 - Stage III/IV
 - Indicated
- Pre-surgical evaluation
 - Indicated to clarify inconclusive conventional imaging
- Recurrence
 - True scar recurrence (persistent disease)
 - Indicated to clarify inconclusive conventional imaging
 - Satellite, in-transit recurrence, nodal or metastatic recurrence
 - Indicated

- Surveillance
 - Stage I
 - **NOT** indicated
 - Stage II
 - Indicated to clarify inconclusive conventional imaging
 - Stage III/IV
 - Indicated annually for 5 years
 - **NOTE:** if additional cross-sectional imaging needed at more frequent intervals in surveillance setting, recommend alternating CT or MRI with PET/CT.

Squamous Cell Skin Cancer ⁽⁶³⁾

Most patients with this disease do not undergo imaging evaluations. Conventional imaging is indicated for suspicion of locally, extensive or metastatic at the discretion of the treating provider. PET/CT is used in rare circumstances to supplement conventional imaging when needed to determine a treatment plan.

- Initial Staging
 - Indicated to clarify inconclusive conventional imaging when needed to direct treatment
- Restaging
 - Indicated to clarify inconclusive conventional imaging when needed to direct treatment
- Pre-surgical evaluation
 - Indicated to clarify inconclusive conventional imaging when needed to direct treatment
- Recurrence
 - Indicated to clarify inconclusive conventional imaging when needed to direct treatment
- Surveillance
 - **NOT** indicated

LEGISLATIVE LANGUAGE

Washington

20181116B – Positron Emission Tomography (PET) scans for lymphoma ⁽⁶⁴⁾

Washington State Health Care Authority Health Technology Assessment

Health Technology Clinical Committee

Findings and Decisions

HTCC Coverage Determination

- PET scans (i.e., PET with computed tomography or PET/CT) for lymphoma is a covered benefit with conditions.

HTCC reimbursement determination

- **Limitations of Coverage**

- An initial staging scan is covered followed by up to three (3) scans per active occurrence of lymphoma:
 - When used to assess a response to chemotherapy, scans should not be done any sooner than three (3) weeks after completion of any chemotherapy cycle, except for advanced stage Hodgkin's lymphoma, after four (4) cycles of ABVD chemotherapy.
 - When used to assess response to radiation therapy, scans should not be done any sooner than eight (8) weeks after completion of radiation or combined chemotherapy and radiation therapy.
- Relapse: Covered when relapse is suspected in the presence of clinical symptoms or other imaging findings suggestive of recurrence

Non-Covered indicators:

Surveillance: Not covered

Arkansas ⁽⁶⁵⁾

APPLICABLE LOB: COMMERCIAL AND EXCHANGE

- Arkansas State
 - State of Arkansas 93rd General Assembly Regular Session 2021 House Bill 1357 an act to continue care for the protection of cancer survivors; concerning coverage for Positron Emission Tomography under a health benefit plan to screen for or diagnose cancer in certain patients; and for other purposes. Arkansas Code Title 23, Chapter 79, Subchapter 1, is amended to add an additional section to read as follows: 25 23-79-164. Coverage for positron emission tomography:
 - A healthcare insurer that offers a health benefit plan in this state shall provide coverage for positron emission tomography to screen for or to diagnose cancer in a patient upon the recommendation of the patient's physician when the patient has a prior history of cancer (subsection (b))
 - Benefits under subsection (b) of this section are subject to any health benefit plan provisions that apply to other services covered by the health benefit plan

CODING AND STANDARDS

Codes

78811, 78812, 78813, 78814, 78815, 78816

Applicable Lines of Business

☒	CHIP (Children’s Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☒	Medicare Advantage

BACKGROUND

PSMA

- Any of the following criteria make PSMA PET indicated for initial staging:
 - Gleason score 8, 9 or 10
 - Primary pattern 4 (Gleason 4+3=7)
 - PSA > 20 **AND** Gleason score 3+3=6 or higher
 - PSA > 10 **AND** Gleason score 3+4=7
 - PSA > 10 **AND** Gleason score 3+3=6 **AND** clinical stage ≥ T2b
 - Clinical stage ≥ T3a **AND** Gleason score 3+3=6 or higher
 - Clinical stage ≥ T2b **AND** Gleason score 3+4=7 or higher
 - ≥ 50% of cores positive for cancer in a random, non-targeted prostate biopsy
 - Grade group 3, 4 or 5 disease

Definitions

- **INITIAL STAGING** refers to imaging that is performed after the diagnosis of cancer is made, and generally before any treatment.
- **RETAGING** refers to imaging that is performed during treatment to determine response to treatment/monitor treatment, a single end of treatment study done within 6 months of completion of treatment, or when there is clinical concern for recurrence (i.e., new

imaging, new signs, rising labs/tumor markers or symptoms relative to type of cancer and entire clinical picture). Recurrence is not required to be biopsy proven.

- Imaging is typically performed 6-12 weeks after surgery
- Imaging is typically performed 12 weeks after radiation (to avoid false positive findings that can be caused by treatment changes or healing).
 - PET/CT can be performed 1 - 3 weeks after neoadjuvant chemotherapy or neoadjuvant chemoradiation if done for presurgical planning to evaluate for distant metastatic disease or to evaluate known metastatic disease located in areas separate from the site(s) being radiated.
- When an end of treatment PET scan performed at an appropriate post-treatment interval (see above) shows indeterminate findings, one additional repeat PET in 3 months is indicated.
- Common exceptions are noted in the guideline. If not noted in the guideline, a valid clinical reason explaining why the interval needs to be shorter is needed.
- **TREATMENT** includes chemotherapy, immunotherapy, radiation, as well as patients on “maintenance therapy” who have known, or existing, metastatic disease being controlled by this treatment. Allogenic bone marrow transplant and CART T-cell therapy should be considered ‘active’ treatment for at least 6 months after infusion/transplant and as such can be approved at 30 days, 100 days, and 6 months after the most recent infusion.
- **INDETERMINATE IMAGING:**
 - When indeterminate imaging is required prior to PET, this typically means conventional imaging (CT, MRI, OR Nuclear Medicine Scan (i.e. bone scan)) shows a finding that is indeterminate **AND** clarification of that finding with PET will potentially change management.
 - The information provided should clearly explain why conventional imaging is insufficient to determine treatment or management.
 - Biopsy guidance:
 - To determine the best location to biopsy either within a tumor that has necrosis on imaging **OR**
 - To determine the best location to biopsy when there are findings on standard imaging that would require a significantly invasive procedure (such as laparoscopic or open surgical procedures) **AND** malignancy is highly suspected based on imaging.
 - When previous conventional imaging has been shown to be negative, yet a concurrent PET scan was positive (i.e. conventional imaging was falsely negative/ missed lesions seen on PET), we do not require repeat conventional imaging prior to every subsequent PET because conventional imaging was already shown to be insufficient. Appropriate interval criteria should still be met.

Further Information

PET with CONTRAINDICATIONS to contrasted CT AND MRI: The inability to image with contrasted conventional imaging includes contraindications to both CT (such as chronic renal failure with GFR < 30 **OR** significant iodinated contrast allergy) **AND** to MRI (such as gadolinium allergy, implanted device that is not MRI compatible, or GFR <40). When requested for surveillance due to the above reasons, PET can be considered during the time that the highest risk of recurrence for that cancer (typically the first two years after completion of treatment).

PET/MR: When PET/MR can be considered per the guideline, if the criteria are met for PET for that cancer and the plan is to do a PET/MR rather than a PET/CT, the PET scan can be approved. In the same way a separate approval for total body CT is not needed when a PET/CT is requested, a separate approval for the total body MR is not typically needed. However, until a PET/MR CPT code is implemented, unlisted MR in addition to PET can be considered on a case-to-case basis.

SUMMARY OF EVIDENCE

PET scans are generally indicated for biopsy-proven cancer or strongly suspected cancer based on other diagnostic testing. The appropriateness of a PET/CT study depends on the type of cancer and the radiopharmaceutical used.

- **Bone Tumors & Sarcomas** ^(1,2): PET/CT is indicated for initial staging, restaging, pre-surgical evaluation, and recurrence in cases like angiosarcoma, clear cell sarcoma, epithelioid sarcoma, Ewing sarcoma, myxoid/round cell liposarcoma, and osteosarcoma. However, it is not indicated for chondrosarcoma and giant cell tumor of bone.
- **Breast Cancer** ⁽³⁾: For stage I and II breast cancer, PET/CT is rarely needed and can be considered on a case-by-case basis. For stage III and IV, it is used to supplement conventional imaging.
- **CNS Cancers** ⁽⁴⁾: PET/CT is used for primary CNS lymphoma and meningioma to determine the extent of disease and monitor response to treatment.
- **Gastrointestinal Tract Cancers** ^(6,7,10): PET/CT is indicated for various gastrointestinal cancers like anal carcinoma, colon cancer, esophageal cancer, gastric cancer, gastrointestinal stromal tumors, rectal cancer, and small bowel adenocarcinoma to clarify inconclusive conventional imaging and evaluate for metastatic disease.
- **Genitourinary Cancers** ^(12,14,15): PET/CT is indicated for muscle-invasive bladder cancer, prostate cancer, and penile cancer to verify staging, clarify inconclusive imaging, and evaluate for metastatic disease.
- **Gynecological Cancers** ^(19,20): PET/CT is used for cervical cancer, uterine neoplasms, gestational trophoblastic neoplasia, ovarian cancer, and vulvar cancer to determine the extent of disease, monitor response to treatment, and evaluate for recurrence.
- **Head & Neck Cancer** ⁽²¹⁾: PET/CT is indicated for initial staging, restaging, pre-surgical evaluation, and recurrence.

- **Leukemias & Lymphomas** ^(22,23,25,26,28,30,31,33,34): PET/CT is used for various types of leukemias and lymphomas to determine the extent of disease and monitor response to treatment.
- **Liver & Hepatobiliary Cancers** ⁽³⁷⁾: PET/CT is indicated for ampullary adenocarcinoma, biliary tract cancers, and hepatocellular carcinoma to clarify inconclusive conventional imaging and evaluate for metastatic disease.
- **Lung Cancers** ^(38–40): PET/CT is used for non-small cell lung cancer and small cell lung cancer to determine the extent of disease and monitor response to treatment.
- **Neuroendocrine & Adrenal Tumors** ⁽⁴¹⁾: PET/CT is indicated for adrenocortical carcinoma, paraganglioma, pheochromocytoma, well-differentiated neuroendocrine tumors, and poorly differentiated neuroendocrine tumors to determine the extent of disease and monitor response to treatment.
- **Non-Malignant Disease** ⁽⁴³⁾: PET/CT is used for dementia, sarcoidosis, and vasculitis in specific circumstances where conventional imaging is insufficient.
- **Other Malignancies** ^(50–52): PET/CT is indicated for histiocytic neoplasms, uveal melanoma, Merkel cell carcinoma, peritoneal mesothelioma, pleural mesothelioma, neuroblastoma, occult primary tumors, thymomas, thymic carcinomas, thyroid carcinoma, Wilms tumor, and pancreatic cancer to determine the extent of disease and monitor response to treatment.

These guidelines are based on evidence from medical literature, societal guidelines, and state/national recommendations.

ANALYSIS OF EVIDENCE

Analysis:

Per NCCN, "Prior to the annual update of the Guidelines, the NCCN Guidelines Team performs a search of the **PubMed database** using appropriate search terms to obtain key literature published since the previous Guidelines update. The PubMed database is used as it remains the most widely used resource for medical literature and indexes peer-reviewed biomedical literature. Articles from additional sources (e.g., e-publications ahead of print, meeting abstracts) deemed as relevant to the Guidelines may also be included in the literature review process. Panels are provided with a resulting list of key articles relevant to the Guidelines in advance of Panel meetings to add a rigorous evidence-based review to the NCCN Guidelines development and update process." For further details on the guideline development and update process, see NCCN.org.

POLICY HISTORY

Date	Summary
July 2025	<ul style="list-style-type: none"> ● Added a Summary of Evidence and analysis of Evidence ● Guideline name was adjusted from PET Scan to; Positron Emission Tomography (PET) Scan, PET Scan with Computed Tomography (CT) for Attenuation
June 2025	<ul style="list-style-type: none"> ● This guideline replaces Evolent Clinical Guideline 070-1 for PET Scan ● Added in general information statement regarding guideline criteria development by reputable sources, standard of care, and best practices ● Surveillance PET section added to all disease types ● Recurrence PET section added to all disease types ● Pre-surgical evaluation section added to all disease types ● Following Cancers to be consistent with updated version of NCCN ● B-cell lymphomas: condensed disease types ● Bladder cancer: added indications for MIBC ● Breast cancer: clarified imaging recommendations by stage ● Gastric cancer: added imaging recommendations for patients with localized disease ● Melanoma: clarified imaging recommendations by stage ● Neuroendocrine: clarified imaging indications based on completely resected vs unresected disease ● Non-malignant disease: added infection section ● Non-small cell lung cancer: added clarification for restaging indications ● Ovarian cancer: added indications for PET ● Penile cancer: clarified indications for initial staging imaging based on clinical features of disease ● Prostate cancer: Removed tracers other than PSMA ● Testicular cancer: clarified indications for non-seminomatous germ cell tumors

Date	Summary
	<ul style="list-style-type: none"> ● Uterine neoplasms: added indications for high-grade carcinomas ● Applicable Line of Business adjusted – Medicare checked
August 2024	<ul style="list-style-type: none"> ● Reorganized: <ul style="list-style-type: none"> ○ Grouped similar cancer types together (e.g. leukemias and lymphomas, gynecological cancers) ● Revised indeterminate imaging and contraindications to conventional imaging sections ● Addition of the use of Amyloid PET for early Alzheimer’s ● Updated: <ul style="list-style-type: none"> ○ Surveillance PET section added to disease type where appropriate ○ Combination imaging added to disease type where appropriate ○ Following Cancers to be consistent with updated version of NCCN <ul style="list-style-type: none"> ■ Adrenal: added indications in limited circumstances ■ Ampullary adenocarcinoma: added section ■ Anal carcinoma: added indications for radiation planning ■ Bone tumors: added combination imaging recommendations, removed age restrictions on PET ■ Cervical cancer: added neuroendocrine small cell carcinoma of the cervix, added surveillance indication ■ Gastrointestinal stromal tumor: added indication for 2-4 weeks after initiation of TKI (tyrosine kinase inhibitor) therapy ■ Gestational trophoblastic neoplasia: added indication for potentially surgically curable metastatic disease ■ Lymphoma: added clarification by sub-type of lymphoma, added indications for combination imaging in pediatric patients, added surveillance indications ■ Melanoma: added indication for patients considering or receiving systemic treatment with immunotherapy ■ Neuroblastoma: added surveillance indications ■ Neuroendocrine: added detail regarding what is needed

Date	Summary
	<p>for restaging in SSTR section</p> <ul style="list-style-type: none"> ■ Non-malignant disease: added dementia section, ■ Non-small cell lung cancer: added qualifiers to restaging indications (Indicated for any of the following: pre-surgical evaluation, suspected or confirmed progression/recurrence, indeterminate findings on conventional imaging, end of treatment evaluation) ■ Penile cancer: added indication for suspected inguinal lymph node positive disease (based on imaging or exam) ■ Pheochromocytoma/Paraganglioma: separated from general neuroendocrine tumors, added clarification to indications for FDG tracer vs. SSTR tracer ■ Prostate cancer: Reorganized section to include all tracers, updated restaging indications ■ Rectal cancer: separated from colon cancer ■ Small cell lung cancer: clarified initial staging indication to indicated if needed to clarify extent of disease ■ Soft tissue sarcomas: added specific indications for sub-categories of soft tissue sarcoma (angiosarcoma, clear cell sarcoma, epithelioid sarcoma, malignant peripheral nerve sheath sarcoma (MPNST), myxoid/round cell liposarcoma), added combination imaging recommendations, removed age restrictions on PET ■ Systemic light chain amyloidosis: added section ■ Testicular cancer: added initial staging indication for all histologies for prior indeterminate imaging when retroperitoneal dissection is under consideration and extent of disease needs clarification ■ Vulvar cancer: added indications for when sentinel lymph node biopsy is positive and when metastases are suspected

LEGAL AND COMPLIANCE

Guideline Approval



Committee

Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee

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