LOUISIANA BLUE

Scintimammography and Gamma Imaging of the Breast and Axilla

Policy # 00438
Original Effective Date: 09/17/2014
Current Effective Date: 01/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services Are Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider use of radiopharmaceutical administration and gamma detection (lymphoscintigraphy) for localization of sentinel lymph nodes in individuals with breast cancer to be **eligible for coverage.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers scintimammography, breast-specific gamma imaging (BSGI), and molecular breast imaging (MBI) in all applications, including but not limited to their use as an adjunct to mammography or in staging the axillary lymph nodes to be **investigational.***

Policy Guidelines

The most commonly used radiopharmaceutical in breast-specific gamma imaging or molecular breast imaging is technetium 99m (Tc 99m) sestamibi.

The 2013 Breast Imaging Reporting and Data System (BI-RADS) breast assessment and breast tissue categories are summarized in Table PG1.

Table PG1. 2013 BI-RADS Breast Assessment and Breast Tissue Categories

Grading Schema	Category
Assessment categories	
	Incomplete

1	Negative
2	Benign
3	Probably benign
4	Suspicious
5	Highly suggestive of malignancy
6	Known biopsy-proven malignancy
Breast tissue categories	
a	Breasts are almost entirely fatty
b	Scattered areas of fibroglandular density
c	Heterogeneously dense
d	Extremely dense

Source: https://www.acr.org/-/media/ACR/Files/RADS/BI-RADS/BIRADS-Poster.pdf.
BI-RADS: Breast Imaging Reporting and Data System.

The most commonly used radiopharmaceuticals for sentinel lymph node detection using either lymphoscintigraphy or hand-held gamma detection include Tc 99m-labeled colloids (eg, sulfur colloid).

Background/Overview

Description

Scintimammography, breast-specific gamma imaging (BSGI), and molecular breast imaging (MBI) use radiotracers with nuclear medicine imaging as a diagnostic tool for abnormalities of the breast. These tests are distinguished by the use of differing gamma camera technology, which may improve diagnostic performance for detecting small lesions. Breast-specific gamma imaging uses a single-head breast-specific gamma camera and a compression device; whereas, MBI uses dual-head breast-specific gamma cameras that also produce breast compression. Preoperative lymphoscintigraphy and/or intraoperative hand-held gamma detection of sentinel lymph nodes is a method of identifying sentinel lymph nodes for a biopsy after radiotracer injection. Surgical removal of 1 or more sentinel lymph nodes is an alternative to full axillary lymph node dissection for staging, evaluation, and management of breast cancer.

Summary of Evidence

Scintimammography, Breast-Specific Gamma Imaging, and Molecular Breast Imaging for Diagnosis

For individuals who have dense breasts or high-risk for breast cancer who receive scintimammography, BSGI, or MBI as an adjunct to mammography, the evidence includes

diagnostic accuracy studies. Relevant outcomes are overall survival (OS), disease-specific survival, test validity, and treatment-related morbidity. Three prospective studies have assessed the incremental difference in diagnostic accuracy when BSGI or MBI is added to mammography in women at increased risk. Sensitivity was higher with combined BSGI or MBI and mammography but specificity was lower. A retrospective study found improved diagnostic accuracy and specificity with BSGI compared to ultrasonography when added to mammography. Studies of women at increased risk of breast cancer and negative mammograms found that a small number of additional cancers were detected. Studies tended to include women at different risk levels (eg, women with dense breasts and those with *BRCA1*). Moreover, any potential benefits need to be weighed against the potential risks of additional radiation exposure. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have indeterminate or suspicious breast lesions who receive scintimammography, BSGI, or MBI, the evidence includes diagnostic accuracy studies. Relevant outcomes are OS, disease-specific survival, test validity, and treatment-related morbidity. In the available studies, compared with biopsy, the negative predictive value of BSGI (or MBI) varied from 83% to 94%. Given the relative ease and diagnostic accuracy of the criterion standard of biopsy, coupled with the adverse consequences of missing a breast cancer, the negative predictive value of BSGI (or MBI) would have to be extremely high to alter treatment decisions. The evidence to date does not demonstrate this level of negative predictive value. Moreover, the value of BSGI in evaluating indeterminate or suspicious lesions must be compared with other modalities that would be used, such as spot views for diagnostic mammography. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have breast cancer undergoing detection of residual tumor after neoadjuvant therapy who receive scintimammography and BSGI, the evidence includes diagnostic accuracy studies and a meta-analysis. Relevant outcomes are OS, disease-specific survival, test validity, and treatment-related morbidity. The meta-analysis of studies evaluating the accuracy of BSGI for detecting residual tumor after neoadjuvant therapy found a pooled sensitivity of 86% and a pooled specificity of 69%, compared with histopathologic analysis. No studies were identified that compared the diagnostic accuracy of BSGI with other imaging approaches, or that investigated the clinical utility of this potential application of BSGI. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have breast cancer undergoing surgical planning for breast-conserving therapy who receive scintimammography and BSGI for disease detection, the evidence includes a retrospective observational study. Relevant outcomes are OS, disease-specific survival, test validity, and treatment-related morbidity. In the retrospective study, results suggested that magnetic resonance imaging identified more patients than BSGI who were not appropriate candidates for breast-conserving therapy. Prospective comparative studies are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Scintimammography and Breast-Specific Gamma Imaging for Treatment
For individuals who have breast cancer undergoing detection of axillary metastases who receive scintimammography and BSGI, the evidence includes diagnostic accuracy studies and systematic reviews of diagnostic accuracy studies. Relevant outcomes are OS, disease-specific survival, test validity, and treatment-related morbidity. A meta-analysis of the available diagnostic accuracy studies found that the sensitivity and specificity of BSGI are not high enough for this technology to replace the current standard practice, surgical nodal dissection. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Radiopharmaceutical and Gamma Detection for Treatment
For individuals who have breast cancer undergoing sentinel lymph node (SLN) biopsy for detection of axillary metastases who receive radiopharmaceutical and gamma detection(lymphoscintigraphy) for localization of SLNs, the evidence includes a randomized controlled trial, nonrandomized studies, and systematic reviews. Relevant outcomes are OS, disease-specific survival, test validity, and treatment-related morbidity. Evidence indicates that using radiopharmaceutical and gamma detection for localization of SLNs yields high success rates in identifying SLNs. Additionally, the diagnostic performance generally offers better detection rates with radiopharmaceuticals than with the blue dye method and similar detection rates to indocyanine green fluorescence. The evidence has indicated that SLN biopsy provides similar long-term outcomes as full axillary lymph node dissection for control of breast cancer and offers more favorable early results with reduced arm swelling and better quality of life. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Several scintillation (gamma) cameras have been cleared for marketing by the FDA through the 510(k) process for "measuring and imaging the distribution of radionuclides in the human body by means of photon detection." Examples of gamma cameras used in BSGI are the Dilon 6800®‡ (Dilon Technologies) and single-head configurations of Discovery NM750b (GE Healthcare). Dual-head cameras used in MBI include LumaGEM™‡ (Gamma Medical) (FDA product code IYX) and Discovery NM750b (GE Healthcare).

Tc-99m sestamibi (Sun Pharmaceutical Industries, Lantheus Medical Imaging, Cardinal Health 414, AnazaoHealth, Curium US, Jubilant Draximage) has been approved by the FDA with the following labeling: "Breast Imaging: Technetium TC 99M Sestamibi is indicated for planar imaging as a second-line diagnostic drug after mammography to assist in the evaluation of breast lesions in patients with an abnormal mammogram or a palpable breast mass. Technetium TC 99M Sestamibi is not indicated for breast cancer screening, to confirm the presence or absence of malignancy, and it is not an alternative to biopsy."

In 2013, Tc 99m tilmanocept (Lymphoseek; Cardinal Health) was approved by the FDA for use in breast cancer and melanoma as a radioactive diagnostic imaging agent to help localize lymph nodes.

Technetium-99m-sulfur colloid was approved by the FDA through the new drug application (NDA; GE Healthcare, NDA 017456; Mallinckrodt, NDA 017724) process although these products appear to be no longer marketed. In addition, in 2011, Technetium Tc 99m Sulfur Colloid Kit (Sun Pharmaceutical Industries) was approved by the FDA through the NDA process (NDA 017858) for use as an injection to localize lymph nodes in breast cancer patients.

In 2018, the FDA granted approval to Northstar Medical Radioisotopes for its RadioGenix™‡ System, which produces molybdenum 99, the material used to generate Tc 99m. Previously, molybdenum 99 was only produced from enriched uranium in facilities outside of the United States.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

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Supplemental Information

Practice Guidelines and Position Statements
Guidelines or position statements will be considered for inclusion in ‘Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Obstetricians and Gynecologists
The American College of Obstetricians and Gynecologists (2017) updated its 2011 practice bulletin on breast cancer screening in average-risk women. There was no discussion or recommendation for scintimammography or any other gamma imaging techniques for routine screening.

American College of Radiology
Appropriateness Criteria from the American College of Radiology rated breast-specific gamma imaging a 1 or 2 (indicating "usually not appropriate" for breast cancer screening), in patients with high or intermediate breast cancer risk (last reviewed in 2021), palpable breast masses (last reviewed in 2022), and workup of breast pain (last reviewed in 2018). Guidelines on screening for breast cancer in above average-risk patients (last reviewed in 2018) do not recommend the use of molecular breast imaging (MBI) for breast cancer screening in any higher-risk population. The guidelines state, “further advances in detector technology to allow lower dosing, more widespread penetration of MBI-guided biopsy capabilities, and additional large prospective trials (to include incidence screening results) will be needed before MBI can be embraced as a screening tool, even in women at elevated risk.” In a 2021 guideline for supplemental breast cancer screening based on breast density, MBI is categorized as "usually not appropriate" regardless of breast density and breast cancer risk.

American Society of Clinical Oncology
The American Society of Clinical Oncology (2016) reaffirmed its 2014 recommendations on the use of sentinel node biopsy for patients with early-stage breast cancer. The recommendations were based on randomized controlled trials, systematic reviews, meta-analyses, and clinical practice guidelines from 2012 through July 2016. The recommendations included:

> "Women without sentinel lymph node (SLN) metastases should not receive axillary lymph node dissection (ALND). Women with 1 to 2 metastatic SLNs who are planning to undergo breast-conserving surgery with whole-breast radiotherapy should not undergo ALND (in most cases). Women with SLN metastases who will undergo mastectomy should be offered ALND. These 3 recommendations are based on randomized controlled trials. Women with operable breast cancer and multicentric tumors, with ductal carcinoma in situ, who will undergo mastectomy, who previously underwent breast and/or axillary surgery, or who received preoperative/neoadjuvant systemic therapy may be offered SNB [sentinel node biopsy]. Women who have large or locally advanced invasive breast cancer (tumor size T3/T4), inflammatory breast cancer, or ductal carcinoma in situ (when breast-conserving surgery is planned) or are pregnant should not undergo SNB."

National Comprehensive Cancer Network
The National Comprehensive Cancer Network's guidelines (v.4.2024) on breast cancer treatment state that sentinel lymph node biopsy is the preferred method for axillary lymph node staging if the patient is a candidate for sentinel lymph node biopsy. If the sentinel nodes are found to be negative on pathologic examination, then no further axillary surgery is suggested (category 1 recommendation).

Network guidelines on breast cancer screening and diagnosis (v4.2024) include the following relevant recommendations:

> "There is emerging evidence that breast scintigraphy and contrast-enhanced mammography may improve detection of early breast cancers among females with mammographically dense breasts; current evidence does *not* support their routine use as alternative screening procedures."

> "Consider contrast-enhanced mammography (CEM) or molecular breast imaging (MBI) whole breast ultrasound for those who qualify for but cannot undergo MRI. Whole breast ultrasound may be done if contrast-enhanced imaging or functional imaging is not available/accessible"

High Risk Individuals (BSCR-A, page 1)

- "In high-risk settings, based on current evidence and considering the FDA safety announcement (gadolinium-based contrast agents), we continue to recommend annual MRI in select populations after shared decision-making. Breast cancer screening MRI may also increase recall and increase benign breast biopsies.

- Abbreviated MRI has a higher cancer detection rate than mammography with tomosynthesis and likely has similar sensitivity compared to full diagnostic protocol breast MRI.
- CEM and MBI are also options for higher risk breast cancer screening. CEM has the risk of iodinated contrast reactions and has a higher breast radiation exposure per exam than standard mammography. MBI has a whole-body effective radiation dose substantially higher than that of mammography.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently ongoing trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT02324387	Tc99m Sestamibi Molecular Breast Imaging	96	Mar 2025
NCT02744053	Multimodality Breast Imaging for the Assessment of Tumor Response to Neoadjuvant Chemotherapy in Triple Negative Breast Cancer Patients	96	Apr 2026
NCT03220893	Density MATTERS [Molecular Breast Imaging (MBI) And Tomosynthesis To Eliminate the ReServoir]	3023 (actual)	Dec 2024
NCT05042687	Comparative Performance of Molecular Breast Imaging (MBI) to Magnetic Resonance Imaging (MRI) of the Breast in Identifying and Excluding Breast Carcinoma in Women at High Risk for Breast Cancer	300	Dec 2024

NCT: national clinical trial.

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Policy History

Original Effective Date: 09/17/2014
Current Effective Date: 01/01/2025

09/04/2014	Medical Policy Committee review
09/17/2014	Medical Policy Implementation Committee approval. New policy.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
09/03/2015	Medical Policy Committee review
09/23/2015	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/03/2016	Medical Policy Committee review
11/16/2016	Medical Policy Implementation Committee approval. New policy statement added for gamma detection following radiopharmaceutical administration for localization of sentinel lymph nodes.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
11/02/2017	Medical Policy Committee review
11/15/2017	Medical Policy Implementation Committee approval. No change to coverage.
11/08/2018	Medical Policy Committee review
11/21/2018	Medical Policy Implementation Committee approval. No change to coverage.
11/07/2019	Medical Policy Committee review
11/13/2019	Medical Policy Implementation Committee approval. No change to coverage.
11/05/2020	Medical Policy Committee review
11/11/2020	Medical Policy Implementation Committee approval. No change to coverage.
11/04/2021	Medical Policy Committee review
11/10/2021	Medical Policy Implementation Committee approval. No change to coverage.

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12/01/2022	Medical Policy Committee review
12/14/2022	Medical Policy Implementation Committee approval. No change to coverage.
12/07/2023	Medical Policy Committee review
12/13/2023	Medical Policy Implementation Committee approval. No change to coverage. Body of policy updated.
12/05/2024	Medical Policy Committee review
12/11/2024	Medical Policy Implementation Committee approval. Eligible for Coverage statement edited to more accurately reflect the intervention reviewed. Coverage eligibility unchanged.

Next Scheduled Review Date: 12/2025

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Louisiana Blue Medical Policy Coverage Guidelines is with Louisiana Blue and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Louisiana Blue Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Louisiana Blue Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	78800, 78801 Add code effective 01/01/2025: 78195 Delete code effective 01/01/2025: 78803
HCPCS	S8080 Add codes effective 01/01/2025: A4641, A9500, A9502, A9520, A9541
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company

recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.