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Approval and implementation dates for specific health plans may vary. Please consult the applicable health plan for more details.

## Clinical Appropriateness Guidelines

# Radiology

# Appropriate Use Criteria: Nuclear Medicine Imaging

### Proprietary

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# Table of Contents

Carelon .....	1
Clinical Appropriateness Guidelines .....	1
Table of Contents.....	2
Description and Application of the Guidelines .....	4
General Clinical Guideline .....	5
Clinical Appropriateness Framework .....	5
Simultaneous Ordering of Multiple Diagnostic or Therapeutic Interventions .....	5
Repeat Diagnostic Intervention.....	5
Repeat Therapeutic Intervention.....	6
Nuclear Medicine Imaging .....	7
Codes .....	7
General Information.....	9
Scope.....	9
Technology Considerations .....	9
Definitions .....	11
Clinical Indications.....	12
Bone Marrow Scintigraphy.....	12
Bone Scintigraphy.....	13
Dacryoscintigraphy .....	19
Esophageal Motility Scintigraphy .....	19
Gallium Scintigraphy .....	19
Gastric Emptying Scintigraphy/Gut Transit Scintigraphy .....	20
Gastrointestinal Blood Loss Scintigraphy .....	20
GERD Scintigraphy (also known as a “milk scan” or “reflux study”) .....	20
Hepatic Scintigraphy .....	20
Hepatobiliary Scintigraphy .....	21
Leukocyte Scintigraphy.....	22
Lymphoscintigraphy .....	23
Meckel’s Scan.....	25
Metaiodobenzylguanidine (MIBG) Scintigraphy.....	25
Parathyroid Scintigraphy.....	26
Perfusion Scintigraphy .....	26
Peritoneal Venous Shunt Scintigraphy .....	27
Pyrophosphate Scintigraphy .....	27
Radionuclide Cisternography.....	28
Radionuclide Cystography .....	28
Renal Scintigraphy.....	29
Somatostatin Receptor Scintigraphy (Octreoscan).....	30

Splenic Scintigraphy .....31

Thallium Scintigraphy.....31

Thyroid Scintigraphy (including Radioactive Iodine Uptake).....31

VQ Scintigraphy .....33

References .....35

History.....39

## Description and Application of the Guidelines

The Carelon Clinical Appropriateness Guidelines (hereinafter “the Carelon Clinical Appropriateness Guidelines” or the “Guidelines”) are designed to assist providers in making the most appropriate treatment decision for a specific clinical condition for an individual. As used by Carelon, the Guidelines establish objective and evidence-based criteria for medical necessity determinations where possible. In the process, multiple functions are accomplished:

- To establish criteria for when services are medically necessary (i.e., in general, shown to be effective in improving health outcomes and considered the most appropriate level of service)
- To assist the practitioner as an educational tool
- To encourage standardization of medical practice patterns
- To curtail the performance of inappropriate and/or duplicate services
- To advocate for patient safety concerns
- To enhance the quality of health care
- To promote the most efficient and cost-effective use of services

The Carelon guideline development process complies with applicable accreditation standards, including the requirement that the Guidelines be developed with involvement from appropriate providers with current clinical expertise relevant to the Guidelines under review and be based on the most up-to-date clinical principles and best practices. Relevant citations are included in the References section attached to each Guideline. Carelon reviews all of its Guidelines at least annually.

Carelon makes its Guidelines publicly available on its website twenty-four hours a day, seven days a week. Copies of the Carelon Clinical Appropriateness Guidelines are also available upon oral or written request. Although the Guidelines are publicly-available, Carelon considers the Guidelines to be important, proprietary information of Carelon, which cannot be sold, assigned, leased, licensed, reproduced or distributed without the written consent of Carelon.

Carelon applies objective and evidence-based criteria, and takes individual circumstances and the local delivery system into account when determining the medical appropriateness of health care services. The Carelon Guidelines are just guidelines for the provision of specialty health services. These criteria are designed to guide both providers and reviewers to the most appropriate services based on a patient’s unique circumstances. In all cases, clinical judgment consistent with the standards of good medical practice should be used when applying the Guidelines. Guideline determinations are made based on the information provided at the time of the request. It is expected that medical necessity decisions may change as new information is provided or based on unique aspects of the patient’s condition. The treating clinician has final authority and responsibility for treatment decisions regarding the care of the patient and for justifying and demonstrating the existence of medical necessity for the requested service. The Guidelines are not a substitute for the experience and judgment of a physician or other health care professionals. Any clinician seeking to apply or consult the Guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient’s care or treatment.

The Guidelines do not address coverage, benefit or other plan specific issues. Applicable federal and state coverage mandates take precedence over these clinical guidelines. If requested by a health plan, Carelon will review requests based on health plan medical policy/guidelines in lieu of the Carelon Guidelines. Pharmaceuticals, radiotracers, or medical devices used in any of the diagnostic or therapeutic interventions listed in the Guidelines must be FDA approved or conditionally approved for the intended use. However, use of an FDA approved or conditionally approved product does not constitute medical necessity or guarantee reimbursement by the respective health plan.

The Guidelines may also be used by the health plan or by Carelon for purposes of provider education, or to review the medical necessity of services by any provider who has been notified of the need for medical necessity review, due to billing practices or claims that are not consistent with other providers in terms of frequency or some other manner.

# General Clinical Guideline

## Clinical Appropriateness Framework

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Critical to any finding of clinical appropriateness under the guidelines for a specific diagnostic or therapeutic intervention are the following elements:

- Prior to any intervention, it is essential that the clinician confirm the diagnosis or establish its pretest likelihood based on a complete evaluation of the patient. This includes a history and physical examination and, where applicable, a review of relevant laboratory studies, diagnostic testing, and response to prior therapeutic intervention.
- The anticipated benefit of the recommended intervention should outweigh any potential harms that may result (net benefit).
- Current literature and/or standards of medical practice should support that the recommended intervention offers the greatest net benefit among competing alternatives.
- Based on the clinical evaluation, current literature, and standards of medical practice, there exists a reasonable likelihood that the intervention will change management and/or lead to an improved outcome for the patient.

If these elements are not established with respect to a given request, the determination of appropriateness will most likely require a peer-to-peer conversation to understand the individual and unique facts that would supersede the requirements set forth above. During the peer-to-peer conversation, factors such as patient acuity and setting of service may also be taken into account.

## Simultaneous Ordering of Multiple Diagnostic or Therapeutic Interventions

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Requests for multiple diagnostic or therapeutic interventions at the same time will often require a peer-to-peer conversation to understand the individual circumstances that support the medical necessity of performing all interventions simultaneously. This is based on the fact that appropriateness of additional intervention is often dependent on the outcome of the initial intervention.

Additionally, either of the following may apply:

- Current literature and/or standards of medical practice support that one of the requested diagnostic or therapeutic interventions is more appropriate in the clinical situation presented; or
- One of the diagnostic or therapeutic interventions requested is more likely to improve patient outcomes based on current literature and/or standards of medical practice.

## Repeat Diagnostic Intervention

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In general, repeated testing of the same anatomic location for the same indication should be limited to evaluation following an intervention, or when there is a change in clinical status such that additional testing is required to determine next steps in management. At times, it may be necessary to repeat a test using different techniques or protocols to clarify a finding or result of the original study.

Repeated testing for the same indication using the same or similar technology may be subject to additional review or require peer-to-peer conversation in the following scenarios:

- Repeated diagnostic testing at the same facility due to technical issues
- Repeated diagnostic testing requested at a different facility due to provider preference or quality concerns
- Repeated diagnostic testing of the same anatomic area based on persistent symptoms with no clinical change, treatment, or intervention since the previous study

- Repeated diagnostic testing of the same anatomic area by different providers for the same member over a short period of time

## **Repeat Therapeutic Intervention**

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In general, repeated therapeutic intervention in the same anatomic area is considered appropriate when the prior intervention proved effective or beneficial and the expected duration of relief has lapsed. A repeat intervention requested prior to the expected duration of relief is not appropriate unless it can be confirmed that the prior intervention was never administered.

# Nuclear Medicine Imaging

## Codes

The following code list is not meant to be all-inclusive. Authorization requirements will vary by health plan. Please consult the applicable health plan for guidance on specific procedure codes.

Specific CPT codes for services should be used when available. Nonspecific or not otherwise classified codes may be subject to additional documentation requirements and review.

### CPT/HCPCS

CPT® (Current Procedural Terminology) is a registered trademark of the American Medical Association (AMA). CPT® five digit codes, nomenclature and other data are copyright by the American Medical Association. All Rights Reserved. AMA does not directly or indirectly practice medicine or dispense medical services. AMA assumes no liability for the data contained herein or not contained herein.

78012	Thyroid uptake, single or multiple quantitative measurement(s) (including stimulation, suppression, or discharge, when performed)
78013	Thyroid imaging (including vascular flow, when performed)
78014	Thyroid imaging (including vascular flow, when performed); with single or multiple uptake(s) quantitative measurement(s) (including stimulation, suppression, or discharge, when performed)
78015	Thyroid carcinoma metastases imaging; limited area (eg, neck and chest only)
78016	Thyroid carcinoma metastases imaging; with additional studies (eg, urinary recovery)
78018	Thyroid carcinoma metastases imaging; whole body
78020	Thyroid carcinoma metastases uptake (List separately in addition to code for primary procedure)
78070	Parathyroid planar imaging (including subtraction, when performed)
78075	Adrenal imaging, cortex and/or medulla
78102	Bone marrow imaging; limited area
78103	Bone marrow imaging; multiple areas
78104	Bone marrow imaging; whole body
78185	Spleen imaging only, with or without vascular flow
78195	Lymphatics and lymph nodes imaging
78201	Liver imaging; static only
78202	Liver imaging; with vascular flow
78215	Liver and spleen imaging; static only
78216	Liver and spleen imaging; with vascular flow
78226	Hepatobiliary system imaging, including gallbladder when present
78227	Hepatobiliary system imaging, including gallbladder when present; with pharmacologic intervention, including quantitative measurement(s) when performed
78230	Salivary gland imaging
78231	Salivary gland imaging; with serial images
78232	Salivary gland function study
78258	Esophageal motility
78261	Gastric mucosa imaging
78262	Gastroesophageal reflux study
78264	Gastric emptying imaging study (eg, solid, liquid, or both);
78265	Gastric emptying imaging study (eg, solid, liquid, or both); with small bowel transit
78266	Gastric emptying imaging study (eg, solid, liquid, or both); with small bowel and colon transit, multiple days
78278	Acute gastrointestinal blood loss imaging
78290	Intestine imaging (eg, ectopic gastric mucosa, Meckel's localization, volvulus)
78291	Peritoneal-venous shunt patency test (eg, for LeVeen, Denver shunt)

78300	Bone and/or joint imaging; limited area
78305	Bone and/or joint imaging; multiple areas
78306	Bone and/or joint imaging; whole body
78315	Bone and/or joint imaging; 3 phase study
78445	Non-cardiac vascular flow imaging (ie, angiography, venography)
78456	Acute venous thrombosis imaging, peptide
78457	Venous thrombosis imaging, venogram; unilateral
78458	Venous thrombosis imaging, venogram; bilateral
78579	Pulmonary ventilation imaging (eg, aerosol or gas)
78580	Pulmonary perfusion imaging (eg, particulate)
78582	Pulmonary ventilation (eg, aerosol or gas) and perfusion imaging
78597	Quantitative differential pulmonary perfusion, including imaging when performed
78598	Quantitative differential pulmonary perfusion and ventilation (eg, aerosol or gas), including imaging when performed
78600	Brain imaging, less than 4 static views;
78601	Brain imaging, less than 4 static views; with vascular flow
78605	Brain imaging, minimum 4 static views;
78606	Brain imaging, minimum 4 static views; with vascular flow
78610	Brain imaging, vascular flow only
78630	Cerebrospinal fluid flow, imaging (not including introduction of material); cisternography
78635	Cerebrospinal fluid flow, imaging (not including introduction of material); ventriculography
78645	Cerebrospinal fluid flow, imaging (not including introduction of material); shunt evaluation
78650	Cerebrospinal fluid leakage detection and localization
78660	Radiopharmaceutical dacryocystography
78700	Kidney imaging morphology;
78701	Kidney imaging morphology; with vascular flow
78707	Kidney imaging morphology; with vascular flow and function, single study without pharmacological intervention
78708	Kidney imaging morphology; with vascular flow and function, single study, with pharmacological intervention (eg, angiotensin converting enzyme inhibitor and/or diuretic)
78709	Kidney imaging morphology; with vascular flow and function, multiple studies, with and without pharmacological intervention (eg, angiotensin converting enzyme inhibitor and/or diuretic)
78725	Kidney function study, non-imaging radioisotopic study
78730	Urinary bladder residual study (List separately in addition to code for primary procedure)
78740	Ureteral reflux study (radiopharmaceutical voiding cystogram)
78761.	Testicular imaging with vascular flow
78800	Radiopharmaceutical localization of tumor or distribution of radiopharmaceutical agent(s); limited area
78801.	Radiopharmaceutical localization of tumor or distribution of radiopharmaceutical agent(s); multiple areas
78802.	Radiopharmaceutical localization of tumor or distribution of radiopharmaceutical agent(s); whole body, single day imaging
78804	Radiopharmaceutical localization of tumor or distribution of radiopharmaceutical agent(s); whole body, requiring 2 or more days imaging



## General Information

### Scope

These guidelines address nuclear medicine imaging in both adult and pediatric populations. For interpretation of the Guidelines, and where not otherwise noted, “adult” refers to persons age 19 and older, and “pediatric” refers to persons age 18 and younger. Where separate indications exist, they are specified as **Adult** or **Pediatric**. Where not specified, indications and prerequisite information apply to persons of all ages.

See the Code section for a list of modalities included in these guidelines.

### Technology Considerations

**Bone marrow scintigraphy** is a nuclear medicine study which may be done in conjunction with other studies such as Gallium or leukocyte scintigraphy for evaluation of marrow involvement. This study is done using technetium 99m-labeled sulfur colloid, the normal biodistribution of which is the reticuloendothelial system (liver, spleen, bone marrow).

**Bone scintigraphy** is a nuclear medicine exam that uses a radiopharmaceutical (typically technetium 99m labeled methylene diphosphonate [MDP] or hydroxydiphosphonate [HDP]) to measure osteoblastic activity throughout the axial and appendicular skeleton. Bone scintigraphy can be limited or whole body and can be performed with planar scintigraphy or with SPECT.

**Dacryoscintigraphy** is a nuclear medicine exam in which a radiopharmaceutical (typically, technetium 99m pertechnetate) is administered via eye dropper or syringe to the surface of the eye. This test is used to evaluate the patency of the nasolacrimal duct.

**Gallium scintigraphy** is a nuclear medicine exam that uses a radiopharmaceutical (typically Gallium-67 citrate) to measure neoplastic, infectious and inflammatory activity involving osseous and soft tissue structures.

A **Gastric emptying study** is a nuclear medicine exam that uses a radiopharmaceutical (typically technetium 99m sulfur colloid) which is mixed into a standardized solid meal or liquid for oral administration. Multiple images are obtained of the abdomen, and the percentage of activity remaining in the stomach is calculated over time. For measurement of gastric emptying only, imaging is typically performed at hourly intervals until 4 hours after solid meal ingestion and for one hour after liquid administration. **Small bowel and whole-gut transit studies** may be performed in conjunction with a gastric emptying study, and typically involve administration of a second radiopharmaceutical, <sup>111</sup>In-DTPA, followed by additional delayed imaging.

**Gastrointestinal blood loss scintigraphy** refers to nuclear medicine evaluation for the source of an active site of gastrointestinal bleeding. This is generally used to evaluate a site of lower GI bleeding, though more proximal sites can also be detected. This test is done using the patient’s red blood cells, which are radiolabeled using technetium 99m either in vitro or in vivo. **GERD scintigraphy** is also known as a “reflux scan” or a “milk scan.” It is a nuclear medicine exam in which a radiopharmaceutical (typically technetium 99m labeled DTPA or sulfur colloid) is administered orally (or by nasogastric or gastrostomy tube) in a liquid meal such as water, juice, or milk. Dynamic imaging is then carried out, typically at 10 seconds per frame for one hour. The number of reflux episodes is determined, as well as the proximal extent of the reflux.

**Hepatic scintigraphy** refers to nuclear medicine imaging of the liver. Depending on the reason for imaging, there are several radiotracers which may be used. Radiolabeled autologous red blood cells may be used for characterization of a liver lesion when it is suspected to be a hemangioma. Radiolabeled sulfur colloid may be used for characterization of a liver lesion when it is suspected to represent focal nodular hyperplasia.

**Hepatobiliary scintigraphy** is a nuclear medicine exam that uses a radiopharmaceutical [a technetium 99m-labeled iminodiacetic acid (IDA) such as DISIDA, BrIDA, or PIPIDA] to evaluate the hepatobiliary system including bile formation and transit through the biliary system into the intestine. Gallbladder ejection fraction (GBEF) can be calculated through the administration of a cholecystikinin analog. Also called HIDA scans after an early form of the primary radiopharmaceutical used in them, these studies are most commonly used in the evaluation of suspected acute cholecystitis, but may also be useful in evaluation of suspected biliary atresia or bile leak.

**Leukocyte scintigraphy** is a nuclear medicine exam that uses a radiopharmaceutical (typically technetium 99m or Indium-111 labeled autologous white blood cells [WBC]) to measure infectious and inflammatory activity involving osseous and soft tissue structures.

**Lymphoscintigraphy** is a nuclear medicine procedure in which a radiopharmaceutical (typically technetium 99m sulfur colloid, filtered to ensure a small particle size) is used to evaluate lymphatic flow and nodal drainage pathways. This test may be used for lymphedema, but is primarily used for sentinel lymph node detection in malignancies such as breast cancer or melanoma.

A **Meckel's scan** is a nuclear medicine examination in which technetium 99m pertechnetate is used to detect a Meckel's diverticulum. These often become clinically apparent because of gastrointestinal bleeding, which in the setting of Meckel's diverticulum almost always indicates the presence of ectopic gastric mucosa. Uptake of pertechnetate is dependent on the presence of gastric mucosa, so this radiopharmaceutical is generally useful in Meckel's diverticula that present with bleeding, but the test may be of less value in other presentations, where the presence of gastric mucosa in the diverticulum may be less likely.

**Perfusion scintigraphy** is a nuclear medicine examination performed with a gamma camera that measures cerebral blood flow using lipophilic radiopharmaceutical agents (typically technetium-99 labeled hexamethylpropylene amine oxide [HMPAO] or ethyl cysteinate dimer [ECD]) with high cerebral retention.

**Peritoneal venous shunt scintigraphy** is a nuclear medicine study in which a radiopharmaceutical (such as technetium 99m macroaggregated albumin [MAA]) is injected into the peritoneal cavity in order to evaluate the patency of a LeVeen or Denver shunt. In the presence of a patent shunt, macroaggregated albumin will travel to the lungs, generally within one hour of injection.

**Planar scintigraphy** refers to static, two-dimensional nuclear medicine imaging. While planar imaging may provide sufficient information in regions where the anatomy is less complex, it is often supplemented by SPECT imaging for improved anatomic localization.

**Radionuclide cisternography** is a minimally invasive procedure which uses a radiopharmaceutical (typically Indium-111 or Technetium 99m-labeled diethylenetriaminepentaacetic acid [DTPA]) injected into the cerebrospinal fluid (CSF) to measure CSF flow and identify sites of leakage.

**Radiopharmaceuticals** are drugs used for diagnosis and therapy which include an isotope (element with the same number of protons but a different number of neutrons and prone to measurable radioactive decay) often coupled to a ligand that binds to a molecule of interest. Examples include technetium 99m-methylene diphosphonate (TC-99 MDP) for bone scintigraphy, iodine 123 for thyroid scintigraphy, and <sup>18</sup>F-fluorodeoxyglucose (FDG) for PET oncologic imaging.

**Renal scintigraphy** refers to several types of nuclear imaging performed to evaluate the structure and/or function of the kidneys: renal cortical scintigraphy uses the radiopharmaceutical technetium 99m-dimercaptosuccinic acid (DMSA) to assess the amount of functioning cortical tissue; renal perfusion/functional imaging uses radiopharmaceutical agents such as technetium 99m-mercaptoacetyltriglycine (MAG3) to assess blood flow to the kidneys as well as excretory function; diuretic renal scintigraphy, which uses MAG3 imaging before and after a diuretic in order to evaluate for the presence of upper urinary tract obstruction; and ACE-inhibitor renal scintigraphy, in which an ACE inhibitor is used alongside MAG3 to assess for renal artery stenosis.

**Single photon emission computed tomography (SPECT)** uses gamma decay from radiopharmaceutical agents captured by gamma cameras to create three-dimensional images of the body, in contrast to the two-dimensional images obtained with planar scintigraphy. SPECT has an improved signal-to-noise ratio relative to planar scintigraphy and is especially useful in regions with complex anatomy that makes localization difficult using two-dimensional imaging alone. **Dopaminergic SPECT** is a brain SPECT exam using a radiopharmaceutical that measures presynaptic dopamine to assess nigrostriatal dysfunction. Ioflupane (I-123) is an FDA approved ligand of dopamine transporters used with SPECT (DaTscan)<sup>1</sup> to diagnose Parkinson's disease in select clinical scenarios.

**Splenic scintigraphy** is generally performed as part of a liver-spleen scan, in which a radiopharmaceutical (such as technetium 99m sulfur colloid or technetium 99m-labeled heat-denatured red blood cells) is administered. Splenic scintigraphy is typically used to evaluate for splenosis, accessory splenic tissue, splenic infarction, or wandering spleen.

**Thallium scintigraphy** has mainly been used in myocardial imaging, both for assessment of perfusion and viability. Thallium is a potassium analog and its intracellular uptake occurs by several pathways, including a co-

transport mechanism in tumor cells. It is taken up by Gallium-avid tumors but, unlike Gallium, does not show significant accumulation in inflammatory or necrotic tissue.<sup>2</sup>

**Thyroid scintigraphy** is a nuclear medicine study in which a radiopharmaceutical (generally iodine-123 or iodine-131, though technetium 99m pertechnetate can also be used for thyroid evaluation, particularly in pediatric patients) is administered in order to evaluate the thyroid gland. This test can be used in the evaluation of thyrotoxicosis or to assist in characterization of thyroid nodules. When an iodine-based radiopharmaceutical is used, radioactive iodine uptake (RAIU) can be measured in conjunction with imaging.

**VQ scintigraphy** is a nuclear medicine study used to evaluate the lungs. This study may evaluate ventilation, perfusion, or both. Ventilation-perfusion scans are generally used in the evaluation of suspected pulmonary embolism. Quantitative lung perfusion scintigraphy is used to evaluate how blood flow is distributed within the lungs, and may be used prior to lung surgery or to evaluate congenital vascular anomalies. Perfusion imaging is performed using technetium 99m-labeled macro-aggregated albumin (MAA). There are several radiopharmaceuticals which may be used for ventilation imaging, including aerosols such as technetium 99m-diethylenetriaminepentaacetic acid (DTPA) or technetium 99m-sulfur colloid, or gases such as <sup>133</sup>Xe (Xenon).

## Definitions

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Phases of the care continuum are broadly defined as follows:

- **Screening** is testing in the absence of signs or symptoms of disease
- **Diagnosis** is testing based on a reasonable suspicion of a particular condition or disorder, usually due to the presence of signs or symptoms
- **Management** is testing to direct therapy of an established condition, which may include preoperative or postoperative imaging, or imaging performed to evaluate the response to nonsurgical intervention
- **Surveillance** is the periodic assessment following completion of therapy, or for monitoring known disease that is stable or asymptomatic

### Statistical terminology

- **Confidence interval (CI)** is a range of values which is likely to contain the cited statistic. For example, 92% sensitivity (95% CI, 89%-95%) means that, while the sensitivity was calculated at 92% on the current study, there is a 95% chance that, if a study were to be repeated, the sensitivity on the repeat study would be in the range of 89%-95%.
- **Diagnostic accuracy** relates to the ability of a test to discriminate between the target condition and health. Diagnostic accuracy is quantified using sensitivity and specificity, predictive values, and likelihood ratios.
- **Hazard ratio** is the odds that an individual in the group with the higher hazard reaches the outcome first. Hazard ratio is analogous to odds ratio and is reported most commonly in time-to-event analysis or survival analysis. A hazard ratio of 1 means that the hazard rates of the 2 groups are equivalent. A hazard ratio of greater than 1 or less than 1 means that there are differences in the hazard rates between the 2 groups.
- **Likelihood ratio** is the ratio of an expected test result (positive or negative) in patients with the disease to an expected test result (positive or negative) in patients without the disease. Positive likelihood ratios, especially those greater than 10, help rule in a disease (i.e., they substantially raise the post-test probability of the disease, and hence make it very likely and the test very useful in identifying the disease). Negative likelihood ratios, especially those less than 0.1, help rule out a disease (i.e., they substantially decrease the post-test probability of disease, and hence make it very unlikely and the test very useful in excluding the disease).
- **Odds ratio** represents the odds that an outcome will occur given a particular exposure, compared to the odds of the outcome occurring in the absence of that exposure. An odds ratio of 1 means that the exposure does not affect the odds of the outcome. An odds ratio greater than 1 means that the exposure is associated with higher odds of the outcome. An odds ratio less than 1 means that the exposure is associated with lower odds of the outcome.

- **Predictive value** is the likelihood that a given test result correlates with the presence or absence of disease. Positive predictive value is defined as the number of true positives divided by the number of test positives. Negative predictive value is defined as the number of true negatives divided by the number of test negative patients. Predictive value is dependent on the prevalence of the condition.
- **Pretest probability** is the probability that a given patient has a disease prior to testing. May be divided into very low (less than 5%), low (less than 20%), moderate (20%-75%), and high (greater than 75%) although these numbers may vary by condition.
- **Relative risk** is the probability of an outcome when an exposure is present relative to the probability of the outcome occurring when the exposure is absent. Relative risk is analogous to odds ratio; however, relative risk is calculated by using percentages instead of odds. A relative risk of 1 means that there is no difference in risk between the 2 groups. A relative risk of greater than 1 means that the outcome is more likely to happen in the exposed group compared to the control group. A relative risk less than 1 means that the outcome is less likely to happen in the exposed group compared to the control group.
- **Sensitivity** is the conditional probability that the test is positive, given that the patient has the disease. Defined as the true positive rate (number of true positives divided by the number of patients with disease). Excellent or high sensitivity is usually greater than 90%.
- **Specificity** is the conditional probability that the test is negative, given that the patient does not have the disease. Defined as the true negative rate (number of true negatives divided by the number of patients without the disease). Excellent or high specificity is usually greater than 90%.

## Clinical Indications

The following section includes indications for which nuclear medicine imaging is considered medically necessary, along with prerequisite information and supporting evidence where available. Indications, diagnoses, or imaging modalities not specifically addressed are considered not medically necessary.

It is recognized that imaging often detects abnormalities unrelated to the condition being evaluated. Such findings must be considered within the context of the clinical situation when determining whether additional imaging is required

## Bone Marrow Scintigraphy

### Extramedullary hematopoiesis

Bone marrow scintigraphy is considered medically necessary for evaluation of an indeterminate mass seen on other imaging studies when extramedullary hematopoiesis is suspected and scintigraphy is being used in order to avoid biopsy.

### Osteomyelitis, when MRI cannot be performed or is nondiagnostic

*Includes chronic regional multifocal osteomyelitis (CRMO).*

Bone marrow scintigraphy is considered medically necessary when done in conjunction with leukocyte scintigraphy for diagnosis and management when radiograph, ultrasound, or arthrocentesis is nondiagnostic or not sufficient to guide treatment.

### Procedure-related imaging

Bone marrow scintigraphy is considered medically necessary when done in conjunction with Gallium scintigraphy or leukocyte scintigraphy for diagnosis and management of periprosthetic infection.

### Rationale

#### SPINE

For periprosthetic infections in the spine, a variety of structural and functional imaging modalities may help define the presence or extent of disease. CT and MRI are commonly performed but evaluation of the surgical bed may be limited by beam

hardening/susceptibility artifact. Gallium and bone scintigraphy are functional imaging alternatives that have a higher diagnostic accuracy than leukocyte scintigraphy in the spine.<sup>3,4</sup>

#### EXTREMITY

Leukocyte scintigraphy is an option in patients with suspected periprosthetic infection<sup>5</sup> and has a high diagnostic accuracy (greater than 90%) for periprosthetic infections of the hip and knee; bone scintigraphy is highly sensitive for infection but is less specific.<sup>6,7</sup>

### Sickle cell disease, when MRI cannot be performed or is nondiagnostic

Bone marrow scintigraphy is considered medically necessary when performed in conjunction with bone scintigraphy to differentiate osteomyelitis from avascular necrosis.

## Bone Scintigraphy

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### Avascular necrosis, when MRI cannot be performed or is nondiagnostic

*Includes sickle cell disease.*

Bone scintigraphy (limited or whole body) is considered medically necessary for diagnosis and management when radiographs are nondiagnostic or not sufficient to guide treatment as in **EITHER** of the following scenarios:

- Diagnosis following negative or inconclusive radiographs
- Preoperative planning for osteonecrosis with femoral head collapse

#### Rationale

When initial radiographs demonstrate avascular necrosis and additional information is needed to guide treatment, MRI without IV contrast is usually appropriate.<sup>8</sup> Consensus among high-quality evidence-based guidelines also suggests that additional MRI imaging for avascular necrosis is also indicated in high-risk patients when radiographs are normal or inconclusive. Bone scan or CT may be substituted when MRI is not available.<sup>9</sup> Bone scintigraphy can also identify avascular necrosis that is occult on radiography but is usually recommended when MRI cannot be performed or is nondiagnostic.<sup>9,10</sup>

### Fracture, when MRI cannot be performed or is nondiagnostic

Bone scintigraphy (limited) is considered medically necessary for detection of occult fracture following nondiagnostic radiographs in **ANY** of the following scenarios:

- Suspected spinal fracture
- Suspected skeletal injury in non-accidental trauma
- Suspected fracture at the following high-risk/weight bearing sites:
  - Femoral neck, proximal femur
  - Tibia (anterior/lateral/plateau)
  - Great toe sesamoid
  - Patella
  - Scaphoid
  - Lunate
  - Talus
  - Navicular
  - Metatarsal base (second and fifth digits)

#### Rationale

Bone scintigraphy is highly sensitive but not specific for the diagnosis of occult fractures; MRI is more specific than sensitive but has a higher overall diagnostic accuracy and is non ionizing. As such, bone scintigraphy may detect MRI false negative occult fractures and may be appropriate as an add-on test when MRI cannot be performed or is nondiagnostic.<sup>11,12</sup>



## Infection, not otherwise specified

*Includes diabetic foot.*

See **Perioperative evaluation, not otherwise specified, including delayed hardware failure for periprosthetic infection.**

Bone scintigraphy is considered medically necessary in **ANY** of the following scenarios:

- Diagnosis of osteomyelitis of the skull base or calvarium (limited or whole body)
- Evaluation of sternal wound infection or dehiscence when CT chest is nondiagnostic (limited or whole body)
- Diagnosis and management of spinal infection when MRI cannot be performed or is nondiagnostic (triple phase)
- Diagnosis and management of chronic regional multifocal osteomyelitis (CRMO) (limited or whole body)
- Diagnosis and management of osteomyelitis at other sites when radiograph, ultrasound, or arthrocentesis is nondiagnostic or not sufficient to guide treatment (triple phase)
- Diagnosis and management of septic arthritis when radiograph, ultrasound, or arthrocentesis is nondiagnostic or not sufficient to guide treatment, and when MRI cannot be performed or is nondiagnostic

### Rationale

#### CHEST

CT chest is usually sufficient for evaluating for sternal wound dehiscence or other forms of chest infection and has the advantage of simultaneous visualization of the mediastinum and lung parenchyma.<sup>13</sup> Historically and in rare circumstances, bone or leukocyte scintigraphy has been used to differentiate superficial and deep infections, although evidence for diagnostic accuracy is limited.<sup>14</sup>

#### SPINE

MRI has high diagnostic accuracy for spondylodiscitis, is widely available, nonionizing, and is recommended as the initial modality by multiple clinical guidelines.<sup>15-17</sup> When MRI cannot be performed or is nondiagnostic, functional imaging with bone scintigraphy with or without gallium scintigraphy is suggested as a weak recommendation based on low quality evidence from the Infectious Disease Society of America (IDSA). While gallium/bone scintigraphy may have moderate-to-high sensitivity for spondylodiscitis<sup>18</sup>, leukocyte scintigraphy has limited sensitivity in the axial skeleton and is not recommended.<sup>15</sup> Functional imaging also offers the advantage of a wider field of view than MRI and can be useful to assess for multifocal or chronic forms of osteomyelitis such as chronic recurrent multifocal osteomyelitis and the Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis (SAPHO) syndrome.

#### OTHER SITES

Functional imaging with bone scintigraphy has historically been used to evaluate for osteomyelitis when radiographs are nondiagnostic. Greater accuracy and the lack of ionizing radiation for MRI have largely made scintigraphy an add-on test when MRI cannot be performed or is nondiagnostic<sup>9, 19, 20</sup>, although bone scintigraphy offers a wider field of view and hence can localize multifocal disease.

## Indeterminate bone lesion of the extremity

Bone scintigraphy (limited or whole body) is considered medically necessary for diagnosis and management following nondiagnostic radiographs and when further characterization is essential to guide management.

## Limping child, age 5 years or younger

Bone scintigraphy (triple phase) is considered medically necessary for diagnosis when MRI and radiographs are nondiagnostic.

## Osseous tumor

Bone scintigraphy (limited or whole body) is considered medically necessary for diagnosis and management.

## Osteoid osteoma

Bone scintigraphy (limited or whole body) is considered medically necessary following negative or inconclusive hip radiographs.

## Paget's disease

Bone scintigraphy (limited or whole body) is considered medically necessary for management of disease in **ANY** of the following scenarios:

- Determine extent of disease in patients with suggestive findings on radiography
- Monitor response to therapy in patients with normal baseline bone turnover markers
- Evaluate for malignant transformation of pagetoid lesions

### Rationale

Paget's disease of bone is a metabolic bone disease characterized by noninflammatory osteoclastic activity followed by osteoblastic activity.<sup>21</sup> The disease can be monostotic or polyostotic. While radiography and elevated serum alkaline phosphatase or other markers of increased bone turnover are often sufficient to make the diagnosis, bone scintigraphy can identify asymptomatic sites and the full extent of disease.<sup>22</sup> While elevated bone turnover markers are usually sufficient to monitor treatment response, bone scintigraphy is an alternative when serum markers are normal.<sup>22</sup>

## Pelvic fracture, when MRI cannot be performed or is nondiagnostic

*Includes sacral insufficiency fracture, stress fracture, and traumatic fracture.*

Bone scintigraphy (limited) is considered medically necessary in **EITHER** of the following scenarios:

- Diagnosis or management of sacral insufficiency fracture
- Diagnosis or management of stress fracture or traumatic fracture following nondiagnostic pelvic or sacral radiographs

## Perioperative evaluation, not otherwise specified, including delayed hardware failure

Bone scintigraphy (limited or three phase) is considered medically necessary for evaluation of clinically suspected periprosthetic infection or aseptic loosening.

### Rationale

#### EXTREMITY

Leukocyte scintigraphy is an option in patients with suspected periprosthetic infection<sup>5</sup> and has a high diagnostic accuracy (greater than 90%) for periprosthetic infections of the hip and knee; bone scintigraphy is highly sensitive for infection but is less specific.<sup>6,7</sup>

#### SPINE

For periprosthetic infections in the spine, a variety of structural and functional imaging modalities may help define the presence or extent of disease. CT and MRI are commonly performed but evaluation of the surgical bed may be limited by beam hardening/susceptibility artifact. Gallium and bone scintigraphy are functional imaging alternatives that have a higher diagnostic accuracy than leukocyte scintigraphy in the spine.<sup>3,4</sup>

## Tumor evaluation

Bone scintigraphy is considered medically necessary for evaluation of lesions of the skull base or calvarium when CT is nondiagnostic.

## Established Malignancy or Neoplasm

### Bladder, renal pelvis, and ureter cancers: invasive

Bone scintigraphy is considered medically necessary for the diagnostic workup and management of documented bladder, renal pelvis, and ureter cancer in the following scenarios:

#### Diagnostic workup

As clinically indicated for **EITHER** of the following scenarios:

- Urothelial cancer with high risk features (T3/T4 disease or stage T2 with hydronephrosis or high-risk histological features)
- Known or suspected malignancy with clinical, radiographic, or biochemical evidence suggestive of bone metastases.

#### Management

Known or suspected malignancy with clinical, radiographic, or biochemical evidence suggestive of bone cancer or bone metastases

*Note: Bone scintigraphy is not indicated when concurrent PET imaging has been performed and is diagnostic for bone metastases*

#### Rationale

##### DIAGNOSTIC WORKUP

The National Comprehensive Cancer Network (NCCN) does not recommend routine evaluation of bone metastases for non-muscle invasive urothelial cancer, and only recommends bone scintigraphy for muscle invasive urothelial cancer in symptomatic high-risk patients or those with laboratory indicators of bone metastasis.<sup>26, 27</sup>

### Breast cancer

Bone scintigraphy is considered medically necessary for the diagnostic workup and management of documented breast cancer in the following scenarios. Routine surveillance imaging following completion of therapy is not considered medically necessary.

#### Diagnostic workup

As clinically indicated for **EITHER** of the following scenarios:

- Stage III or higher invasive breast cancer
- Known or suspected malignancy with clinical, radiographic, or biochemical evidence suggestive of bone metastases.

#### Management

Known or suspected malignancy with clinical, radiographic, or biochemical evidence suggestive of bone cancer or bone metastases.

*Note: Bone scintigraphy is not indicated when concurrent PET imaging has been performed and is diagnostic for bone metastases.*

#### Rationale

##### DIAGNOSTIC WORKUP

In a large single-institution retrospective study of newly diagnosed asymptomatic breast cancer, bone scan detected bony metastases in 6% of patients (stage I 5%, stage II 6%, and stage III 14%), liver ultrasound detected hepatic metastases in 0.7% of patients (stage I or II 0% and stage III 6%), and chest x-ray detected lung metastases in 0.9% of patients (stage I or II 0% and stage III 7%). However, there was an unacceptably high rate of false positives: 6% for bone scans, 6% for liver ultrasounds, and 3% for chest x-rays.<sup>28</sup> Ravaioli et al. reported the rate of metastases detection in asymptomatic breast cancer patients was 1.46% for stage I and II vs 10.68% for stage III.<sup>29</sup> A review of 20 studies similarly showed that bone scan detected skeletal metastases in 0.5%-6.8% of those with stage I, 2.4%-8.8% with stage II, and 8.3%-24.5% with stage III breast cancer.<sup>30</sup> The detection of liver and bone metastases ranged from 0%-1.7% in stage I-II patients and 1.7%-2% for stage III patients. False-positive rates were 10%-22% for bone scan, 33%-66% for liver ultrasonography, and 0%-23% for chest



radiography. Based on the poor sensitivity and specificity of imaging in asymptomatic early stage breast cancer, imaging should be reserved for evaluation of specific signs or symptoms suggestive of metastatic disease.

## Colorectal cancer

Bone scintigraphy is considered medically necessary for diagnostic workup and management of documented colorectal cancer with clinical, radiographic, or biochemical evidence suggestive of bone cancer or bone metastases.

*Note: Bone scintigraphy is not indicated when concurrent PET imaging has been performed and is diagnostic for bone metastases.*

### Rationale

#### DIAGNOSTIC WORKUP

The use of bone scintigraphy for staging of asymptomatic patients is not recommended by the NCCN.<sup>31,32</sup>

## Melanoma

Bone scintigraphy is considered medically necessary for diagnostic workup and management of documented melanoma in the following scenarios:

### Diagnostic workup

As clinically indicated for **EITHER** of the following scenarios:

- Stage III or higher cutaneous melanoma
- Known or suspected malignancy with clinical, radiographic, or biochemical evidence suggestive of bone metastases

### Management

Known or suspected malignancy with clinical, radiographic, or biochemical evidence suggestive of bone cancer or bone metastases.

*Note: Bone scintigraphy is not indicated when concurrent PET imaging has been performed and is diagnostic for bone metastases.*

### Rationale

#### DIAGNOSTIC WORKUP

Bone scintigraphy is generally not required, especially if a FDG-PET/CT is planned. The NCCN recommends sentinel lymph node detection in patients with stage IA with adverse features, stage IB, stage II, in-transit and local recurrence and clinically negative lymph node cutaneous melanoma. The use of sentinel lymph node detection has been shown to decrease extent and morbidity of surgery without compromise to outcome.<sup>33</sup>

## Prostate cancer

*Note: The following information addresses adenocarcinoma of the prostate; however, applicability and coverage include all cancers originating in the prostate unless expressly addressed in another Carelon imaging guideline. Specific imaging considerations are addressed below.*

Bone scintigraphy is considered medically necessary for diagnostic workup and management of documented prostate cancer in the following scenarios:

### Diagnostic workup

As clinically indicated for **ANY** of the following scenarios:

- Unfavorable intermediate risk, if T2 disease and PSA > 10
- High or very high risk disease
- Regional lymph node involvement
- Metastatic prostate cancer

- Known or suspected malignancy with clinical, radiographic, or biochemical evidence suggestive of bone metastases

### Management

As clinically indicated for known or suspected malignancy with clinical, radiographic, or biochemical evidence suggestive of bone cancer or bone metastases.

*Note: Bone scintigraphy is not indicated when concurrent PET imaging has been performed and is diagnostic for bone metastases.*

*Unfavorable intermediate-risk group (ONE or more of the following):*

- 2 or 3 intermediate-risk factors: T2b-T2c; Grade group 2 or 3; or PSA 10-20ng/ml
- Grade group 3
- $\geq 50\%$  biopsy cores positive

*High risk (no very high-risk features and at least ONE of the following high-risk features):*

- T3a
- Grade group 4 or Grade group 5
- PSA > 20ng/ml

*Very high risk (at least ONE of the following):*

- T3b-T4
- Primary Gleason pattern 5
- 2 or 3 high-risk features
- 4 cores with Grade group 4 or 5

### Rationale

#### DIAGNOSTIC WORKUP

Neither the NCCN<sup>34</sup> nor the American College of Radiology<sup>35</sup> recommends bone scintigraphy in asymptomatic patients with low to favorable intermediate risk prostate cancer. A summary of 23 studies evaluating bone imaging to stage prostate cancer found bone metastases in 2.3% of patients with a PSA level of less than 10 ng/mL and in 5% of patients with a low Gleason score.<sup>36</sup> In a systematic review from 2004, Abuzallouf reported that among 23 studies examining the role of bone scan, metastases were detected in 2.3%, 5.3%, and 16.2% of patients with PSA levels less than 10, 10.1 to 19.9, and 20 to 49.9 ng/ml, respectively.<sup>36</sup> Scanning detected metastases in 6.4% of men with organ-confined cancer and 49.5% with locally advanced disease. Detection rates were 5.6% and 29.9% for Gleason scores 7 or less and 8 or greater, respectively.

morbidity of surgery without compromise to outcome.<sup>33</sup>

### Sarcoma of the bone and soft tissue

Imaging is considered medically necessary for the diagnostic workup and management of documented bone, cartilage, connective tissue, and other soft tissue sarcoma as clinically indicated for evaluation of clinical, radiographic, or biochemical evidence suggestive of bone cancer or bone metastases.

*Note: Bone scintigraphy is not indicated when concurrent PET imaging has been performed and is diagnostic for bone metastases.*

### Rationale

#### DIAGNOSTIC WORKUP

Bone scintigraphy can also be considered for primary bone cancer or suspected malignancy based on clinical, radiographic, or biochemical evidence.

### Suspected metastases, not otherwise specified

Bone scintigraphy is considered medically necessary for diagnostic workup and management of patients with a documented malignancy and signs or symptoms concerning for bony metastatic disease.

*Note: Bone scintigraphy is not indicated when concurrent PET imaging has been performed and is diagnostic for bone metastases.*

## Dacryoscintigraphy

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### Lacrimal duct obstruction

Dacryoscintigraphy is considered medically necessary for diagnosis of functional or mechanical obstruction of the lacrimal duct.

## Esophageal Motility Scintigraphy

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### Gastroesophageal reflux disease, when esophagram cannot be performed or is nondiagnostic

Esophageal motility scintigraphy is considered medically necessary for diagnosis.

## Gallium Scintigraphy

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### Lymphoma

For diagnosis and management of lymphoma when PET imaging cannot be performed and when standard imaging (CT or MRI) does not provide sufficient information to guide management.

### Osteomyelitis of the skull base or calvarium, when CT or MRI cannot be performed or is nondiagnostic

Gallium scintigraphy is considered medically necessary for diagnosis.

### Perioperative evaluation, not otherwise specified, including delayed hardware failure

*Also see Bone Marrow Scintigraphy.*

Gallium scintigraphy, with or without bone marrow scintigraphy, is considered medically necessary for diagnosis and management of periprosthetic infection.

#### Rationale

For periprosthetic infections in the spine, a variety of structural and functional imaging modalities may help define the presence or extent of disease. CT and MRI are commonly performed but evaluation of the surgical bed may be limited by beam hardening/susceptibility artifact. Gallium and bone scintigraphy are functional imaging alternatives that have a higher diagnostic accuracy than leukocyte scintigraphy in the spine.<sup>3,4</sup>

### Spinal infection, when MRI cannot be performed or is nondiagnostic

Gallium scintigraphy is considered medically necessary for diagnosis and management of spinal infection, including but not limited to epidural abscess, arachnoiditis, discitis, and osteomyelitis.

#### Rationale

MRI has high diagnostic accuracy for spondylodiscitis, is widely available, nonionizing, and is recommended as the initial modality by multiple clinical guidelines.<sup>15-17</sup> When MRI cannot be performed or is nondiagnostic, functional imaging with bone scintigraphy with or without gallium scintigraphy is suggested as a weak recommendation based on low quality evidence from the Infectious Disease Society of America (IDSA). While gallium/bone scintigraphy may have moderate-to-high sensitivity for spondylodiscitis<sup>18</sup>, leukocyte scintigraphy has limited sensitivity in the axial skeleton and is not recommended.<sup>15</sup> Functional imaging also offers the advantage of a wider field of view than MRI and can be useful to assess for multifocal or chronic forms of osteomyelitis such as chronic recurrent multifocal osteomyelitis and the Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis (SAPHO) syndrome.

## Gastric Emptying Scintigraphy/Gut Transit Scintigraphy

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### Gastrointestinal motility, including gastric outlet obstruction and gastroparesis

Imaging is considered medically necessary for diagnosis and management in **ANY** of the following scenarios:

- Gastric emptying study for evaluation of delayed gastric emptying or dumping syndrome
- Whole gut transit scintigraphy for evaluation of patients with severe constipation not responsive to conservative management
- Small bowel transit scintigraphy for evaluation of patients with severe constipation not responsive to conservative management

#### Rationale

Gastric and whole gut transit scintigraphy are standardized techniques to establish impairments in gastrointestinal motility. Gastric emptying studies may help identify gastroparesis in diabetic patients with upper gastrointestinal symptoms, in endoscopy negative dyspepsia, or following gastric surgery.<sup>44, 45</sup> Gastric emptying can also be used to establish abnormally rapid gastric emptying as seen in the dumping syndrome.<sup>44</sup>

Small bowel/colonic transit or whole gut studies are uncommonly performed but may help to establish abnormal motility by measuring total and regional transit times in a standardized manner. In patients with constipation, transit scintigraphy can be useful to the extent that it alters management, for instance when surgical intervention for a regional transit abnormality is being considered.<sup>46</sup>

## Gastrointestinal Blood Loss Scintigraphy

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### Hematoma/hemorrhage within the abdomen or unexplained hypotension

Gastrointestinal blood loss scintigraphy is considered medically necessary for diagnosis and management of active lower gastrointestinal bleeding unexplained by colonoscopy.

## GERD Scintigraphy (also known as a “milk scan” or “reflux study”)

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### Gastroesophageal reflux (Pediatric only)

GERD scintigraphy is considered medically necessary to evaluate symptoms of severe gastroesophageal reflux as an alternative to fluoroscopic evaluation or pH monitoring.

#### Rationale

Gastroesophageal reflux is a common and typically mild condition in infants and children that becomes gastroesophageal reflux disease (GERD) only when symptoms are troublesome. The gold standard for GERD detection is pH monitoring, but the technique is not widely available and minimally invasive. Fluoroscopy and scintigraphy are alternative modalities for the initial investigation of GERD. Scintigraphy can evaluate both reflux and gastric emptying<sup>44</sup> although diagnostic accuracy is moderate.<sup>47</sup>

## Hepatic Scintigraphy

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### Diffuse liver disease

*Includes chronic hepatitis, cirrhosis, glycogen storage diseases, hemochromatosis, and Wilson’s disease.*

Hepatic scintigraphy is considered medically necessary for evaluation of suspected liver disease based on clinical findings or abnormal liver function tests when ultrasound is nondiagnostic and further evaluation is required

#### Rationale

Hepatosplenic scintigraphy, typically performed with sulfur colloid, can be used to assess the function of the reticuloendothelial system and may be appropriate when results will determine whether a liver biopsy is performed or whether a potentially hepatotoxic medication is continued.<sup>48</sup>

## Indeterminate liver lesion, when either CT or MRI is nondiagnostic

Hepatic scintigraphy is considered medically necessary for evaluation of an indeterminate liver lesion > 1 cm in size, to evaluate for focal nodular hyperplasia or hemangioma.

### Rationale

Cavernous hemangiomas are common; autopsy studies have shown that they occur in up to 7% of the population.<sup>49, 50</sup> Hemangiomas appear as a homogenous hyperechoic mass, usually less than 3 cm in diameter with acoustic enhancement and sharp margins and are important to identify because they are benign lesions with a characteristic imaging appearance. Confident diagnosis of hemangioma can therefore avoid further biopsy and intervention. Triphasic CT and MRI are usually sufficient to establish the diagnosis.<sup>51</sup> Hemangiomas usually show radiotracer uptake on RBC scintigraphy with high positive likelihood ratios and good interobserver agreement.<sup>52, 53</sup> However, this is a historical technique that offers less information about alternative diagnosis and is typically reserved in situations where ultrasound is nondiagnostic and neither triphasic MRI or CT can be performed. Similarly, sulfur colloid scintigraphy has been used to further characterize suspected focal nodular hyperplasia<sup>54</sup> but is rarely performed as both MRI and CT are usually diagnostic.

## Hepatobiliary Scintigraphy

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### Ascites

Hepatobiliary scintigraphy is considered medically necessary for evaluation of suspected bile leak or biloma.

### Congenital and developmental conditions, not otherwise specified

Hepatobiliary scintigraphy is considered medically necessary for diagnosis and management in the following scenarios:

#### Adult

- To evaluate for choledochocoele following nondiagnostic ultrasound, CT, or MRI

#### Pediatric

- To evaluate for neonatal jaundice, biliary atresia, or choledochocoele when ultrasound is nondiagnostic

### Rationale

Ultrasound is the initial modality for evaluation of congenital hepatobiliary disease.<sup>56, 57</sup> Although it requires ionizing radiation, hepatobiliary scintigraphy has high specificity (greater than 98%) and moderate sensitivity (70%) for the diagnosis of biliary atresia with very large positive predictive value sufficient to establish the diagnosis.<sup>58</sup>

### Cholecystitis

Hepatobiliary scintigraphy is considered medically necessary for diagnosis and management in **EITHER** of the following scenarios:

- Acute or chronic cholecystitis (including chronic acalculous cholecystitis) following nondiagnostic ultrasound
- Complications of acute cholecystitis or cholecystectomy including perforation, abscess, gangrenous or hemorrhagic cholecystitis, gallstone ileus, Mirizzi's syndrome, and bile leak

### Rationale

In a large systematic review (57 studies and 5859 patients) on the comparative diagnostic accuracy of imaging for acute cholecystitis, hepatobiliary scintigraphy was found to have higher sensitivity (96%; 95% CI, 94%-97%) than ultrasound (81%; 95% CI, 75%-87%) and similar specificity, equating to higher positive and similar negative likelihood ratios and greater overall diagnostic accuracy.<sup>59</sup> However, ultrasound is typically preferred in the initial evaluation of hepatobiliary abnormalities, including acute cholecystitis, and is recommended by multiple clinical guidelines for this purpose.<sup>56, 57, 60</sup> Ultrasound offers net benefit because it is noninvasive, widely available, nonionizing, and with moderate-to-high diagnostic accuracy is usually sufficient for patient management. Hepatobiliary scintigraphy is typically an add-on test in situations where ultrasound is nondiagnostic.

## Leukocyte Scintigraphy

### Fever of unknown origin, when contrast-enhanced CT cannot be performed or is nondiagnostic

Leukocyte scintigraphy is considered medically necessary in **EITHER** of the following scenarios:

- Fever of duration greater than 3 weeks which is unexplained following a standard diagnostic evaluation to identify the source
- Unexplained fever in immunocompromised patient

#### Rationale

CT is usually the first line advanced imaging modality performed in the evaluation of fever of unknown origin (FUO)<sup>61</sup>. When a source remains unidentified following a comprehensive clinical and laboratory evaluation and CT, nuclear medicine imaging may be an option. Leukocyte scintigraphy has historically been used in the work up of FUO. It is specific (83%; 95% CI, 61%-94%) but not sensitive (33%; 95% CI, 24%-44%) for FUO, because it is limited to the identification of infectious sources<sup>62</sup>. However, leukocyte scintigraphy may play a role in further characterizing abnormalities on CT, or when CT is negative and an infectious source is suspected.

### Inflammatory bowel disease, including Crohn's disease and ulcerative colitis, when CT or MRI is nondiagnostic

Leukocyte scintigraphy is considered medically necessary in **EITHER** of the following scenarios:

- Diagnosis of suspected Crohn's disease following nondiagnostic colonoscopy in **ANY** of the following clinical scenarios when a patient:
  - Meets criteria for irritable bowel syndrome with a normal colonoscopy and an elevated fecal calprotectin OR C-reactive protein (CRP) level
  - Has concurrent upper gastrointestinal signs or symptoms with a nondiagnostic upper endoscopy
  - Does not meet criteria for irritable bowel syndrome and does not have concurrent upper gastrointestinal signs or symptoms
- Management of new or worsening symptoms to confirm exacerbation or evaluate for complications, including stricture, abscess, toxic megacolon, or fistula

#### Rationale

Leukocyte scintigraphy also has the advantage of full gastrointestinal visualization and can detect sites of inflammatory bowel disease with the small and large bowel.<sup>63,64</sup> Relative to CT/MRI, leukocyte scintigraphy has lower spatial resolution, higher radiation doses, and is less widely available; hence, it is typically reserved as an add-on test when CT or MR enterography are nondiagnostic.

### Osteomyelitis and septic arthritis

*Also see Bone Marrow Scintigraphy.*

Leukocyte scintigraphy is considered medically necessary in **EITHER** of the following scenarios:

- For diagnosis and management of osteomyelitis of the skull base or calvarium when CT or MRI cannot be performed or is nondiagnostic
- For diagnosis and management of osteomyelitis or septic arthritis at other sites (with or without bone marrow scintigraphy) when radiograph, ultrasound, or arthrocentesis is nondiagnostic or not sufficient to guide treatment and when MRI cannot be performed or is nondiagnostic.

#### Rationale

Functional imaging with bone scintigraphy has historically been used to evaluate for osteomyelitis when radiographs are nondiagnostic. Greater accuracy and the lack of ionizing radiation for MRI have largely made scintigraphy an add-on test when MRI cannot be performed or is nondiagnostic<sup>9,19,20</sup>, although bone scintigraphy offers a wider field of view and hence can

localize multifocal disease. Similarly, leukocyte scintigraphy is usually not appropriate in the initial evaluation of osteomyelitis<sup>19</sup> but may play a complementary role to bone scintigraphy in specific scenarios such as multifocal disease.

## Perioperative evaluation, not otherwise specified, including delayed hardware failure

Also see *Bone Marrow Scintigraphy*.

Leukocyte scintigraphy (with or without bone marrow scintigraphy) is considered medically necessary for diagnosis and management of periprosthetic infection.

### Rationale

#### EXTREMITY

Leukocyte scintigraphy is an option in patients with suspected periprosthetic infection<sup>5</sup> and has a high diagnostic accuracy (greater than 90%) for periprosthetic infections of the hip and knee; bone scintigraphy is highly sensitive for infection but is less specific.<sup>6, 7</sup>

#### SPINE

For periprosthetic infections in the spine, a variety of structural and functional imaging modalities may help define the presence or extent of disease. CT and MRI are commonly performed but evaluation of the surgical bed may be limited by beam hardening/susceptibility artifact. Gallium and bone scintigraphy are functional imaging alternatives that have a higher diagnostic accuracy than leukocyte scintigraphy in the spine.<sup>3, 4</sup>

## Infectious and inflammatory conditions, not otherwise referenced

Leukocyte scintigraphy is considered medically necessary for diagnosis and management in **EITHER** of the following scenarios:

- To evaluate for sternal wound infection or dehiscence when CT chest is nondiagnostic
- To evaluate sites of intra-abdominal infection suspected by CT or MRI

### Rationale

#### CHEST

CT chest is usually sufficient for evaluating for sternal wound dehiscence or other forms of chest infection and has the advantage of simultaneous visualization of the mediastinum and lung parenchyma.<sup>13</sup> Historically and in rare circumstances, bone or leukocyte scintigraphy has been used to differentiate superficial and deep infections, although evidence for diagnostic accuracy is limited.<sup>14</sup>

#### ABDOMEN AND PELVIS

CT or MRI is usually sufficient to evaluate for complications of intra-abdominal infection such as abscess and are widely available and commonly performed. However, factors such as distorted anatomy, ileus, ascites, and healing wounds can complicate the structural assessment of infection.<sup>64</sup> When diagnostic uncertainty remains following CT and/or MRI, leukocyte scintigraphy may be helpful as an add-on test to further characterize suspected sites of infection such as infected surgical material including vascular grafts, shunts, or abscess.<sup>63, 64</sup>

## Lymphoscintigraphy

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### Lymphedema

Lymphoscintigraphy is considered medically necessary for evaluation when diffuse and unexplained by venous ultrasound.

### Rationale

Diffuse swelling of the extremities has a variety of causes including lymphedema due to chronic lymphatic insufficiency.<sup>65</sup> Lymphoscintigraphy can help to determine whether obstruction to lymphatic flow is responsible for diffuse swelling and help to direct both medical and surgical interventions.<sup>65, 66</sup>

### Breast cancer

Lymphoscintigraphy is considered medically necessary in **EITHER** of the following scenarios:



- For localization of sentinel lymph nodes in stage I-III invasive breast cancer and clinically negative lymph nodes
- For localization of sentinel lymph nodes in ductal carcinoma in situ (DCIS) when mastectomy is planned

### Rationale

The NCCN recommends the use of sentinel lymph node detection in patients with stage I-III and clinically lymph node-negative breast cancer performed prior to systemic therapy or in selected patients after systemic therapy. The use of sentinel lymph node detection has been shown to decrease extent and morbidity of surgery without compromise to outcome. Patients with higher stage disease may require full lymph node dissections.<sup>67-69</sup>

## Cervical cancer

Lymphoscintigraphy is considered medically necessary as clinically indicated for localization of sentinel lymph nodes in stage IA1 with LVI, stage IA2, stage 1B1, or stage IIA1 cervical cancer with clinically negative lymph nodes.

### Rationale

The NCCN recommends sentinel lymph node detection in patients with stage IA1 with LVI, IA2, 1B1, and IIA1 and clinically lymph node-negative cervical cancer. The use of sentinel lymph node detection has been shown to decrease extent and morbidity of surgery without compromise to outcome. Patients with higher stage disease may require full lymph node dissections.<sup>68, 70</sup>

## Head and neck cancer

Lymphoscintigraphy is considered medically necessary as clinically indicated for localization of sentinel lymph nodes in T1-T2 squamous cell carcinoma of the oral cavity with clinically negative lymph nodes.

### Rationale

The NCCN recommends sentinel lymph node detection in patients with T1-T2 tumors and clinically lymph node-negative oral cavity squamous cell carcinoma.<sup>71</sup> The use of sentinel lymph node detection has been shown to decrease extent and morbidity of surgery without compromise to outcome. Patients with higher stage disease may require full lymph node dissections.<sup>68, 71</sup>

## Melanoma

Lymphoscintigraphy is considered medically necessary as clinically indicated for localization of sentinel lymph nodes in stage IA with adverse features, stage IB, stage II, in-transit, or locally recurrent melanoma with clinically negative lymph nodes.

### Rationale

The NCCN recommends sentinel lymph node detection in patients with stage IA with adverse features, IB, II, in-transit, and local recurrence and clinically negative lymph node melanoma. The use of sentinel lymph node detection has been shown to decrease extent and morbidity of surgery without compromise to outcome.<sup>33, 68, 72</sup>

## Merkel cell carcinoma

Lymphoscintigraphy is considered medically necessary as clinically indicated for localization of sentinel lymph nodes in Merkel cell carcinoma with clinically negative lymph nodes.

### Rationale

#### DIAGNOSTIC WORKUP

The NCCN recommends sentinel lymph node detection in patients with clinically lymph node-negative Merkel cell carcinoma. Sentinel lymph node biopsy is an important staging tool. This procedure and subsequent treatment impact for regional control for patients with positive sentinel lymph node, but the impact of sentinel lymph node biopsy on overall survival is unclear. If sentinel lymph node biopsy is not performed concurrently, it is recommended that sentinel lymph node biopsy be performed prior to definitive excision with exhaustive histologic margin assessment (i.e., Mohs micrographic surgery).<sup>73</sup>



## Penile, vaginal, and vulvar cancers

*Note: The following information primarily addresses squamous cell carcinomas of the vagina, vulva, and penis; however, applicability and coverage include all cancers originating in the vagina, vulva, and penis unless expressly addressed elsewhere in oncologic indications. Specific imaging considerations are addressed below.*

Lymphoscintigraphy is considered medically necessary as clinically indicated for localization of sentinel lymph nodes in **EITHER** of the following scenarios:

- Penile cancer with clinically negative lymph nodes
- Vulvar cancer (T1 or T2) with clinically negative lymph nodes

### Rationale

The NCCN recommends sentinel lymph node detection in patients with T1 or T2 and clinically lymph node-negative vulvar cancer. The use of sentinel lymph node detection has been shown to decrease extent and morbidity of surgery without compromise to outcome. Patients with higher stage disease may require full lymph node dissections.<sup>74</sup>

The NCCN recommends sentinel lymph node detection for clinically lymph node-negative penile cancer. The use of sentinel lymph node detection has been shown to decrease extent and morbidity of surgery without compromise to outcome. Patients with higher stage disease may require full lymph node dissections.<sup>75</sup>

## Uterine cancer

Lymphoscintigraphy is considered medically necessary as clinically indicated for localization of sentinel lymph nodes of uterine cancer confined to the uterus with clinically negative lymph nodes.

### Rationale

The NCCN recommends sentinel lymph node detection in patients with uterine confined and clinically lymph node-negative uterine cancer. Prospective and retrospective studies demonstrate that compared to systemic lymphadenectomy, sentinel lymph node mapping with ultrastaging may increase the detection of lymph node metastasis with low false-negative rates in women with apparent uterine-confined disease. Recent evidence indicates that sentinel lymph node mapping may also be used in high-risk histologies (serous carcinoma, clear cell carcinoma, carcinosarcoma).<sup>76</sup>

## Meckel's Scan

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### Meckel's diverticulum

A Meckel's scan is considered medically necessary for diagnosis of Meckel's diverticulum or for further characterization of a lesion suspected to contain gastric mucosa, in patients with a history of unexplained gastrointestinal bleeding or anemia.

### Rationale

A variety of advanced structural and functional imaging modalities may be needed in the diagnosis and management of select intra-abdominal congenital abnormalities. More common anomalies of the gastrointestinal system including pyloric stenosis, midgut volvulus, Hirschsprung's disease, and small left colon syndrome are usually diagnosed with upper GI series or barium enema. Meckel's scan is useful to diagnose ectopic functioning gastric mucosa, typically in a Meckel's diverticulum<sup>45</sup> and has moderate-to-high diagnostic accuracy in patients with subacute unexplained gastrointestinal bleeding.<sup>77-79</sup>

## Metaiodobenzylguanidine (MIBG) Scintigraphy

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### Neuroendocrine tumors

MIBG scintigraphy is considered medically necessary for the diagnostic workup and management of documented neuroendocrine cancer in the following scenarios:

### Diagnostic workup

As clinically indicated for neuroblastoma or tumors of the autonomic nervous system (pheochromocytoma, paraganglioma, ganglioneuroma) in **ANY** of the following scenarios:

- Suspected metastatic disease

- Suspected neuroblastoma or tumors of the autonomic nervous system (pheochromocytoma, paraganglioma, ganglioneuroma) based on CT, MRI or abnormal serum or urine metanephrine levels
- For pheochromocytoma/paraganglioma prior to planned I131 iobenguane treatment

### Management

As clinically indicated for pheochromocytoma/paraganglioma prior to planned I131 iobenguane treatment.

### Rationale

#### DIAGNOSTIC WORKUP

The NCCN does not recommend MIBG scintigraphy as routine imaging in patients with pheochromocytoma and paraganglioma. However, in patients with high-risk disease or suspected metastases, the addition of MIBG, especially with its higher specificity, may provide additional information which could affect definitive therapy. CT and MRI have a 98%-100% sensitivity for detection of pheochromocytoma. However, the specificity only approaches 70%. In a 2010 meta-analysis of 22 studies, the sensitivity and specificity of MIBG were reported to be 94% (95% CI, 91%-97%) and 92% (95% CI, 87%-98%). Individual prospective and retrospective studies also appear to support the continued role of MIBG scintigraphy.<sup>80</sup>

#### MANAGEMENT

MIBG scintigraphy is indicated prior to 131I iobenguane treatment. In an open-label, single-arm, multicenter phase II clinical trial (Study IB12B [NCT00874614]) that prompted the approval of 131I iobenguane (Azedra), patients were required have positive MIBG scintigraphy prior to therapeutic treatment.

## Parathyroid Scintigraphy

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### Parathyroid adenoma, when ultrasound is normal or nondiagnostic

Parathyroid scintigraphy is considered medically necessary in **EITHER** of the following scenarios:

- To identify an adenoma for surgical planning in patients with primary hyperparathyroidism
- Localization of residual parathyroid tissue in patients with recurrent or persistent disease following parathyroidectomy.

### Rationale

Ultrasound and sestamibi scintigraphy are the most common initial imaging tests used to evaluate suspected parathyroid adenoma and have a diagnostic accuracy of above 80%.<sup>81</sup> A meta-analysis of 12 diagnostic accuracy studies with over 500 patients found comparable sensitivity for ultrasound (80%, CI 77%-83%) and planar sestamibi scintigraphy (84%, CI 80%-87%) and slightly higher specificity for sestamibi (87%, CI 83%-91%) vs ultrasound (77%, CI 71%-82%).<sup>82</sup> When ultrasound and sestamibi exams are not diagnostic, 4-dimensional CT, including dynamic contrast enhancement, has high sensitivity (94%) and specificity (96%).<sup>83</sup> This is consistent with clinical practice/consensus-based guidelines on parathyroid scintigraphy.<sup>84, 85</sup>

## Perfusion Scintigraphy

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### Seizure, refractory

Ictal perfusion scintigraphy is considered medically necessary for preoperative planning, to identify a focus of seizure activity in patients refractory to medical therapy.

### Rationale

Ictal (including immediate postictal) perfusion scintigraphy is an older technology largely supplanted by FDG PET and difficult to perform. Meta-analysis of perfusion scintigraphy found a low (< 60%) sensitivity for inter-ictal, moderate (62%-88%) sensitivity for post-ictal and moderate-to-high (73%-100%) sensitivity for ictal imaging.<sup>86</sup>

### Stroke or transient ischemic attack

Perfusion scintigraphy is considered medically necessary for evaluation of non-acute ischemia to determine candidacy for vascular intervention.

## Rationale

The role for perfusion scintigraphy in the diagnosis and management of stroke is limited. Perfusion scintigraphy may be helpful to determine cerebral vascular reserve after a vasodilation challenge or in patients being considered for carotid artery sacrifice.<sup>87</sup>

## Peritoneal Venous Shunt Scintigraphy

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### Ascites

Peritoneal venous shunt scintigraphy is considered medically necessary following nondiagnostic ultrasound to assess LeVeen or Denver shunt patency in patients with cirrhosis and refractory ascites.

## Pyrophosphate Scintigraphy

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### Amyloidosis

For evaluation of cardiac amyloidosis in **ANY** of the following scenarios:

- Patient who is a carrier of the TTR gene mutation in **ANY** of the following scenarios:
  - Baseline screening for cardiac amyloidosis in asymptomatic carrier
  - Surveillance at two (2) yearly intervals in asymptomatic carrier
  - New or worsening symptoms suggestive of amyloidosis (cardiac or extracardiac)
- New onset symptomatic heart failure when **ANY** of the following apply:
  - African-American patient > 60 years old with **EITHER** of the following:
    - Heart failure of unknown etiology
    - Mean left ventricular wall thickness > 12 mm on echocardiography
  - Non-African-American patient > 60 years old with **BOTH** of the following:
    - Heart failure of unknown etiology
    - Mean left ventricular wall thickness > 12 mm on echocardiography
  - Patient with known or suspected familial amyloidosis
  - Patient with unexplained peripheral sensorimotor neuropathy
  - Patient > 60 years old with low-flow, low-gradient aortic stenosis
  - Patient > 60 years old with unexplained biceps tendon rupture
- Established extracardiac transthyretin amyloidosis (ATTR) with new or worsening cardiac symptoms
- Bilateral carpal tunnel syndrome (with or without heart failure) in patients who are > 60 years old
- Other testing suggestive of cardiac amyloidosis in patients - **EITHER** of the following:
  - Echocardiogram consistent with amyloidosis
  - Cardiac MRI consistent with amyloidosis

### Rationale

Cardiac amyloidosis results from the deposition of an abnormal protein in the extracellular matrix of the myocardium. The most common types of cardiac amyloidosis which manifest clinically are transthyretin amyloidosis (ATTR) and light chain amyloidosis (AL). The clinical presentation of cardiac amyloidosis is variable does not differentiate ATTR from AL. Echocardiography and Cardiac MR imaging provide suggestive evidence of cardiac amyloidosis but are not diagnostic and cannot differentiate between AL and ATTR. However, this differentiation is important in selection of optimal treatment, prognostication, and genetic counseling.

99mT-PYP imaging can lead to a diagnosis of ATTR without the need for biopsy when there are Echo or Cardiac MRI findings consistent with amyloidosis and laboratory markers of AL (serum and urine immunofixation electrophoresis and serum kappa/lambda ratio) are absent. False positive 99mT-PYP imaging studies can occur in the setting of AL.

## Radionuclide Cisternography

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### Brain and spinal cord malignancies

Radionuclide cisternography is considered medically necessary for leptomeningeal metastases in **EITHER** of the following scenarios:

- If symptoms or conventional imaging suggest CSF flow blockage and intra-CSF chemotherapy is planned
- After primary treatment when flow abnormalities were demonstrated on previous CSF flow scan

### Cerebrospinal fluid leak of the skull base

Radionuclide cisternography is considered medically necessary for diagnosis and management when cerebrospinal fluid (CSF) leak is suspected and **EITHER** of the following is present:

- CSF rhinorrhea when fluid is positive for beta-2 transferrin
- History of skull base trauma or surgery

### Hydrocephalus/ventricular assessment, when MRI cannot be performed or is nondiagnostic

Radionuclide cisternography is considered medically necessary for evaluation of suspected hydrocephalus or shunt malfunction.

#### Rationale

Compared to MRI, radionuclide cisternography is a minimally invasive test with comparatively lower spatial and contrast resolution that also requires ionizing radiation and hence is not routinely recommended in the evaluation of NPH.<sup>43, 88</sup> Cisternography may be useful when MRI cannot be performed or is indeterminate and can help identify the site of CSF obstruction.<sup>88, 89</sup> Cisternography is a functional study that may can help identify the site of CSF obstruction<sup>88</sup> and has a wider field of view, making it a useful add-on test for suspected shunt malfunction.<sup>89</sup>

### Spontaneous (idiopathic) intracranial hypotension, when MRI cannot be performed or is nondiagnostic

Radionuclide cisternography is considered medically necessary for diagnosis and management.

## Radionuclide Cystography

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### Urinary tract infection (Pediatric only)

Radionuclide cystography is considered medically necessary as an alternative to voiding cystourethrography (VCUG) to evaluate for vesicoureteral reflux in **ANY** of the following scenarios:

- Ultrasound suggestive of high grade vesicoureteral reflux
- First febrile urinary tract infection that is atypical
- Recurrent febrile urinary tract infection

#### Rationale

Imaging is useful to evaluate for anatomic abnormalities associated with vesicoureteral reflux (VUR) and to assess the severity of disease. Ultrasound is the recommended initial imaging modality for infants with febrile UTI.<sup>90, 91</sup> Voiding cystourethrography (VCUG) has the highest diagnostic accuracy for VUR evaluation and is the most commonly performed test, although radionuclide cystography is an alternative test especially in girls that offers lower spatial resolution but lower radiation

exposure. However, guidelines do not recommend either form of ionizing VUR imaging following the first febrile UTI. Criteria for VUR imaging include atypical and recurrent UTI or abnormalities of ultrasound suggesting high grade VUR.<sup>90,92</sup>

## Renal Scintigraphy

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### Congenital and developmental conditions, not otherwise specified

Renal scintigraphy is considered medically necessary in **EITHER** of the following scenarios:

- Known or suspected ureteropelvic junction obstruction, megaureter, or multicystic dysplastic kidney (MCDK) when ultrasound is nondiagnostic
- Split function evaluation in congenital renal anomalies

#### Rationale

A variety of advanced structural and functional imaging modalities may be needed in the diagnosis and management of select intra-abdominal congenital abnormalities. Renal scintigraphy can be useful to establish the diagnosis of congenital anomalies of the kidney and ureter<sup>93,94</sup> or for differential estimation of renal function, especially in the presence of an ectopic, malrotated, or hypoplastic kidney.<sup>94</sup>

### Hydronephrosis

Renal scintigraphy is considered medically necessary following nondiagnostic ultrasound, CT, or MRI to differentiate obstructive from nonobstructive hydronephrosis.

#### Rationale

Renal scintigraphy is a functional study that can help differentiate obstructive from nonobstructive hydronephrosis and so determine the clinical significance of suspected hydronephrosis, including the impact on renal function and the presence or absence of obstructive uropathy.<sup>93-96</sup>

### Kidney cancer/Renal cell carcinoma

Renal scintigraphy is considered medically necessary for the diagnostic workup and management of documented kidney cancer.

### Perioperative evaluation, not otherwise specified, including transplant

Renal scintigraphy is considered medically necessary for diagnosis and management in **EITHER** of the following scenarios:

- Split renal function evaluation prior to nephrectomy
- Renal transplant viability

#### Rationale

A variety of complications--both acute and delayed--can occur following renal transplant. Ultrasound is a commonly performed initial imaging study since it is widely available, nonnephrotoxic, minimally invasive, nonionizing, and can evaluate both the perinephric space and both renal parenchyma and vasculature. However, ultrasound is operator dependent and findings may be nonspecific. Limited evidence and guidelines are available to inform the optimal diagnostic testing strategy following renal transplant. Renal scintigraphy may be a complementary or add-on imaging test and may be helpful in evaluating transplant viability including differentiating acute rejection from acute tubular necrosis.<sup>25</sup> Renal scintigraphy may also be helpful in evaluating renal function prior to nephrectomy.

### Renal artery stenosis/Renovascular hypertension

Renal scintigraphy is considered medically necessary to assess renal split function in patients with an established diagnosis of renal artery stenosis.

### Trauma, not otherwise specified

Renal scintigraphy is considered medically necessary to further characterize fluid collections suspected to be urinomas.

## Urinary tract infection (Pediatric only)

Renal scintigraphy is considered medically necessary to evaluate for renal scarring at least 4 months following urinary tract infection in **EITHER** of the following scenarios:

- Age less than 3 years with atypical urinary tract infection
- Recurrent urinary tract infection

### Rationale

Renal scintigraphy using dimercaptosuccinic acid (DMSA) is sensitive for the detection of renal scarring following urinary tract infection or pyelonephritis. Renal scintigraphy is not routinely indicated in initial evaluation of a urinary tract infection (UTI), but may be used to help direct management including use of prophylactic antibiotics in children under 3 years of age with atypical UTIs (including features such as septicemia, infection with non *Escherichia coli* organisms, and other markers of serious illness) or in patients with recurrent UTI.<sup>91,92</sup>

## Somatostatin Receptor Scintigraphy (Octreoscan)

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### Neuroendocrine cancer

Somatostatin receptor imaging is considered medically necessary for the diagnostic workup and management of documented well-differentiated neuroendocrine cancer in **EITHER** of the following scenarios:

- Diagnostic workup in **EITHER** of the following scenarios:
  - Biopsy-proven well-differentiated neuroendocrine tumor
  - Suspected well-differentiated neuroendocrine tumor based on endoscopy, conventional imaging, or biochemical markers when not amenable to biopsy
- Management in **EITHER** of the following scenarios:
  - Prior to planned peptide receptor radioligand therapy (PRRT) for well-differentiated neuroendocrine tumor
  - When identification of more extensive disease will change management and ANY of the following criteria are met:
    - Equivocal findings of disease progression on conventional imaging
    - Clinical or biochemical progression with negative conventional imaging
    - When the original disease was only detectable by somatostatin receptor-based imaging

### Rationale

#### DIAGNOSTIC WORKUP

Neuroendocrine cancer is staged using the American Joint Committee on Cancer TNM system. As an adjunct to TNM staging, the World Health Organization classification scheme also takes into account proliferation rate (Ki-67) in grading of tumors. Carcinoid is a highly vascular tumor and multiphasic imaging should be used to improve detection.<sup>97</sup> MRI is more sensitive than CT for detection of liver metastases; however, one study found no statistically significant difference between these modalities for this indication.<sup>98</sup> Smaller lesions, especially in the small bowel and appendix, may be difficult to visualize with either modality. Somatostatin receptor-based imaging should also be considered in well-differentiated neuroendocrine tumors. MRI brain with contrast is indicated for poorly differentiated tumors arising from the thorax.

Somatostatin receptor imaging is recommended by multiple professional societies including ACR, NCCN, and ENTS as a part of initial staging of well-differentiated neuroendocrine tumors (NETs) when indicated. 68Ga dotatate PET is generally preferred. In the FDA review, OctreoScan when compared to conventional imaging was consistent with the final diagnosis in 267 of 309 evaluable patients (86.4%). In patients with nonfunctioning NETs, OctreoScan successfully detected NETs in 27 of 32 patients (84.4%). OctreoScan localized previously unidentified tumors in 57 of 204 patients. In a small subgroup of 39 patients who had tissue confirmation, the sensitivity rate for OctreoScan scintigraphy was 85.7%; for CT/MRI the rate was 68%. The specificity rate for OctreoScan scintigraphy was 50%, the rate for CT/MRI was 12%. In a 2018 systematic review of 15 studies with 679 patients evaluating the diagnostic accuracy of SSTR-PET with OctreoScan, 18FDG PET or CT/MRI, Hope et al. reported that SSTR-PET was associated with greater sensitivity than OctreoScan (difference in sensitivity ranged from 14% to 56%) as well as CT and/or MRI (differences in sensitivity ranged from 12% to 49%). Multiple prospective trials confirm the overall superiority of 68Ga dotatate PET to somatostatin receptor scintigraphy. Several other systematic reviews, a meta-analysis, and prospective studies of variable quality have consistently shown that 68Ga dotatate has a moderate-to-high



diagnostic accuracy for the staging of de novo, recurrent, or suspected neuroendocrine cancer with a moderate-to-high positive likelihood ratio in the range of 5-13 and a high negative likelihood ratio in the range of 0.04-0.21 to exclude neuroendocrine cancer. In addition, comparative studies with <sup>111</sup>In pentetretotide SPECT/CT and conventional imaging confirms its superior diagnostic accuracy and sensitivity in this setting, although these studies have several methodological limitations.<sup>99, 100</sup>

## MANAGEMENT

Imaging to assess disease response to therapy should be performed with the same modality used to detect the initial abnormality and the same modality should be used over time. For most cases, CT chest, abdomen, and pelvis with or without contrast is sufficient. Limited evidence supports the use of <sup>68</sup>Ga dotatate for monitoring disease during treatment.

Somatostatin analog receptor imaging is vital prior to PRRT. Based on the increased sensitivity for detection of somatostatin receptors and expected change in management, <sup>68</sup>Ga dotatate also appears to play a role prior to therapy. <sup>68</sup>Ga dotatate changed management in 13%-60% of patients, with a wide variation depending on the clinical scenario in which the radiotracer is used. No study has compared the utility of SSTR-PET with alternative imaging modalities for predicting response to PRRT or somatostatin analog therapy.<sup>99</sup>

## Splenic Scintigraphy

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### Splenic tissue, ectopic or wandering

Splenic scintigraphy is considered medically necessary for diagnosis and management when CT or MRI is nondiagnostic.

#### Rationale

Splenosis is the autotransplantation of splenic tissue to ectopic locations in the lungs and abdomen usually following trauma.<sup>101</sup> CT, ultrasound, or MRI are usually sufficient to characterize splenic tissue.<sup>102</sup> Literature on this rare condition is limited to case reports or small retrospective studies, the majority of which demonstrate the utility of <sup>99</sup>Tc sulfur colloid scintigraphy to characterize a mass outside the spleen suspected to be splenic tissue, especially one with atypical features on ultrasound, CT, or MRI when a positive result on scintigraphy would avoid the need for biopsy or more invasive methods of diagnosis.<sup>101, 103, 104</sup>

## Thallium Scintigraphy

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### Intracranial mass

Thallium scintigraphy is considered medically necessary for evaluation of HIV-positive patients with an intracranial mass.

#### Rationale

In a systematic review comparing the diagnostic accuracy of thallium scintigraphy, FDG-PET, and MR spectroscopy in distinguishing CNS lymphoma from toxoplasmosis in HIV positive patients, Yang et al. found high (> 90%) diagnostic accuracy with moderate sample sizes for scintigraphy and PET. Limited data for MR spectroscopy suggests lower and widely ranging diagnostic accuracy.<sup>105</sup>

## Thyroid Scintigraphy (including Radioactive Iodine Uptake)

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### Thyroid cancer

Thyroid scintigraphy is considered medically necessary for the diagnostic workup, management, and surveillance of documented thyroid cancer.

#### Diagnostic workup

As clinically indicated for differentiated thyroid cancer in **ANY** of the following scenarios:

- Prior to planned definitive radioactive iodine therapy in low risk patients
- Post thyroidectomy when radioactive iodine therapy is planned (except in low risk patients)
- For known or suspected metastatic disease when radioactive iodine therapy is planned

#### Management

As clinically indicated for differentiated thyroid cancer in **ANY** of the following scenarios:

- Immediately following radioactive iodine therapy
- Evaluation of persistent disease found on post radioactive iodine therapy imaging
- Evaluation for suspected recurrent thyroid cancer found during surveillance (i.e., elevated Tg, stable or rising antithyroglobulin antibodies, abnormal ultrasound during surveillance)

### Surveillance

As clinically indicated for intermediate or high risk differentiated thyroid cancer 6 to 12 months after therapy has been completed.

*Note: Low risk papillary thyroid cancer*

- *Classic papillary thyroid cancer*
- *Largest primary tumor < 2 cm*
- *Intrathyroidal*
- *Unifocal or multifocal (all foci  $\leq$  1 cm)*
- *No detectable anti-Tg antibodies*
- *Postoperative unstimulated Tg < 1 ng/mL*

*Note: Low risk follicular and Hurthle cell thyroid cancer*

- *Largest primary tumor < 2 cm*
- *Intrathyroidal*
- *No vascular invasion*
- *Clinical N0*
- *Postoperative unstimulated Tg < 1 ng/mL*

### Rationale

#### DIAGNOSTIC WORKUP

High quality evidence and medical society recommendations support the use of thyroid scintigraphy after thyroidectomy in patients with intermediate to high-risk differentiated thyroid cancer and in whom radioactive iodine treatment is planned. In a large systematic review, no clear improvement in overall survival or disease free survival was seen in low risk patients treated with radioactive iodine.<sup>106</sup> In a retrospective review of 1298 patients with low-risk differentiated thyroid cancer, radioactive iodine resulted in a 10-year overall survival of 95.8% while patients not treated with radioactive iodine after surgery had a 10-year overall survival of 94.6%.<sup>107</sup> Conversely, a review of the NCI database of 21,870 patients with intermediate-risk differentiated thyroid cancer who underwent total thyroidectomy with or without radioactive iodine showed improved overall survival ( $P < .001$ ). After a multivariate adjustment for demographic and clinical factors, radioactive iodine was associated with a 29% reduction in the risk of death, with a hazard risk 0.71 (95% CI, 0.62-0.82;  $P < .001$ ).<sup>108</sup> In a 2015 NTCTCS Registry analysis of 4941 patients, improved overall survival was seen in stage III patients who received radioactive iodine (risk ratio, 0.66;  $P = .04$ ) and stage IV patients who received both total/near-total thyroidectomy and radioactive iodine (risk ratio, 0.66 and 0.70; combined  $P = .049$ ).<sup>109</sup>

#### MANAGEMENT

Relatively weak evidence and medical society recommendations support the use of thyroid scintigraphy after radioactive iodine treatment evaluation. Up to 25% of images show lesions that may be clinically important but which were not originally detected on diagnostic imaging. In a retrospective study comparing whole body scans obtained before and after radioactive iodine in patients ( $N = 93$ ) with thyroid carcinoma, in 27% of treatment cycles, the results of posttreatment and pretreatment scans differed. Only 10% of post-treatment scans detected new locations of metastatic disease.

#### SCREENING AND SURVEILLANCE

Biochemical monitoring remains the most vital component for surveillance of differentiated thyroid cancer, although conventional imaging may also be considered when clinically indicated. High quality evidence and medical society recommendations do not support the use of thyroid scintigraphy for asymptomatic surveillance of patients without evidence of disease. Both the American Thyroid Association and NCCN give consideration to a single exam after completion of therapy in intermediate-risk and high-risk differentiated thyroid cancer patients. The value of continued monitoring if no evidence of disease is seen is controversial.<sup>110, 111</sup>



## Thyroid nodule or thyromegaly (goiter)

Thyroid scintigraphy is considered medically necessary for diagnosis following nondiagnostic ultrasound in **ANY** of the following scenarios:

- For characterization of nodule(s) in patients with a low thyroid-stimulating hormone (TSH)/thyrotoxicosis
- To identify ectopic thyroid tissue in patients with unexplained (subclinical) hyperthyroidism or when suspected based on other imaging studies
- To confirm the diagnosis of retrosternal goiter

### Rationale

There is a limited role for thyroid scintigraphy in the diagnosis of thyroid nodules typically as an add-on test following a nondiagnostic thyroid ultrasound. Thyroid scintigraphy has a wider field of view and can identify ectopic thyroid tissue in patients with unexplained thyrotoxicosis or when suspected based on structural imaging. Thyroid scintigraphy can also determine the functional status of nodules and may avert the need for biopsy in “hot” nodules due to their low pre test probability for malignancy (weak recommendation based on low-quality evidence).<sup>110</sup>

## Thyrotoxicosis (including hyperthyroidism and Graves’ disease)

Imaging is considered medically necessary in **EITHER** of the following scenarios:

- Diagnosis
  - Radioactive iodine uptake (RAIU) and/or thyroid scintigraphy to determine the etiology of thyrotoxicosis when not apparent on initial clinical and biochemical evaluation
- Management
  - RAIU prior to radioactive iodine (RAI) therapy

## VQ Scintigraphy

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### Congenital heart disease

VQ scintigraphy is considered medically necessary to evaluate for cardiac shunts in patients with congenital heart disease.

### Congenital pulmonary airway malformation (Pediatric only)

VQ scintigraphy is considered medically necessary for diagnosis and management of **EITHER** of the following conditions:

- Congenital lobar emphysema
- Congenital cystic adenomatoid malformation

### Congenital thoracic anomalies

VQ scintigraphy is considered medically necessary for diagnosis and management.

### Lung cancer, small cell and non-small cell

VQ scintigraphy is considered medically necessary for diagnostic workup and management of documented small cell and non-small cell lung cancer.

### Malignant pleural mesothelioma

VQ scintigraphy is considered medically necessary as part of surgical evaluation when FEV1 is less than 80%.

## Perioperative evaluation, including evaluation prior to lung transplant

VQ scintigraphy is considered medically necessary to quantify pulmonary function prior to pneumonectomy or lobectomy.

### Pulmonary artery hypertension

VQ scintigraphy is considered medically necessary for diagnosis and management in **EITHER** of the following scenarios:

- To diagnose chronic thromboembolic pulmonary artery hypertension (CTEPH) as a cause of patients with established pulmonary artery hypertension
- To manage confirmed chronic thromboembolic pulmonary artery hypertension (CTEPH) by evaluating the anatomic extent of disease in patients being considered for surgery when CTA cannot be performed or is nondiagnostic

#### Rationale

Guidelines do not recommend routine use of advanced imaging in asymptomatic patients following venous thromboembolism<sup>112</sup>, but suggest VQ scintigraphy for the initial evaluation of symptomatic patients due to the higher sensitivity of this modality for pulmonary perfusion abnormalities and high negative likelihood ratio.<sup>112-114</sup> In patients with established chronic pulmonary thromboembolism, CTA is suggested instead of VQ scintigraphy to evaluate the anatomic extent of surgically accessible disease and MRA is not recommended.<sup>112</sup>

### Pulmonary embolism

#### Adult: In pregnant patients or when CT/CTA cannot be performed or is nondiagnostic

VQ scintigraphy is considered medically necessary in **ANY** of the following scenarios:

- Pulmonary embolism *likely* based on modified Wells criteria<sup>115</sup> (> 4 points)
- Pulmonary embolism *unlikely* based on modified Wells criteria<sup>115</sup> ( $\leq$  4 points) with a positive D-dimer
- Suspected pulmonary embolism in pregnancy

#### Pediatric

VQ scintigraphy is considered medically necessary in **EITHER** of the following scenarios:

- Moderate or high clinical suspicion of pulmonary embolism
- Concern for recurrent embolism in patients on adequate medical therapy

#### Rationale

For patients with suspected pulmonary embolism of moderate-to-high pretest probability, the majority of high-quality evidence-based guidelines recommend the use of VQ scintigraphy as an add-on test when CTA is nondiagnostic or cannot be performed due to contrast allergy or nephrotoxicity.<sup>40, 87</sup> While systematic reviews of comparative diagnostic accuracy are mixed<sup>116, 117</sup>, many cited studies used earlier generations of CT technology, limiting the applicability of this literature to contemporary clinical practice. CT has fewer nondiagnostic studies<sup>118</sup> and is widely available. Comparative effective radiation dose between VQ scintigraphy and CT is also controversial, but a normal VQ or Q scan may offer a lower radiation dose than CT and confidently exclude pulmonary embolism when negative (negative likelihood ratio 0.05).<sup>116</sup> Scintigraphy is also recommended by consensus-based guidelines as an alternative test in pregnant patients.<sup>119</sup>

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## History

Status	Review Date	Effective Date	Action
Revised	11/11/2021	09/11/2022	Independent Multispecialty Physician Panel (IMPP) review. Revised indications for Lymphoscintigraphy.
Revised	11/11/2021	06/12/2022	IMPP review. Added and/or revised indications for Lymphoscintigraphy and Pyrophosphate Scintigraphy.
Updated	-	09/12/2021	Removed codes 78071 and 78072 (moved to SPECT document).
Revised	07/08/2020	01/01/2021	IMPP review. Added and/or revised indications for Bone Marrow scintigraphy, Bone scintigraphy, Gallium scintigraphy, Hepatic scintigraphy, Hepatobiliary scintigraphy, Leukocyte scintigraphy, Meckel's scan, Radionuclide cisternography, Renal scintigraphy, Thyroid scintigraphy, and VQ scintigraphy. Added Esophageal motility scintigraphy. Moved criteria for Dopaminergic SPECT to a separate SPECT imaging guideline. Moved CPT 78803, 78830, 78831, and 78832 to SPECT guideline.
Revised	05/11/2020	09/01/2020	Original effective date. Consolidated nuclear medicine content into Nuclear Medicine imaging guidelines. IMPP review. Revised Oncologic imaging guidelines.
Revised	02/03/2020	-	IMPP review. Revised Brain imaging and Head and Neck imaging guidelines.
Revised	10/29/2019	-	IMPP review. Revised Chest imaging and Oncologic imaging guidelines.
Revised	08/12/2019	-	IMPP review. Revised Vascular imaging guidelines.
Created	03/25/2019	-	IMPP review. Created nuclear medicine content in Chest, Abdomen and Pelvis, Vascular, and Oncologic imaging guidelines.
Created	01/28/2019	-	IMPP review. Created nuclear medicine content in Brain, Extremity, Spine, and Oncologic imaging guidelines.