National Imaging Associates, Inc.*	
Clinical guidelines **PET SCANS**	**Original Date: September 1997**
	Last Revised Date: June 2021
Guideline Number: NIA_CG_070-1	**Implementation Date: January 2022**

GENERAL NOTES:

ADULT AND PEDIATRIC MALIGNANCIES (NCCN, 2019, 2020):

~~The appropriateness of an ordered PET/CT study is fully dependent on the answer to the question of which radiopharmaceutical will be used for the PET/CT.~~ **ONCOLOGICAL PET IS 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 which radiopharmaceutical will be used for the PET/CT.** ~~This guideline only covers the radiopharmaceuticals F^{18} FDG, Ga^{68} Dotatate, F^{18} Fluciclovine (Axumin).~~

FDG-PET/CT (fluorodeoxyglucose-positron emission tomography)

~~**For Lung Nodule**~~**LUNG NODULE** seen on LDCT or CT+ contrast~~:~~

- Solid Component of Dominant Nodule ≥ 8mm **or Part solid/mixed nodules with the solid component 8 mm or larger**
- Mixed nodule (i.e., ground glass and solid nodule) with solid component of the nodule ≥ 4mm on LDCT when there has been
  - ~~o~~ Interval growth of the solid component of at least 1.5mm on subsequent LDCT scans
  - ○

    OR
  - ~~o~~ Interval development of a new mixed nodule on subsequent LDCT with the solid nodule component ≥ 4mm
  - ○

USEFUL DEFINITIONS (to aide in using the following table(s)):

* National Imaging Associates, Inc. (NIA) is a subsidiary of Magellan Healthcare, Inc.

- **INITIAL STAGING refers to imaging that is performed AFTER the diagnosis of cancer is made, and generally before any treatment.**
- **RESTAGING includes scans that are either needed during active treatment* (subsequent treatment strategy**) to determine response to treatment, within 6 months after the end of treatment, or when there is clinical concern for recurrence (~~i~~ei.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)**
- ***ACTIVE TREATMENT includes traditional chemotherapy, immunotherapy, radiation, as well as patients on "maintenance therapy" who have known, or existing, metastatic disease being held in check 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.**
- ****SUBSEQUENT TREATMENT STRATEGY~~:~~**
    - **For restaging or monitoring response during active treatment (including immunotherapy), and/or a single evaluation after completion/cessation of therapy. The interval should ideally‡* be 6-12 weeks after surgery, and 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.**

‡*NOTE: a valid clinical reason explaining why the interval needs to be shorter than ideal must be present

- **INCONCLUSIVE IMAGING see Background section at end of guidelines**
- **SURVEILLANCE PET is generally not approvable. Surveillance means no active treatment, no current suspicion of recurrence and occurs 6 months or more after completion of treatment. ~~(~~Possible exceptions† where PET "may be considered" for surveillance:**
    - **Ewing's**
    - **~~,~~Osteosarcoma**
    - **~~,~~Breast (Stage 4)**
    - **~~,~~Cervical (stage 2-4)**
    - **~~,~~Diffuse Large B Cell Lymphoma when disease was only seen previously on PET**

- ~~,~~ Melanoma (stage 2b-4)
- ~~,~~ Myeloma/plasmacytoma (ideally use same type imaging as was used in initial dx, up to 5 yrs after the diagnosis of plasmacytoma)
- ~~,~~ Seminoma (Stage 2b, 2c and 3)~~.~~

†NOTE: These cases would need to include a clinical reason why PET is needed (i.e., being considered), rather than conventional imaging (CT, MRI, bone scan). Generally, this would be accepted only when ordered by the treating oncologist or clearly at their recommendation (not as routine follow~~-~~up ordered by PCP).

~~INDICATED FOR BIOPSY PROVEN CANCER OR STRONGLY SUSPECTED, BASED ON OTHER DIAGNOSTIC TESTING, INCLUDING:~~

~~ONCOLOGICAL INDICATIONS FOR FDG PET~~

~~(SEE SPECIAL TRACERS SECTIONS FOR INDICAIONS OTHER TRACERS)~~

ONCOLOGICAL INDICATIONS FOR FDG PET

(SEE SPECIAL TRACERS SECTIONS FOR INDICATIONS OTHER TRACERS)

CANCER TYPE~~(FDG PET/CT)~~	INITIAL STAGING	RESTAGING
~~Adrenal~~ ADRENAL (other than pheochromocytoma/ paraganglioma)	**Not Indicated**	**Not Indicated**
~~AIDS~~ AIDS-**related** ~~Kaposi~~ KAPOSI SARCOMA~~arcoma~~	with prior inconclusive imaging	**Not Indicated**
~~ALL (~~ACUTE~~cute Lymphoblastic~~ LYMPHOBLASTIC ~~Leukemia~~LEUKEMIA (ALL)	lymphomatous extramedullary disease	lymphomatous extramedullary disease
~~AML (~~Acute CUTE MYELOGENOUS ~~yelogenous~~ L~~eukemia~~EUKEMIA (AML)	If suspected extramedullary involvement	If suspected/known extramedullary involvement
~~Anal~~ANAL	with prior inconclusive imaging (can be done with PET (PET/CT or PET/MR‡‡ if available))	with prior inconclusive imaging
~~Anaplastic Thyroid Cancer~~	~~with prior inconclusive imaging~~	~~with prior inconclusive imaging~~
~~BCC~~B ~~(Basal~~ASAL ~~Cell~~ CELL ~~Carcinoma~~ (BCC of the skin)~~)~~	**Not Indicated**	**Not Indicated**

ONCOLOGICAL INDICATIONS FOR FDG PET

(SEE SPECIAL TRACERS SECTIONS FOR INDICATIONS OTHER TRACERS)

CANCER TYPE~~(FDG PET/CT)~~	INITIAL STAGING	RESTAGING
~~Bladder~~BLADDER	Muscle invasive only, with prior inconclusive imaging	Metastatic only, with prior inconclusive imaging
~~Breast~~BREAST	Indicated for stage IIb and above (if only T and N are provided, this equates to T3 (tumor > 50mm); or T4 (tumor of any size with direct extension to chest wall and/or skin); or N2 (>3 axillary LN, ipsilateral internal mammary node); or the combination of T2 (tumor >20mm but <50mm) plus N1 (any positive lymph node involvement)	with prior inconclusive imaging OR if initial stagging was done with PET
~~Castleman's disease~~	~~Indicated~~	~~Indicated~~
~~Cervical~~CERVICAL	Indicated (can consider PET/MR‡‡ if available)	Indicated
~~Chordoma~~CHORDOMA	with prior inconclusive imaging	**Not Indicated**
~~CLL (Chronic Lymphocytic Leukemia) /SLL (Small Lymphocytic Leukemia)~~	~~For suspected high-grade transformation or to guide biopsy~~	~~with accelerated CLL or to guide biopsy~~
~~Colorectal~~CHOLANGIOCARCINOMA	with prior inconclusive imaging ~~with prior inconclusive imaging~~	with prior inconclusive imagingwith prior inconclusive imaging

ONCOLOGICAL INDICATIONS FOR FDG PET

(SEE SPECIAL TRACERS SECTIONS FOR INDICATIONS OTHER TRACERS)

CANCER TYPE~~(FDG PET/CT)~~	INITIAL STAGING	RESTAGING
CHONDROSARCOMA (bone)	Not Indicated	Not Indicated
~~Chondrosarcoma~~ CHONDOSARCOMA (bone)	~~Not Indicated~~	~~Not Indicated~~
COLORECTAL	with prior inconclusive imaging (PET/CT indicated if potentially surgically curable M1 disease, when considered for image-guided liver directed therapies)	with prior inconclusive imaging
~~Endometrial~~ENDOMETRIAL	with prior inconclusive imaging	with prior inconclusive imaging
~~Esophageal~~ ESOPHOGEAL and EGJ (esophagogastric junction epicenter < 2m into stomach)	Indicated	Indicated
E~~wing sarcoma~~WING SARCOMA- Osseous	Indicated (all ages)~~with MR/CT of local area disease and Chest CT and prior inconclusive bone scan~~	Patients <30 yrs old: Indicated~~with prior inconclusive bone scan; or prior PET/CT demonstrated disease not seen on other imaging modalities~~ Patients >30 yrs old: when initial staging showed metastatic disease Or other signs (PE/imaging) worrisome for progression beyond localized disease
~~FALLOPIAN TUBE CANCER~~	~~with prior inconclusive imaging~~	~~with prior inconclusive imaging~~

ONCOLOGICAL INDICATIONS FOR FDG PET

(SEE SPECIAL TRACERS SECTIONS FOR INDICATIONS OTHER TRACERS)

CANCER TYPE~~(FDG PET/CT)~~	INITIAL STAGING	RESTAGING
FALLOPIAN TUBE CANCER ~~Extrahepatic Cholangiocarcinoma~~	with prior inconclusive imaging ~~with prior inconclusive imaging~~	with prior inconclusive imaging ~~with prior inconclusive imaging~~
G~~Gallbladder~~ ALLBLADDER	with prior inconclusive imaging	with prior inconclusive imaging
G~~astric Cancer~~ASTRIC (include EGJ tumors with epicenter >2cm into stomach)	with prior inconclusive imaging or if radiation is being considered **(Not indicated for T1N0M0 or M1)**	with prior inconclusive imaging. PET/CT is indicated for post radiation imaging
~~Gestational~~ GESTATIONAL ~~trophoblastic~~ TROPHOBLASTIC ~~cancer~~CANCER	with prior inconclusive imaging	with prior inconclusive imaging
~~Head~~ HEAD **and** ~~neck~~ NECK (including mucosal melanoma of the head and neck)	Indicated • ~~-~~May be done in conjunction with a dedicated face/neck ~~CT/~~MRI when surgery or radiation is planned	Indicated • ~~-~~Can concurrently approve a Neck MRI and PET 3-4 months after definitive • ~~(~~treatment in patients with locoregionally advanced disease or with altered anatomy. • • ~~-~~PET should not be done earlier than 12 weeks after definitive treatment unless signs or symptoms of recurrence • • ~~-~~If final PET/CT is equivocal or borderline for residual disease, a repeat PET/CT at

ONCOLOGICAL INDICATIONS FOR FDG PET

(SEE SPECIAL TRACERS SECTIONS FOR INDICATIONS OTHER TRACERS)

CANCER TYPE~~(FDG PET/CT)~~	INITIAL STAGING	RESTAGING
		≥ 6 weeks may help identify those that can be safely observed without additional surgery~~)~~
~~Hepatocellular~~HEPATOCELLULAR~~ / Intrahepatic Cholangiocarcinoma~~	with prior inconclusive imaging	with prior inconclusive imaging
~~Langerhans Cell Histiocytosis~~ ~~-predominantly osseous disease~~ ~~-non osseous disease~~	~~Indicated~~	~~Indicated~~
LEUKEMIA (refer to specific types listed in table when possible)	~~Not indicated~~ If there is lymph node involvement (lymphomatous features), soft tissue and/or extramedullary involvement (myeloid sarcoma) and/or if forms "chloromas" (leukemia tumor balls)	~~Not indicated~~If there is lymph node involvement (lymphomatous features), soft tissue and/or extramedullary involvement (myeloid sarcoma) and/or if forms "chloromas" (leukemia tumor balls)
~~Lung~~ LUNG • ~~ALL~~ ~~Nn~~on-~~s~~Small ~~Ce~~ell	Indicated	Indicated
•		
•	Indicated	Indicated
• -Limited stage small cell ~~S~~stage I-III	Not indicated	Not indicated
•		
○ Except -T3/T4		
• -Extensive small cell Stage IV and T3 or T4 disease		
○		
~~Lung~~	~~Not indicated~~	~~Not Indicated~~

ONCOLOGICAL INDICATIONS FOR FDG PET

(SEE SPECIAL TRACERS SECTIONS FOR INDICATIONS OTHER TRACERS)

CANCER TYPE~~(FDG PET/CT)~~	INITIAL STAGING	RESTAGING
~~Extensive small cell~~ (Stage ~~IV~~Stage IV a and T3 ~~or T4 disease~~ ~~T3/T4)~~		
LYMPHOCYTIC LEUKEMIA • ~~-~~Chronic (CLL) and Small (SLL)	For suspected high-grade transformation or to guide biopsy with prior inconclusive imaging	with accelerated CLL or to guide biopsy with prior inconclusive imaging (includes negative CT with rising tumor markers or if conventional imaging documents mets, IF clearly considering resection)
~~Lymphoma~~ LYMPHOMA (Non~~n~~ -Hodgkins and Hodgkins)	Indicated (can consider PET/MR‡‡)	Indicated (can consider PET/MR‡‡)
~~Medullary Thyroid Cancer~~	~~FDG Not Indicated (see Dotatate below)~~	~~when calcitonin levels ≥ 150 pg/ml or CEA levels >5 ng/ml post-surgery with prior insufficient Dotatate scan~~
~~Melanoma~~MELANOMA (See Uveal melanoma below for indications)	only stage III, IV	only stage III, IV
M~~erkel cell~~ERKEL CELL	Indicated	Indicated
~~Mesothelioma~~ MESOTHELIOMA (pleural)	Indicated only prior to surgery for stage I-IIIA	Indicated only prior to surgery for stage I-IIIA
MULTIPLE MYELOMA~~ultiple Myeloma~~ • ~~-~~S~~s~~moldering myeloma (asymptomatic) •	Indicated	~~Indicated - Active myeloma/plasmacytoma only~~ Not indicated (unless labs suggest progression to active myeloma)

ONCOLOGICAL INDICATIONS FOR FDG PET

(SEE SPECIAL TRACERS SECTIONS FOR INDICATIONS OTHER TRACERS)

CANCER TYPE~~(FDG PET/CT)~~	INITIAL STAGING	RESTAGING
-	Indicated Indicated	Indicated Indicated
• ~~A~~active myeloma		
•		
• ~~P~~plasmacytoma	~~Indicated when MIBG is negative, inconclusive, or there are discordant findings between MIBG and pathology~~	~~Indicated when the FDG PET was used for initial staging~~
~~NEUROBLASTOMA~~		
~~NEUROENDICRINE TUMORS-NET UNDIFFERENTIATED/DEDIFFERENTIATED (including pheochromocytoma, paraganglioma, extrapulmonary large/small cell)~~	~~Indicated if used after prior negative or inconclusive Ga68 Dotatate scan~~	~~Indicated when FDG was used for initial staging, or when used after prior negative/inconclusive Ga68 Dotatate scan (or MIBG scan) OR after inconclusive conventional imaging~~
NEUROBLASTOMA	Indicated when MIBG is negative, inconclusive, or there are discordant findings between MIBG and pathology	Indicated when the FDG PET was used for initial staging
NEUROENDICRINE TUMORS-NET UNDIFFERENTIATED/DEDIFFERENTIATED (including pheochromocytoma, paraganglioma, extrapulmonary large/small cell)	Indicated if used after prior negative or inconclusive Ga68 Dotatate scan	Indicated when FDG was used for initial staging, or when used after prior negative/inconclusive Ga68 Dotatate scan (or MIBG scan) OR after inconclusive conventional imaging

ONCOLOGICAL INDICATIONS FOR FDG PET

(SEE SPECIAL TRACERS SECTIONS FOR INDICATIONS OTHER TRACERS)

CANCER TYPE~~(FDG PET/CT)~~	INITIAL STAGING	RESTAGING
~~Ovarian~~OVARIAN~~/Fallopian tube Cancer/ Primary peritoneal cancer~~	with prior inconclusive imaging	with prior inconclusive imaging
~~Occult primary~~OCCULT PRIMARY	with prior inconclusive imaging (can consider PET/MR‡‡)	with prior inconclusive imaging
~~Osteosarcoma~~OSTEOSARCOMA ~~Osseous~~ • Osseous	For patients >30 years old: Indicated when the prior bone scan is inconclusive or negative (i.e. the primary bone tumor is not seen on bone scan). PET can be approved in conjunction with MR of primary site~~with MR/CT of local area disease and Chest CT and prior inconclusive bone scan~~ For patients <30 years old: Indicated	For patients >30 yrs old: Indicated when disease is positive on prior FDG-PET or when there is inconclusive conventional imaging. PET can be approved in conjunction with MR of primary site~~with prior inconclusive bone scan or prior PET/CT demonstrated disease not seen on other imaging modalities~~ Indicated
~~Other malignancies~~ PANCREATIC	W~~w~~ith prior inconclusive imaging OR with any of the following high-risk features: ~~o~~ borderline resectable • disease ~~o~~ markedly elevated • CA19-9 >180 U/ml ~~o~~ large primary tumor/ • lymph nodes ~~o~~ very symptomatic (jaundice, symptomatic	~~with prior inconclusive imaging~~ Not Indicated

ONCOLOGICAL INDICATIONS FOR FDG PET

(SEE SPECIAL TRACERS SECTIONS FOR INDICATIONS OTHER TRACERS)

CANCER TYPE~~(FDG PET/CT)~~	INITIAL STAGING	RESTAGING
	~~gastric outlet~~ ~~obstruction, venous~~ ~~thromboembolism,~~ ~~extreme pain and~~ • ~~excessive weight loss~~~~with prior inconclusive imaging~~	
~~Pancreatic cancer~~	~~with prior inconclusive imaging OR with any of the following high-risk features:~~ ○ ~~borderline resectable disease~~ ○ ~~markedly elevated CA19-9 >180 U/ml~~ ○ ~~large primary tumor/ lymph nodes~~ ○ ~~very symptomatic (jaundice, symptomatic gastric outlet obstruction, venous thromboembolism, extreme pain and excessive weight loss~~	
~~Penil~~PeENILE	with prior inconclusive imaging	with prior inconclusive imaging
PERITONEAL CANCER (PRIMARY)~~Poorly differentiated or dedifferentiated neuroendocrine tumors (includes Pheochromocytoma/ paraganglioma, extrapulmonary large/small cell)~~	with prior inconclusive imaging~~with prior negative or inconclusive Ga68 Dotatate scan~~ ~~Indicated when the diagnosis is made OR if suspected based on abnormal PE, abnormal imaging or abnormal labs (i.e.~~	with prior inconclusive imaging~~with prior negative or inconclusive Ga68 Dotatate scan~~ ~~For pheochromocytoma/ paraganglioma, extrapulmonary large/small cell- FDG PET/CT may be done before a Dotatate scan after inconclusive CT~~

ONCOLOGICAL INDICATIONS FOR FDG PET

(SEE SPECIAL TRACERS SECTIONS FOR INDICATIONS OTHER TRACERS)

CANCER TYPE~~(FDG PET/CT)~~	INITIAL STAGING	RESTAGING
~~POST TRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD)~~	~~significantly elevated or rising viral titers)~~	~~Indicated~~
POST TRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD)	Indicated when the diagnosis is made OR if suspected based on abnormal PE, abnormal imaging or abnormal labs (i.e. significantly elevated or rising viral titers)	Indicated
~~Prostate~~ PROSTATE (~~this applies to~~ FDG PET ~~/CT~~ only) *See other PET tracer section~~F18-Fluciclovine section~~ below for prostate cancer*	**Not Indicated**	**Not Indicated**
~~Renal~~RENAL	**Not Indicated**	**Not Indicated**
~~Skin squamous cell~~SKIN SQUAMOUS CELL	with prior inconclusive imaging	**Not Indicated**
~~Small bowel adenocarcinoma~~SMALL BOWEL CARCINOMA	**Not indicated**	with prior inconclusive imaging
~~Soft tissue sarcoma~~SOFT TISSUE ~~S~~SARCOMA (including ~~e.g.,~~ soft tissue/extraosseous Ewing sarcoma and soft tissue/extraosseous osteosarcoma)/ GIST/ Rhabdomyosarcoma	For patients >30 years old: with prior inconclusive imaging For patients <30 years old~~Pediatric~~: ~~Indicated~~Indicated (does not	For patients >30yrs old with prior inconclusive imaging For patients <30 yrs old~~Pediatric~~:~~-~~ Indicated (does not require inconclusive conventional imaging)

ONCOLOGICAL INDICATIONS FOR FDG PET

(SEE SPECIAL TRACERS SECTIONS FOR INDICATIONS OTHER TRACERS)

CANCER TYPE~~(FDG PET/CT)~~	INITIAL STAGING	RESTAGING
	require inconclusive conventional imaging)	
~~Testicular~~TESTICULAR • ~~-~~Seminoma	~~Seminoma -~~Not Indicated	~~Seminoma -~~with prior inconclusive imaging or residual mass >3cm or 6 weeks post chemotherapy (If final PET/CT is equivocal or borderline for residual disease PET/CT, a repeat PET/CT a ≥ 6 weeks may help identify those that can be safely observed without additional surgery) ~~Non-seminoma -~~ Not Indicated
• ~~-~~Non-Seminoma	Not Indicated ~~Non-seminoma - Not Indicated~~	
~~Thymoma and thymic cancer~~THYMOMA/THYMIC CANCER	Indicated	Indicated
~~Thyroid~~ THYROID • ~~-(P~~papillary, ~~/F~~follicular, ~~/~~Hurthle~~)~~	Not Indicated	~~1. A thyroidectomy and radioiodine ablation initially; AND~~ Indicated with the following 3 criteria: • ~~1.~~ A thyroidectomy and radioiodine ablation were done initially; AND

ONCOLOGICAL INDICATIONS FOR FDG PET

(SEE SPECIAL TRACERS SECTIONS FOR INDICATIONS OTHER TRACERS)

CANCER TYPE~~(FDG PET/CT)~~	INITIAL STAGING	RESTAGING
		~~2.~~ Serum thyroglobulin is >2 ng/ml (unstimulated or stimulated) OR there is a high anti- thyroglobulin • antibody (anti-Tg Ab) >1 year after treatment AND • ~~3.~~ A Negative current I-131/123 scan OR a Negative prior stimulated whole body I-131/ I-123 scan done at TG level similar to the current TG level (a current scan is needed if on radioiodine sensitizing medications)
• Anaplastic • Medullary	With prior inconclusive imaging Not Indicated (see Dotatate indications below)	~~2. Stimulated serum thyroglobulin >2 ng/ml or high anti- thyroglobulin antibody (anti-Tg Ab) >1 year after treatment AND~~ With prior inconclusive imaging with prior inconclusive imaging when calcitonin levels ≥ 150 pg/ml or CEA levels >5 ng/ml post-surgery with prior insufficient Dotatate scan ~~3. Current OR two prior stimulated whole body I-131/ I-123 scans are negative (a current scan is needed if on radioiodine sensitizing medications).~~
~~Anaplastic~~	~~with prior inconclusive imaging~~	~~with prior inconclusive imaging~~

ONCOLOGICAL INDICATIONS FOR FDG PET

(SEE SPECIAL TRACERS SECTIONS FOR INDICATIONS OTHER TRACERS)

CANCER TYPE~~(FDG PET/CT)~~	INITIAL STAGING	RESTAGING
~~Medullary~~	~~Not Indicated (see Dotatate indications below)~~	~~when calcitonin levels ≥ 150 pg/ml or CEA levels >5 ng/ml post-surgery with prior insufficient Dotatate scan~~ with prior inconclusive imaging
~~Uterine~~ UTERINE	with prior inconclusive imaging	
~~Uveal Melanoma~~UVEAL MELANOMA	Not Indicated	w~~W~~ith prior inconclusive imaging
VAGINAL	Indicated	Indicated
VULVAR	≥T2 or after prior inconclusive imaging	Indicated
~~Vaginal~~VAGINAL ~~Indicated~~		
~~Vulvar~~VULVAR ~~≥T2 or after prior inconclusive Indicated inconclusive imaging~~		

MISCELLANEOUS (NON ONCOLOGIC) INDICATIONS FOR FDG PET

(excluding brain and cardiac PET which have separate Guidelines)

CANCER TYPE	INITIAL STAGING	RESTAGING
CASTELMAN'S DISEASE	Indicated	Indicated

MISCELLANEOUS (NON ONCOLOGIC) INDICATIONS FOR FDG PET
(excluding brain and cardiac PET which have separate Guidelines)

CANCER TYPE	INITIAL STAGING	RESTAGING
LANGERHANS CELL HISTIOCYTOSIS		
• Predominantly osseous disease	Indicated	Indicated
• Non-osseous disease	Not Indicated	Not Indicated

~~MISCELLANEOUS (NON ONCOLOGIC) INDICATIONS FOR FDG PET (excluding brain and cardiac PET which have separate Guidelines)~~

~~CASTELMAN'S DISEASE indicated for initial and restaging~~

~~LANNGERHANS CELL HISTIOCYTOSIS~~
~~predominantly osseous disease indicated for initial and restaging~~
~~non osseous disease not indicated for initial nor restaging~~

~~OTHER (NON FDG) PET TRACERS~~ covered

~~GA68A[68] DOTATATE, GA68-DOTATOC and CU64 DOTATATE~~

~~CANCER INITIAL (GA68 DOTATATE PET/CT)~~	~~INITIAL STAGING AND RESTAGING~~

OTHER (NON-FDG) PET TRACERS covered
GA68-DOTATATE, GA68-DOTATOC and CU64-DOTATATE

CANCER TYPE	INITIAL STAGING	RESTAGING
CARCINOID EXTRAPULMONARY LARGE AND SMALL CELL MEN-1/MEN-2 SYNDOMES NEUROENDOCRINE TUMORS (NET) PHEOCHROMOCYTOMA	• Biopsy proven AND to determine eligibility for somatostatin receptor (SSR) therapy (such Lutetium, Octreotide, Sandostatin) OR	• for restaging or monitoring response to active treatment, and/or evaluation for suspicion of recurrence due to new or changing signs/symptoms

PARAGANGLIOMA	• **Biopsy proven AND prior CT/ MRI has been or is reasonably expected to be insufficient for any the following reasons:** ○ **to determine extent of treatment plan** ○ **to determine if candidate for invasive diagnostic/ therapeutic procedure** ○ **to determine optimal anatomic location for invasive procedure** • **(can consider PET/MR‡‡)**	**when CT/MR is negative but biomarkers are rising** • **PET/MR‡‡ can be considered with negative CT/MR and rising biomarkers** • **asymptomatic surveillance is not approvable**
MEDULLARY THYROID	**Prior CT/ MRI insufficient to** • **Determine extent of treatment plan** • **Determine if candidate for invasive diagnostic/ therapeutic procedure** • **Determine optimal anatomic location for invasive procedure**	**When calcitonin levels ≥ 150 pg/ml or CEA levels >5 ng/ml post-surgery**

F18 FLUCICLOVINE (AXUMIN®), PSMA TRACERS (such as F18 piflufolastat (Pylarify®) and GA68) and C11 CHOLINE

CANCER ~~(F18 FLUCICLOVINE (AXUMIN))~~	INITIAL STAGING	RESTAGING
~~Prostate Cancer~~PROSTATE (PET/CT or PET/MRI‡‡) • After a negative Axumin® PET, a subsequent PSMA PET is not covered until a repeat PSA (done at least 3 months later) shows a progressive rise • 11-Choline should be approved only if PSMA and/or Axumin® are not available. Order of preference typically would be PSMA, then Axumin®, then 11-Choline	Only PSMA (not Axumin® or Choline) is indicated for high risk defined as 1 or more of the following: • T3a or higher, • PSA>20, • Gleason Score* 8-10, • Grade Group** 4-5 • Gleason Primary Pattern*** 5 Pelvic MRI can be approved concurrently if needed for surgical planning~~With prior inconclusive bone scan with no CT/MRI correlate; or inconclusive bone SPECT/CT~~	For post-surgery/radiation with persistent or rising PSA (two separate PSA levels required) as below:~~With rising/persistent PSA AND after CT/MRI has been performed and is insufficient for detection of metastases~~ • PSA <2 PMSA indicated and DOES NOT require prior conventional imaging • PSA<2 Axumin® indicated if prior bone scan and CT/MRI are negative or inconclusive • PSA>2 PSMA, Axumin® or Choline indicated if prior bone scan and CT/MRI are negative or inconclusive

*Equivalent Scorings:

Grade Group	Gleason Score	Gleason Pattern
4	8	4+4 3+5 5+3
5	9 or 10	4+5 5+4 5+5

**The Primary Pattern refers to the 1st number in the Gleason Pattern

‡‡NOTE: If PET/MR study is requested, there is no specific CPT Code for this imaging study and a Health Plan review will be required.

~~*Equivalent scorings~~

~~Grade Group Gleason Score Gleason Pattern~~

~~4 8 4+4, 3+5, 5+3~~
~~5 9 or 10 4+5, 5+4, 5+5~~
~~**The Primary Pattern refers to the 1st number in the Gleason Pattern~~**~~SUBSEQUENT TREATMENT STRATEGY:~~**

- ~~For restaging or monitoring response to active treatment (including immunotherapy), and/or a single evaluation after completion/cessation of therapy. The interval should ideally be 6-12 weeks after surgery, and 12 weeks after radiation.~~
- ~~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.~~
- ~~Asymptomatic surveillance~~ **~~is not~~** ~~approvable.~~

BACKGROUND

Inconclusive Imaging includes the following:

- Equivocal or ambiguous other prior standard ~~imaging, if~~**imaging if** results will change management
- Biopsy guidance (e.g., tumors with necrosis)
- High suspicion of metastases due to clinical or histopathological or laboratory considerations but with no evidence of metastases on standard initial staging
- Clinical or laboratory disease progression with negative standard imaging
- Contraindications to IV contrast, including allergy and chronic renal failure precluding MRI in a patient with a known or highly suspected malignancy
    - PET/CT may be indicated if CT cannot be performed due to significant iodinated contrast allergy or chronic renal failure **AND** MRI cannot be performed due to significant gadolinium contrast allergy or if renal failure with GFR < 30 (RSNA, 2018).
- Evaluation for other distant metastases prior to surgical resection of limited metastases/local disease and otherwise negative prior standard imaging
- Response to neoadjuvant therapy when CT/MR insufficient
- Residual masses after completion of therapy
- Target definition for radiation planning
- **If previous conventional imaging has been inconclusive, and it seems reasonable to expect that to still be the case, new conventional imaging is NOT required**

In situations where there is questionable disease in an area that requires significantly invasive procedures to obtain tissue (such as open surgical procedures), and malignancy is high on the radiographic differential diagnosis, it is reasonable and medically appropriate to attempt to gain as much information about diagnosis from imaging prior to subjecting the patient to tissue diagnosis that has real risk of morbidity/mortality.

Definition of Disease Progression:
For any signs of progression, as noted below, that could not be confirmed by other imaging, PET/CT is needed. Findings concerning for progression of disease include:

- Worsening of symptoms such as pain or dyspnea
- Evidence of worsening or new disease on physical examination
- Declining performance status
- Unexplained weight loss
- Increasing alkaline phosphatase, alanine aminotransferase (ALT), aspartate transaminase (AST), or bilirubin
- Hypercalcemia
- New radiographic abnormality or increase in the size of pre-existing radiographic abnormality
- New areas of abnormality on functional imaging (e.g., bone scan, PET/CT)
- Increasing tumor markers (e.g., carcinoembryonic antigen [CEA], CA 15-3, CA27.29)

PET/CT also helps to differentiate active tumor from necrotic or inactive scar tissue, malignant from benign tissue, and recurrent tumor from nondescript benign changes.

Positron emission tomography-Computed Tomography (PET/CT) is a rapidly developing and changing technology that is able to detect biochemical reactions, e.g., metabolism, or abnormal distribution of cell receptors within body tissues. A radioactive tracer is used during the procedure. Unlike other nuclear medicine examinations, PET/CT can measure metabolic activity of the cells of body tissues, providing information about the functionality and structure of the particular organ or tissue examined. PET/CT may also detect biochemical changes that help to evaluate malignant tumors and other lesions.

TYPICALLY, separate CT/MR scans being requested concurrently with a PET are not needed. There should be very few instances where separate studies are needed, and when this does happen, it is usually SITE-SPECIFIC. Most PET scanners now in use can "simultaneously" perform PET and CT (whether CT Attenuation or a Diagnostic CT). Contrast can be given for the CT portion of the PET/CT. A separate request for diagnostic CTs in addition to PET is therefore not needed. The ordering MDO can specify to the imaging provider details about what type of CT scan is desired to be done with the PET portion. "Exceptions" generally occur when CT is needed in a plane other than standard axial imaging (for example: coronal CT for facial bone imaging that might be needed for surgical reconstruction). Separate MRIs are

likewise rarely needed, but are perhaps somewhat more frequently needed than additional, separate CTs, since MRI does allow multiple imaging planes and may provide additional information. When evaluating for these "exceptions", the reason additional separate imaging is needed should be clearly delineated before approval.

The degree of radioactive tracer uptake may indicate increased metabolism in the cells of body tissues or an abnormal distribution of cell receptors. Cancer cells may show increased radioactive tracer relative to tissue not involved with tumor. Radioactive tracer uptake is often higher in fast-growing tumors; PET/CT is often not as beneficial for slow growing tumors. Radioactive tracer uptake may occur in various types of active inflammation and is not specific for cancer. **FDG is the most widely known and frequently requested radiotracer; however, the use of "special tracers" is a rapidly progressing field. These "special tracers" are typically somewhat specific to a certain cancer type due to their physiological properties. As such, a particularly careful review should be made when there is concern that a "special tracer" is needed or requested, regardless of whether the ST icon is present. If the notes clearly indicate the desired tracer (and guidelines are met for the tracer and cancer type), the case should be adjudicated according to the notes rather than the presence or absence of the ST icon. However, if the notes do not clearly indicate what tracer is requested, this needs to be clarified when there is discrepancy between notes and the ST icon (or lack thereof).**

Patients with certain malignancies may benefit more from PET/MRI since it detects brain and liver metastases better when compared with PET/CT. NCCN does suggest consideration of PET/MR in some malignancies (see table for specific cancers), but not specifically replacing PET/CT. PET/MRI should only be considered for certain malignancies and in specific situations (such as when extensive travel would be needed, for pediatric cases, particularly those requiring sedation or when reasonably expect a need for multiple PET scans where radiation exposure from CT would be a significant factor). Typically, PET/CT should suffice; however, under some circumstances, with clear explanation of why PET/MR is preferred rather than PET/CT, ~~PET/MR~~ PET/MR may be an appropriate study‡‡ (NCCN, 2020). ~~may be approvable.~~

Langerhans Cell Histiocytosis (Jessop, 2020; Daldrup-Link, 2001; Obert, 2017; Phillips, 2009) **is** ~~t~~The most common type of histiocytosis, with variable presentations and sites involvement. The osseous structures are the most common site of involvement. PET/CT is highly sensitive and specific for whole body evaluation as FDG is a metabolite of the histocyte cell and allows for a reproducible evaluation for response to effectiveness of treatment on restaging exams. Some studies suggest PET/CT ~~that~~ may be more effective in detecting bone lesions compared with MRI and bone scans in assessing disease response as healing/treatment changes of bone lesions on conventional imaging maybe delayed. PET/CT is, however, not the modality of choice in assessing disease response of lung or brain lesions; ~~,~~ in these scenarios, Chest CT (HRCT) and Brain MRI would be the test of choice, respectively.

POLICY HISTORY

Date	Summary
June 2021	**Added:** • **Definitions** • **CART T info** • **PTLD information added** • **PET/MRI information** • **Updated/added details for Prostate cancer and PSMA, Axumin and Choline** • **Minor adjustments to the PET FDG table, such as added details from NCCN, clarifications, separation of non-malignant uses**
May 2020	• **Modified to table format** • **Added section of follow up of a new or interval growth of a mixed pulmonary lung nodule on subsequent LDCT (NCCN 2020)** • **Initial staging indicated** ○ **Changed AML to extramedullary disease (previously lymphomatous involvement)** ○ **Changed Breast cancer stage IIb and above (previously III and IV)** ○ **Added Castleman's disease** ○ **Added for Chronic Lymphocytic Leukemia to guide biopsy** ○ **Changed Mesothelioma to only prior to surgery for stage I-IIIA** ○ **Added "soft tissue" sarcoma in pediatric patient** ○ **Added Thymoma and thymic cancer** ○ **Added Langerhans Cell Histiocytosis-predominantly osseous disease (previously not included)** • **Initial staging which is only indicated after prior inconclusive imaging (NCCN 2019/2020)** ○ **Added AIDS related Kaposi sarcoma** ○ **Changed Anal carcinoma (previously indicated)** ○ **Added Ewing sarcoma-osseous** ○ **Added Gestational trophoblastic disease** ○ **Added Hepatocellular/Intrahepatic Cholangiocarcinoma (previously not included)** ○ **Added Fallopian tube and primary peritoneal cancer** ○ **Added Osteosarcoma-osseous** ○ **Changed Penile cancer (previously indicated with palpable nodes)** • **Initial staging NOT indicated (NCCN 2019/2020)**

	○ Changed testicular (previously indicated) ○ Added Uveal Melanoma ○ Added Langerhans Cell Histiocytosis-predominantly non-osseous disease (previously not included) • Restaging indicated (NCCN 2019/2020) ○ Added Castleman's disease ○ Added for accelerated Chronic Lymphocytic Leukemia and to guide biopsy ○ Added Gastric Cancer post radiation treatment ○ Changed Mesothelioma to only prior to surgery for stage I-IIIA ○ Added "soft tissue" to sarcoma in pediatric patient ○ Added Thymoma and thymic cancer ○ Added Langerhans Cell Histiocytosis-predominantly osseous disease (previously not included) • Restaging which are only indicated after prior inconclusive imaging (NCCN 2019/2020) ○ Removed for resectable disease in Colorectal cancer ○ Removed for if candidate for surgery/locoregional therapy for endometrial cancer ○ Specified Ewings sarcoma-osseous ○ Added Extrahepatic Cholangiocarcinoma (previously not indicated) ○ Added Gallbladder carcinoma (previously not indicated) ○ Changed Gastric Cancer to prior inconclusive imaging or if radiation planning considered (previously indicated if no metastasis or early disease) ○ Added Gestational trophoblastic disease ○ Added Hepatocellular/Intrahepatic Cholangiocarcinoma (previously not included) ○ Changed Ovarian cancer (previously indicated for greater than Stage I) ○ Added Fallopian tube and all stages of primary peritoneal cancer ○ Added Osteosarcoma- osseous ○ Added that for pheochromocytoma/ paraganglioma, extrapulmonary large/small cell, restaging FDG PET/CT can be done after inconclusive CT ○ Modified Seminoma with residual mass >3cm or 6 weeks post chemotherapy (previously indicated) ○ Added Uveal melanoma • Restaging NOT indicated (NCCN 2019/2020) ○ Added AIDS related Kaposi sarcoma

	○ Changed Testicular non seminoma (previously indicated) ○ Added Langerhans Cell Histiocytosis-predominantly non-osseous disease (previously not included) • Added CT face/neck may be done in conjunction with PET when surgery or radiation is planned • Added to head and neck cancer that if a final PET is equivocal or borderline for residual disease PET, a repeat PET/CT a > 6 weeks may help identify those that can be safely observed without additional surgery • Medullary thyroid: added FDG restaging indicated when CEA >5ng/ml post-surgery and after prior insufficient Dotatate scan • Modified pancreatic cancer symptoms to excessive weight loss • Added to Seminoma: if final PET is equivocal or borderline for residual disease PET, a repeat PET/CT a > 6 weeks may help identify those that can be safely observed without additional surgery) • Thyroid FDG- changed serum thyroglobulin level to >2ng/ml (previously >5ng/ml) and added 'current OR two prior stimulated whole body I-131/ I-123 scans are negative (a current scan is needed if on radioiodine sensitizing medications)' • GA^{68} Dotatate- added restaging calcitonin levels ≥ 150 pg/ml or CEA levels >5 ng/ml post-surgery • F18 Fluciclovine (Axumin) ○ Initial staging changed to: With prior inconclusive bone scan with no CT/MRI correlate; or inconclusive bone SPECT/CT ○ Restaging changed to with rising/persistent PSA and after CT/MRI has been performed and is insufficient for detection of metastases • Added Inconclusive imaging features to background as noted in NCCN 2020 • Added Disease progression to Background as noted in NCCN 2020 • Added Section of Langerhans Cell Histiocytosis to background section
September 2019	• Removed Introduction section • Removed "Important Note" • Changed title "The following are noncovered for all other indications including (but not limited to):" to "The following

	are noncovered for F^{18} FDG, Ga^{68} Dotatate, F^{18} Fluciclovine (NCCN 2019):" • Under noncovered for F^{18} FDG, Ga^{68} Dotatate, F^{18} Fluciclovine section, added the following: ○ Breast cancer - Initial Staging for Stage I and II Breast Cancer ○ Melanoma - Initial and Restaging for Stage I and II Melanoma (NCCN 2016) ○ Bladder Cancer - non muscle invasive (by imaging or tissue sample) ○ Vulvar Cancer < T2 or no suspicion of metastatic disease ○ Prostate Cancer - Initial or Restaging ○ Small cell lung cancer - Staging (Initial or Restaging) for extensive disease ○ Ovarian Cancer - Restaging if stage I ○ Pancreatic Cancer - Restaging ○ Renal Cancer - Initial and Restaging ○ Skin Squamous Cell Carcinoma - Restaging ○ Gastric Cancer - Initial staging if there is evidence of metastases (M1), or very early disease (T1) ○ Malignant Pleural Mesothelioma - Initial staging except if stage I-IIIA and pre-surgical ○ Hepatocellular / Intrahepatic Cholangiocarcinoma - Initial and Restaging ○ Gallbladder/ Extrahepatic Cholangiocarcinoma - Restaging ○ Small bowel adenocarcinoma - Initial Staging ○ Chordoma – Restaging ○ Adrenal (except pheochromocytoma/ paraganglioma) - Initial or Restaging ○ Smoldering Myeloma - except to discern smoldering from active myeloma with negative skeletal survey ○ ALL (Acute Lymphoblastic Leukemia)/ AML (Acute Myelogenous Leukemia) - Unless prior imaging suggests lymphomatous involvement ○ BCC (Basal Cell Carcinoma (of the skin)) ○ Infection and/or Inflammation: removed "- PET for chronic osteomyelitis, infection of hip arthroplasty, and fever of unknown origin." • Under indications for oncological PET heading, added: "Note: for radiation treatment planning, contact health plan directly" • Under Initial Treatment Strategy, the first sentence now specifies "active myeloma" instead of "myeloma" previously

	• Under Initial Treatment Strategy, the last sentence now replaces "after a" with "AND": "To determine the optimal anatomic location for an invasive procedure AND prior imaging insufficient" • "CLL – chronic lymphocytic leukemia (PET/CT is generally not useful in CLL/SLL but may be necessary to direct nodal tissue sampling when high-grade histologic transformation is suspected) (NCCN, 2018)." has been changed to "CLL (Chronic Lymphocytic Leukemia): only when high-grade histologic transformation is suspected (NCCN, 2018)" • Changed references for SPN to "(Bueno, 2018; MacMahon, 2017)" from previous "(Vansteenkiste, 2006)" • Removed the section: " Excluding • ALL- acute lymphoblastic leukemia o Unless prior CT imaging suggest lymphomatous involvement • AML – acute myelogenous leukemia o Unless clinical suspicion for extramedullary disease • BCC – basal cell carcinoma (of the skin) • Prostate cancer (NCCN, 2018)" • Added "EXCEPT for the following, which are only indicated after prior inconclusive imaging (NCCN 2019): ○ Colorectal ○ Ovarian/ fallopian ○ Sarcoma/ GIST/ Uterine/Rhabdomyosarcoma ○ Chordoma ○ Muscle invasive bladder cancer ○ Endometrial Cancer ○ Penile (for palpable nodes only) ○ Occult Primary ○ Pancreatic Cancer (unless high risk features: borderline resectable, markedly elevated CA19-9 > 180 U/ml, large primary tumor/ lymph nodes) ○ Skin squamous Cell Carcinoma ○ Gallbladder/ Extrahepatic Cholangiocarcinoma ○ Poorly differentiated neuroendocrine tumors with prior negative Ga68 Dotatate/ MIBG/Octreotide scan (includes Pheochromocytoma/ paraganglioma, extrapulmonary large/small cell)" • Under subsequent Treatment Strategy, first line has been modified by adding parenthesis as follows: Restaging or

	monitoring response to active treatment (including immunotherapy)" • Under subsequent Treatment Strategy, changed "not to be performed within 4 weeks of completion of therapy (ideally F^{18} FDG, Ga^{68} Dotatate, F^{18} Fluciclovine PET is delayed 2 - 3months after surgical therapy, 2 - 3 months after radiation therapy if locoregional assessment is the imaging goal), and/or evaluation for suspicion of recurrence due to new or changing signs/symptoms. (Asymptomatic surveillance is not approvable) (NCCN, 2018)." to "The interval should ideally be 6 - 12 weeks after surgery, and 12 weeks after radiation. PET can be performed 1-3 weeks after neoadjuvant chemotherapy or neoadjuvant chemoradiation to assess stage for surgery. PET evaluation can also be done for suspicion of recurrence due to new or changing signs/symptoms or rising tumor markers, or inconclusive findings on CT. Asymptomatic surveillance is not approvable. (NCCN 2018, 2019)" • List of cancers under subsequent imaging (without needing prior inconclusive imaging) has been changed. The following were removed: Breast cancer (female and males), colorectal cancer (including colon, rectal, appendiceal or anal cancer), ovarian cancer. The following were changed as follows: • "Lung cancer - Non-small cell" to "Lung cancer - Non-small cell and limited stage small cell cancer" • "Esophageal cancer" to "Esophageal and esophagogastric cancer" • "Melanoma" to Melanoma- only stage III, IV (excludes uveal melanoma) • "Myeloma to "Active Myeloma/plasmacytoma" • Added for Soft tissue sarcoma: "only stage II/III for response to neoadjuvant Rx" • Added Merkel cell carcinoma • Added "Mesothelioma, if also presurgical" • Individual References were removed for soft tissue sarcoma and vulvar/ vaginal cancer. • Statement regarding subsequent PET scans needing prior inconclusive imaging has been modified from "only" if other imaging (ie. US, CT, MRI, NM) is inconclusive in determining a treatment plan or unable to be performed " to " only if other imaging (ie. US, CT, MRI, NM) is inconclusive/ insufficient in determining a treatment plan or unable to be performed or with rising tumor markers and negative/ insufficient other

	imaging. PETCT is to be used only if the cancer is known to be generally F^{18} FDG, Ga^{68} Dotatate, F^{18} Fluciclovine avid. It may be indicated if iodinated and gadolinium contrast are both contraindicated due to significant allergy or chronic renal failure without dialysis (NCCN 2019). " • Under subsequent PET scans needing prior inconclusive imaging, the following were changed: ○ Added: Breast cancer (female and males), Bladder cancer, only if metastatic, Colorectal Cancer – resectable metastatic disease only, Anal/ Vulvar/ Penile Carcinoma, Bone Sarcoma, Sarcoma/ GIST/ Uterine/Rhabdomyosarcoma, Ovarian/ malignant germ cell tumors/primary peritoneal cancer – Stage II-IV, Endometrial cancer if candidate for surgery/locoregional therapy; Poorly differentiated Cancers, or Dedifferentiated neuroendocrine tumors with prior negative Ga68 Dotatate/ MIBG/Octreotide scan • Removed: prostate cancer, pancreatic cancer, individual references for cancers • Changed: "Lung cancer -Small cell" to "Extensive small cell lung cancer"; "Tumor of unknown Origin" to "Occult primary"; "Neuroendocrine cancer (e.g. carcinoid, pheochromocytoma, etc)" to "Poorly differentiated or dedifferentiated neuroendocrine tumors with prior negative Ga68 Dotatate/ MIBG/Octreotide scan (includes Pheochromocytoma/ paraganglioma, extrapulmonary large/small cell)". • Last sentence has been changed from "Other malignancies where the tumor has been shown to be F^{18} FDG, Ga^{68} Dotatate, F^{18} Fluciclovineavid on prior PET/CT imaging if done, and other imaging (ie: US, CT, MRI, NM) is inconclusive in determining a treatment plan or unable to be performed " to "Other malignancies where other imaging (i.e., US, CT, MRI, NM) is inconclusive in determining a treatment plan or unable to be performed." • Under thyroid Cancer, ○ Added references "(NCCN 2019, ATA 2015)" to subsequent treatment strategy for papillary/follicular/ hurthle cancers ▪ Changed "Stimulated serum thyroglobulin > 2 ng/ml" to "Stimulated serum thyroglobulin > 5

	ng/ml or high anti- thyroglobulin antibody (anti-Tg Ab) > 1 year after treatment (Na SJ 2012)" ▪ Changed "Current whole body I-131 scan is negative (Kloos, 2005)" to "Current stimulated whole body I-131/ I-123 scan is negative (Alzahranj 2012)" ○ Changed "Medullary thyroid cancer when calcitonin levels > 150 pg/ml post-operatively (Wells, 2015)" to "Medullary thyroid cancer when calcitonin levels ≥ 150 pg/ml post primary treatment (NCCN 2019, Souteiro 2019)" ○ Changed "Anaplastic 3-6 months after initial treatment, 3-6 month interval if persistent structural disease (Smallridge, 2012)" to "Anaplastic: Initial and Restaging after prior inconclusive/ insufficient CT/MRI (NCCN 2019)" • Added pediatric cancers section as follows: "PEDIATRIC CANCERS (for indications different from adult guidelines): ○ Sarcoma - Initial and Restaging (Quartuccio 2015) ○ Neuroblastoma/ other cancers under Ga68 imaging: only with prior negative/ inconclusive MIBG/ Octreotide/ Ga68 PETCT (Uslu 2015, Alexander 2018, Kong 2016, Li 2018, Elkhatib 2017) ○ Nasopharyngeal Cancer- Initial staging after inconclusive/ insufficient MRI; Restaging. (Cheuk 2012) • For Gallium 68 Dotatate PET: ○ Added references for initial or subsequent treatment strategy: (NCCN 2019, Deppen, 2016 a, b) ○ Added under neuroendocrine tumors: "Medullary Thyroid Cancer for Initial staging; and Restaging when calcitonin ≥ 150 pg/ml" ○ Modified last part of the last sentence as follows: "and rising biomarkers (asymptomatic surveillance is not approvable). " • Under 18F-Fluciclovine PET/CT SCAN: ○ Added "(Axumin)" after 18F-Fluciclovine ○ Removed reference "(Bach-Gansmo, 2017)" ○ Changed "18F-Fluciclovine PET/CT scans should be performed only if other imaging (CT, MRI, US, NM) is inconclusive/insufficient AND the patient has not already been evaluated with an F18 FDG, Ga68 Dotatate, F18 Fluciclovine PET/CT Scan" to "Known prostate cancer for workup of recurrence and response to treatment, only if other imaging (CT, MRI) AND Bone

	scan is inconclusive/insufficient. (NCCN 2019, Andriole 2019, Bach-Gansmo 2017)" ○ Removed:" Known prostate cancer for workup of recurrence and response to treatment:" ○ "Initial treatment by radical prostatectomy with" was replaced by "Post radical prostatectomy with" ○ "Initial treatment radiation therapy with" was replaced by "Post radiation therapy with" ○ "Post-RT rising PSA or positive digital exam and is candidate for local therapy" was replaced by "rising/persistent PSA (increase should be >2ng/ml unless doubling time ≤ 8 months or pt is a candidate for local salvage therapy)" • Removed: "NOTE: Not all plans cover 18F-Fluciclovine (A9588), such as Magellan Complete Care of Florida and Magellan Complete Care of Arizona. If you are unsure, you should check with the Health Plan prior to requesting a PET with Fluciclovine from NIA." • Added Background section as follows: "BACKGROUND: Positron emission tomography (PET) is a rapidly developing and changing technology that is able to detect biochemical reactions, e.g., metabolism, or abnormal distribution of cell receptors within body tissues. A radioactive tracer is used during the procedure. Unlike other nuclear medicine examinations, PET can measure metabolic activity of the cells of body tissues, providing information about the functionality and structure of the particular organ or tissue examined. PET may also detect biochemical changes that help to evaluate malignant tumors and other lesions. The degree of radioactive tracer uptake may indicate increased metabolism in the cells of body tissues or an abnormal distribution of cell receptors. Cancer cells may show increased radioactive tracer relative to tissue not involved with tumor. Radioactive tracer uptake is often higher in fast-growing tumors; PET is often not as beneficial for slow growing tumors. Radioactive tracer uptake may occur in various types of active inflammation and is not specific for cancer."

~~September 2019~~

- ~~Removed Introduction section~~

- ~~Removed "Important Note"~~
- ~~Changed title "The following are noncovered for all other indications including (but not limited to):" to "The following are noncovered for F^{18} FDG, Ga^{68} Dotatate, F^{18} Fluciclovine (NCCN 2019):"~~
- ~~Under noncovered for F^{18} FDG, Ga^{68} Dotatate, F^{18} Fluciclovine section, added the following:~~
    - ~~Breast cancer – Initial Staging for Stage I and II Breast Cancer~~
    - ~~Melanoma – Initial and Restaging for Stage I and II Melanoma (NCCN 2016)~~
    - ~~Bladder Cancer - non muscle invasive (by imaging or tissue sample)~~
    - ~~Vulvar Cancer < T2 or no suspicion of metastatic disease~~
    - ~~Prostate Cancer - Initial or Restaging~~
    - ~~Small cell lung cancer - Staging (Initial or Restaging) for extensive disease~~
    - ~~Ovarian Cancer - Restaging if stage I~~
    - ~~Pancreatic Cancer - Restaging~~
    - ~~Renal Cancer – Initial and Restaging~~
    - ~~Skin Squamous Cell Carcinoma – Restaging~~
    - ~~Gastric Cancer – Initial staging if there is evidence of metastases (M1), or very early disease (T1)~~
    - ~~Malignant Pleural Mesothelioma – Initial staging except if stage I-IIIA and pre-surgical~~
    - ~~Hepatocellular / Intrahepatic Cholangiocarcinoma – Initial and Restaging~~
    - ~~Gallbladder/ Extrahepatic Cholangiocarcinoma – Restaging~~
    - ~~Small bowel adenocarcinoma - Initial Staging~~
    - ~~Chordoma – Restaging~~
    - ~~Adrenal (except pheochromocytoma/ paraganglioma) - Initial or Restaging~~
    - ~~Smoldering Myeloma - except to discern smoldering from active myeloma with negative skeletal survey~~
    - ~~ALL (Acute Lymphoblastic Leukemia)/ AML (Acute Myelogenous Leukemia) - Unless prior imaging suggests lymphomatous involvement~~
    - ~~BCC (Basal Cell Carcinoma (of the skin))~~
    - ~~Infection and/or Inflammation: removed "– PET for chronic osteomyelitis, infection of hip arthroplasty, and fever of unknown origin."~~
- ~~Under indications for oncological PET heading, added: "Note: for radiation treatment planning, contact health plan directly"~~
- ~~Under Initial Treatment Strategy, the first sentence now specifies "active myeloma" instead of "myeloma" previously~~
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- ~~"CLL – chronic lymphocytic leukemia (PET/CT is generally not useful in CLL/SLL but may be necessary to direct nodal tissue sampling when high-grade histologic transformation is suspected) (NCCN, 2018)." has been changed to "CLL (Chronic Lymphocytic Leukemia): only when high-grade histologic transformation is suspected (NCCN, 2018)"~~

- ~~Changed references for SPN to "(Bueno, 2018; MacMahon, 2017)" from previous "(Vansteenkiste, 2006)"~~
- ~~Removed the section:~~
  ~~" Excluding~~
    - ~~ALL- acute lymphoblastic leukemia~~
      - ~~o Unless prior CT imaging suggest lymphomatous involvement~~
    - ~~AML – acute myelogenous leukemia~~
      - ~~o Unless clinical suspicion for extramedullary disease~~
    - ~~BCC – basal cell carcinoma (of the skin)~~
    - ~~Prostate cancer (NCCN, 2018)"~~
- ~~Added "EXCEPT for the following, which are only indicated after prior inconclusive imaging (NCCN 2019):~~
  - ~~Colorectal~~
  - ~~Ovarian/ fallopian~~
  - ~~Sarcoma/ GIST/ Uterine/Rhabdomyosarcoma~~
  - ~~Chordoma~~
  - ~~Muscle invasive bladder cancer~~
  - ~~Endometrial Cancer~~
  - ~~Penile (for palpable nodes only)~~
  - ~~Occult Primary~~
  - ~~Pancreatic Cancer (unless high risk features: borderline resectable, markedly elevated CA19-9 > 180 U/ml, large primary tumor/ lymph nodes)~~
  - ~~Skin squamous Cell Carcinoma~~
  - ~~Gallbladder/ Extrahepatic Cholangiocarcinoma~~
  - ~~Poorly differentiated neuroendocrine tumors with prior negative Ga68 Dotatate/ MIBG/Octreotide scan (includes Pheochromocytoma/ paraganglioma, extrapulmonary large/small cell)"~~
- ~~Under subsequent Treatment Strategy, first line has been modified by adding parenthesis as follows: Restaging or monitoring response to active treatment (including immunotherapy)"~~
- ~~Under subsequent Treatment Strategy, changed "not to be performed within 4 weeks of completion of therapy (ideally F^{18} FDG, Ga^{68} Dotatate, F^{18} Fluciclovine PET is delayed 2 – 3months after surgical therapy, 2 – 3 months after radiation therapy if locoregional assessment is the imaging goal), and/or evaluation for suspicion of recurrence due to new or changing signs/symptoms. (Asymptomatic surveillance is not approvable) (NCCN, 2018)." to "The interval should ideally be 6 – 12 weeks after surgery, and 12 weeks after radiation. PET can be performed 1-3 weeks after neoadjuvant chemotherapy or neoadjuvant chemoradiation to assess stage for surgery. PET evaluation can also be done for suspicion of recurrence due to new or changing signs/symptoms or rising tumor markers, or inconclusive findings on CT. Asymptomatic surveillance is not approvable. (NCCN 2018, 2019)"~~
- ~~List of cancers under subsequent imaging (without needing prior inconclusive imaging) has been changed. The following were removed: Breast cancer (female and males),~~

colorectal cancer (including colon, rectal, appendiceal or anal cancer), ovarian cancer. The following were changed as follows:

- "Lung cancer - Non-small cell" to "Lung cancer - Non-small cell and limited stage - small cell cancer"
- "Esophageal cancer" to "Esophageal and esophagogastric cancer"
- "Melanoma" to Melanoma -only stage III, IV (excludes uveal melanoma)
- "Myeloma to "Active Myeloma/plasmacytoma"
- Added for Soft tissue sarcoma: "only stage II/III for response to neoadjuvant Rx"
- Added Merkel cell carcinoma
- Added "Mesothelioma, if also presurgical"
- Individual References were removed for soft tissue sarcoma and vulvar/ vaginal cancer.
- Statement regarding subsequent PET scans needing prior inconclusive imaging has been modified from ""only" if other imaging (ie. US, CT, MRI, NM) is inconclusive in determining a treatment plan or unable to be performed " to " only if other imaging (ie. US, CT, MRI, NM) is inconclusive/ insufficient in determining a treatment plan or unable to be performed or with rising tumor markers and negative/ insufficient other imaging. PETCT is to be used only if the cancer is known to be generally F^{18} FDG, Ga^{68} Dotatate, F^{18} Fluciclovine avid. It may be indicated if iodinated and gadolinium contrast are both contraindicated due to significant allergy or chronic renal failure without dialysis (NCCN 2019). "
- Under subsequent PET scans needing prior inconclusive imaging, the following were changed:
    - Added: Breast cancer (female and males), Bladder cancer, only if metastatic, Colorectal Cancer – resectable metastatic disease only, Anal/ Vulvar/ Penile Carcinoma, Bone Sarcoma, Sarcoma/ GIST/ Uterine/Rhabdomyosarcoma, Ovarian/ malignant germ cell tumors/primary peritoneal cancer – Stage II-IV, Endometrial cancer if candidate for surgery/locoregional therapy; Poorly differentiated Cancers, or Dedifferentiated neuroendocrine tumors with prior negative Ga68 Dotatate/ MIBG/Octreotide scan
    - Removed: prostate cancer, pancreatic cancer, individual references for cancers
    - Changed: "Lung cancer -Small cell" to "Extensive small cell lung cancer"; "Tumor of unknown Origin" to "Occult primary"; "Neuroendocrine cancer (e.g. carcinoid, pheochromocytoma, etc)" to "Poorly differentiated or dedifferentiated neuroendocrine tumors with prior negative Ga68 Dotatate/ MIBG/Octreotide scan (includes Pheochromocytoma/ paraganglioma, extrapulmonary large/small cell)".
    - Last sentence has been changed from "Other malignancies where the tumor has been shown to be F^{18} FDG, Ga^{68} Dotatate, F^{18} Fluciclovineavid on prior PET/CT imaging if done, and other imaging (ie: US, CT, MRI, NM) is inconclusive in determining a treatment plan or unable to be performed " to "Other malignancies where other imaging (i.e., US, CT, MRI, NM) is inconclusive in determining a treatment plan or unable to be performed."

- Under thyroid Cancer,

- ~~Added references "(NCCN 2019, ATA 2015)" to subsequent treatment strategy for papillary/follicular/ hurthle cancers~~
    - ~~Changed "Stimulated serum thyroglobulin > 2 ng/ml" to "Stimulated serum thyroglobulin > 5 ng/ml or high anti- thyroglobulin antibody (anti-Tg Ab) > 1 year after treatment (Na SJ 2012)"~~
    - ~~Changed "Current whole body I-131 scan is negative (Kloos, 2005)" to "Current stimulated whole body I-131/ I-123 scan is negative (Alzahrani 2012)"~~
  - ~~Changed "Medullary thyroid cancer when calcitonin levels > 150 pg/ml post-operatively (Wells, 2015)" to "Medullary thyroid cancer when calcitonin levels ≥ 150 pg/ml post primary treatment (NCCN 2019, Souteiro 2019)"~~
  - ~~Changed "Anaplastic 3-6 months after initial treatment, 3-6 month interval if persistent structural disease (Smallridge, 2012)" to "Anaplastic: Initial and Restaging after prior inconclusive/ insufficient CT/MRI (NCCN 2019)"~~
- ~~Added pediatric cancers section as follows: "PEDIATRIC CANCERS (for indications different from adult guidelines):~~
  - ~~Sarcoma - Initial and Restaging (Quartuccio 2015)~~
  - ~~Neuroblastoma/ other cancers under Ga68 imaging: only with prior negative/ inconclusive MIBG/ Octreotide/ Ga68 PETCT (Uslu 2015, Alexander 2018, Kong 2016, Li 2018, Elkhatib 2017)~~
  - ~~Nasopharyngeal Cancer- Initial staging after inconclusive/ insufficient MRI; Restaging. (Cheuk 2012)~~
- ~~For Gallium-68 Dotatate PET:~~
  - ~~Added references for initial or subsequent treatment strategy: (NCCN 2019, Deppen, 2016 a, b)~~
  - ~~Added under neuroendocrine tumors: "Medullary Thyroid Cancer for Initial staging; and Restaging when calcitonin ≥ 150 pg/ml"~~
  - ~~Modified last part of the last sentence as follows: "and rising biomarkers (asymptomatic surveillance is not approvable). "~~
- ~~Under 18F-Fluciclovine PET/CT SCAN:~~
  - ~~Added "(Axumin)" after 18F-Fluciclovine~~
  - ~~Removed reference "(Bach-Gansmo, 2017)"~~
  - ~~Changed "18F-Fluciclovine PET/CT scans should be performed only if other imaging (CT, MRI, US, NM) is inconclusive/insufficient AND the patient has not already been evaluated with an F^{18} FDG, Ga^{68} Dotatate, F^{18} Fluciclovine PET/CT Scan" to "Known prostate cancer for workup of recurrence and response to treatment, only if other imaging (CT, MRI) AND Bone scan is inconclusive/insufficient. (NCCN 2019, Andriole 2019, Bach-Gansmo 2017)"~~
  - ~~Removed:" Known prostate cancer for workup of recurrence and response to treatment:"~~
  - ~~"Initial treatment by radical prostatectomy with" was replaced by "Post radical prostatectomy with"~~

- ~~"Initial treatment radiation therapy with" was replaced by "Post radiation therapy with"~~
- ~~"Post-RT rising PSA or positive digital exam and is candidate for local therapy" was replaced by "rising/persistent PSA (increase should be >2ng/ml unless doubling time ≤ 8 months or pt is a candidate for local salvage therapy)"~~

- ~~Removed: "NOTE: Not all plans cover 18F-Fluciclovine (A9588), such as Magellan Complete Care of Florida and Magellan Complete Care of Arizona. If you are unsure, you should check with the Health Plan prior to requesting a PET with Fluciclovine from NIA."~~
- ~~Added Background section as follows:~~

~~"BACKGROUND:~~

~~Positron emission tomography (PET) is a rapidly developing and changing technology that is able to detect biochemical reactions, e.g., metabolism, or abnormal distribution of cell receptors within body tissues. A radioactive tracer is used during the procedure. Unlike other nuclear medicine examinations, PET can measure metabolic activity of the cells of body tissues, providing information about the functionality and structure of the particular organ or tissue examined. PET may also detect biochemical changes that help to evaluate malignant tumors and other lesions.~~

~~The degree of radioactive tracer uptake may indicate increased metabolism in the cells of body tissues or an abnormal distribution of cell receptors. Cancer cells may show increased radioactive tracer relative to tissue not involved with tumor. Radioactive tracer uptake is often higher in fast-growing tumors; PET is often not as beneficial for slow-growing tumors. Radioactive tracer uptake may occur in various types of active inflammation and is not specific for cancer."~~

~~May 2020~~

- ~~Modified to table format~~
- ~~Added section of follow-up of a new or interval growth of a mixed pulmonary lung nodule on subsequent LDCT (NCCN 2020)~~
- ~~Initial staging indicated~~
  - ~~Changed AML to extramedullary disease (previously lymphomatous involvement)~~
  - ~~Changed Breast cancer stage IIb and above (previously III and IV)~~
  - ~~Added Castleman's disease~~
  - ~~Added for Chronic Lymphocytic Leukemia to guide biopsy~~
  - ~~Changed Mesothelioma to only prior to surgery for stage I-IIIA~~
  - ~~Added "soft tissue" sarcoma in pediatric patient~~
  - ~~Added Thymoma and thymic cancer~~
  - ~~Added Langerhans Cell Histiocytosis predominantly osseous disease (previously not included)~~
- ~~Initial staging which is only indicated after prior inconclusive imaging (NCCN 2019/2020)~~
  - ~~Added AIDS-related Kaposi sarcoma~~
  - ~~Changed Anal carcinoma (previously indicated)~~

- ~~Added Ewing sarcoma-osseous~~
- ~~Added Gestastional trophoblastic disease~~
- ~~Added Hepatocellular/Intrahepatic Cholangiocarcinoma (previously not included)~~
- ~~Added Fallopian tube and primary peritoneal cancer~~
- ~~Added Osteosarcoma-osseous~~
- ~~Changed Penile cancer (previously indicated with palpable nodes)~~

- ~~Initial staging NOT indicated (NCCN 2019/2020)~~
  - ~~Changed testicular (previously indicated)~~
  - ~~Added Uveal Melanoma~~
  - ~~Added Langerhans Cell Histiocytosis-predominantly non-osseous disease (previously not included)~~
- ~~Restaging indicated (NCCN 2019/2020)~~
  - ~~Added Castleman's disease~~
  - ~~Added for accelerated Chronic Lymphocytic Leukemia and to guide biopsy~~
  - ~~Added Gastric Cancer post radiation treatment~~
  - ~~Changed Mesothelioma to only prior to surgery for stage I-IIIA~~
  - ~~Added "soft tissue" to sarcoma in pediatric patient~~
  - ~~Added Thymoma and thymic cancer~~
  - ~~Added Langerhans Cell Histiocytosis-predominantly osseous disease (previously not included)~~
- ~~Restaging which are only indicated after prior inconclusive imaging (NCCN 2019/2020)~~
  - ~~Removed for resectable disease in Colorectal cancer~~
  - ~~Removed for if candidate for surgery/locoregional therapy for endometrial cancer~~
  - ~~Specified Ewings sarcoma-osseous~~
  - ~~Added Extrahepatic Cholangiocarcinoma (previously not indicated)~~
  - ~~Added Gallbladder carcinoma (previously not indicated)~~
  - ~~Changed Gastric Cancer to prior inconclusive imaging or if radiation planning considered (previously indicated if no metastasis or early disease)~~
  - ~~Added Gestastional trophoblastic disease~~
  - ~~Added Hepatocellular/Intrahepatic Cholangiocarcinoma (previously not included)~~
  - ~~Changed Ovarian cancer (previously indicated for greater than Stage I)~~
  - ~~Added Fallopian tube and all stages of primary peritoneal cancer~~
  - ~~Added Osteosarcoma- osseous~~
  - ~~Added that for pheochromocytoma/ paraganglioma, extrapulmonary large/small cell, restaging FDG PET/CT can be done after inconclusive CT~~
  - ~~Modified Seminoma with residual mass >3cm or 6 weeks post chemotherapy (previously indicated)~~
  - ~~Added Uveal melanoma~~
- ~~Restaging NOT indicated (NCCN 2019/2020)~~
  - ~~Added AIDS related Kaposi sarcoma~~
  - ~~Changed Testicular non-seminoma (previously indicated)~~

- Added Langerhans Cell Histiocytosis-predominantly non-osseous disease (previously not included)

- Added CT face/neck may be done in conjunction with PET when surgery or radiation is planned
- Added to head and neck cancer that if a final PET is equivocal or borderline for residual disease PET, a repeat PET/CT a ≥ 6 weeks may help identify those that can be safely observed without additional surgery
- Medullary thyroid: added FDG restaging indicated when CEA >5ng/ml post-surgery and after prior insufficient Dotatate scan
- Modified pancreatic cancer symptoms to excessive weight loss
- Added to Seminoma: if final PET is equivocal or borderline for residual disease PET, a repeat PET/CT a ≥ 6 weeks may help identify those that can be safely observed without additional surgery)
- Thyroid FDG- changed serum thyroglobulin level to >2ng/ml (previously >5ng/ml) and added 'current OR two prior stimulated whole body I-131/ I-123 scans are negative (a current scan is needed if on radioiodine sensitizing medications)'
- GA^{68} Dotatate- added restaging calcitonin levels ≥ 150 pg/ml or CEA levels >5 ng/ml post-surgery
- F18 Fluciclovine (Axumin)
  - Initial staging changed to: With prior inconclusive bone scan with no CT/MRI correlate; or inconclusive bone SPECT/CT
  - Restaging changed to with rising/persistent PSA and after CT/MRI has been performed and is insufficient for detection of metastases
- Added Inconclusive imaging features to background as noted in NCCN 2020
- Added Disease progression to Background as noted in NCCN 2020

Added Section of Langerhans Cell Histiocytosis to background section

June 2021

Definitions
CART T info
PTLD information added
PET/MRI information
Updated/added details for Prostate cancer and PSMA, Axumin and Choline
Minor adjustments to the PET FDG table, such as added details from NCCN, clarifications, separation of non-malignant uses

- Added PET/MRI information in background and to table for cancers where NCCN says "consider" or "when available
- Added PSMA and updated prostate cancer special tracers GL and table
- Adjusted FDG PET table to reflect recent updates in NCCN
- Minor change to thyroid FDG PET indication

- ~~Added definitions section for use in table, including CART T~~
- ~~Added PTLD to FDG table~~
- ~~Minor rearrangement of FDG PET table~~

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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.