MEDICAL POLICY

POLICY TITLE	POSITRON EMISSION MAMMOGRAPHY
POLICY NUMBER	MP 5.008

CLINICAL BENEFIT	☐ MINIMIZE SAFETY RISK OR CONCERN. ☒ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☐ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☐ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	**7/1/2024**

I. POLICY

Note: For the use of mammography for preventive screening for adult Members covered under commercial products, refer to the Schedule of Preventive Care Services

Positron Emission Mammography (PEM)

The use of positron emission mammography (PEM) is considered **investigational.** There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

The National Comprehensive Cancer Network (NCCN) is a nonprofit alliance of cancer centers throughout the United States. NCCN develops the Clinical Practice Guidelines in Oncology which are recommendations aimed to help health care professionals diagnose, treat, and manage patients with cancer. Guidelines evolve continuously as new treatments and diagnostics emerge and may be used by Capital Blue Cross when determining medical necessity according to this policy.

***Cross References*:**

MP 5.021 Scintimammography and Gamma Imaging of the Breast and Axilla

II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross. Please see additional information below, and subject to benefit variations as discussed in Section VI below.

FEP PPO -
Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at: https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies.

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NOTE: On October 5, 2015, the Pennsylvania Insurance Department provided guidance to health Insurers regarding coverage of 3D Mammography (Digital Breast Tomosynthesis) Under this state law, 3D mammograms, also known as digital breast tomosynthesis, must be covered at no cost in the same manner as traditional two-dimensional mammograms.

III. DESCRIPTION/BACKGROUND

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Positron Emission Mammography (PEM)

Positron emission mammography (PEM) is a form of positron emission tomography (PET) that uses a high-resolution, mini-camera detection technology for imaging the breast. As with PET, a radiotracer (usually fluorine 18 fluorodeoxyglucose) is administered, and the camera is used to provide a higher resolution image of a limited section of the body than would be achievable with fluorine 18 fluorodeoxyglucose PET. Gentle compression is used, and the detector(s) are mounted directly on the compression paddle(s).

PEM was developed to overcome the limitations of PET for detecting breast cancer tumors. Patients are usually supine for PET procedures; further, breast tissue may spread over the chest wall, making it potentially difficult to differentiate breast lesions from other organs that take up the radiotracer. PET's resolution is generally limited to approximately 5 mm, which may not detect early breast cancer tumors. PEM allows for the detection of lesions as small as 2 to 3 mm and creates images that are more easily compared with mammography because they are acquired in the same position. Three-dimensional reconstruction of PEM images also is possible. As with PET, PEM provides functional rather than anatomic information about the breast. In PEM studies, exclusion criteria have included some patients with diabetes (e.g., Berg et al [2011, 2012]).

Radiation Dose Associated With PEM

The label-recommended dose of FDG for PEM is 370 MBq (10 mCi). Hendrick (2010) calculated mean glandular doses, and from the doses was able to determine lifetime attributable risk (LAR) of cancer for film mammography, digital mammography, breast-specific gamma imaging (BSGI), and PEM.8 The author used BEIR VII Group risk estimates to gauge the risks of radiation-induced cancer incidence and mortality from breast imaging studies. Estimated LAR of cancer for a patient with average-sized compressed breast during mammography of 5.3 cm (risks would be higher for larger breasts) for a single breast procedure at age 40 years is:

- 5 per 100,000 for digital mammography (breast cancer only);
- 7 per 100,000 for screen film mammography (breast cancer only);
- 55 to 82 per 100,000 for BSGI (depending on the dose of technetium 99m sestamibi); and
- 75 per 100,000 for PEM.

The corresponding LAR of cancer mortality at age 40 years is:

- 1.3 per 100,000 for digital mammography (breast cancer only);
- 7 per 100,000 for screen film mammography (breast cancer only);
- 26 to 39 per 100,000 for BSGI; and
- 31 per 100,000 for PEM.

A major difference in the impact of radiation between mammography and BSGI or PEM is that in mammography radiation dose is limited to the breast; whereas with BSGI and PEM, all organs are irradiated. Furthermore, as one ages, the risk of cancer induction from radiation exposure decreases more rapidly for the breast than for other radiosensitive organs. Organs at highest risk for cancer are the bladder with PEM and the colon with BSGI; these cancers, along with lung cancer, are also less curable than breast cancer. Thus, the distribution of radiation throughout the body adds to the risks associated with BSGI and PEM. Hendrick concluded that:

> "… BSGI and PEM are not good candidate procedures for breast cancer screening because of the associated higher risks for cancer induction per study compared with the risks associated with existing modalities such as mammography, breast US [ultrasound], and breast MR [magnetic resonance] imaging. The benefit-to-risk ratio for BSGI and PEM may be different in women known to have breast cancer, in whom additional information about the extent of disease may better guide treatment."

O'Connor et al (2010) estimated the LAR of cancer and cancer mortality from the use of digital mammography, screen-film mammography, PEM, and molecular breast imaging. Only results for digital mammography and PEM are reported here. The authors concluded that, in a group of 100,000 women at age 80 years, a single digital mammogram at age 40 years would induce 4.7 cancers with 1.0 cancer deaths; 2.2 cancers with 0.5 cancer deaths for a mammogram at age 50; 0.9 cancers with 0.2 cancer deaths for a mammogram at age 60; and 0.2 cancers with 0.0 cancer deaths for a mammogram at age 70. Comparable numbers for PEM would be 36 cancers and 17 cancer deaths for PEM at age 40; 30 cancers and 15 cancer deaths for PEM at age 50; 22 cancers and 12 cancer deaths for PEM at age 60; and 9.5 cancers and 5.2 cancer deaths for PEM at age 70. The authors also analyzed the cumulative effect of annual screening between the ages of 40 and 80, as well as between the ages of 50 and 80. For women at age 80 who were screened annually from the ages of 40 to 80, digital mammography would induce 56 cancers with 15 cancer deaths; for PEM, the analogous numbers were 800 cancers and 408 cancer deaths. For women at age 80 who were screened annually from the ages of 50 to 80, digital mammography would induce 21 cancers with 6 cancer deaths; for PEM, the analogous numbers were 442 cancers and 248 cancer deaths. However, background radiation from age 0 to 80 is estimated to induce 2174 cancers and 1011 cancer deaths.

These calculations, like all estimated health effects of radiation exposure, are based on several assumptions. When comparing digital mammography with PEM, 2 conclusions become clear: Many more cancers are induced by PEM than by digital mammography; and for both modalities, adding annual screening from age 40 to 49 roughly doubles the number of induced cancers. In a benefit-risk calculation performed for digital mammography but not for PEM, O'Connor et al (2010) nevertheless reported that the benefit-risk ratio of annual screening is still approximately 3 to 1 for women in their 40s, although it is much higher for women age 50 and older. Like Hendrick, the authors concluded that "if molecular imaging techniques [including PEM] are to be of value in screening for breast cancer, then the administered doses need to be substantially reduced to better match the effective doses of mammography."

The American College of Radiology has assigned a relative radiation level (effective dose) of 10 to 30 mSv to PEM. The College has also stated that, because of radiation dose, PEM and BSGI in their present form are not indicated for screening.

Because the use of BSGI and molecular breast imaging have been proposed for women at high risk of breast cancer, it should be noted there is controversy and speculation whether some women (e.g., those with *BRCA* variants) have heightened radiosensitivity. If women with *BRCA* variants are more radiosensitive than the general population, the previous estimates may underestimate the risks they face from breast imaging with ionizing radiation (i.e., mammography, BSGI, molecular breast imaging, PEM, single-photon emission computed tomography, breast-specific computed tomography, and tomosynthesis; ultrasound and magnetic resonance imaging do not use radiation). More research will be needed to resolve this issue. Also, risks associated with radiation exposure will be greater for women at high risk of breast cancer (regardless of whether they are more radiosensitive) because they start screening at a younger age when the risks associated with radiation exposure are increased.

REGULATORY STATUS

In 2003, the PEM 2400 PET Scanner (PEM Technologies) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. FDA determined that this device was substantially equivalent to existing devices for “medical purposes to image and measure the distribution of injected positron emitting radiopharmaceuticals in human beings for the purpose of determining various metabolic and physiologic functions within the human body.”

In 2009, the Naviscan PEM Flex™ Solo II™ High Resolution PET Scanner (Naviscan) was cleared for marketing by FDA through the 510(k) process for the same indication. The PEM 2400 PET Scanner was the predicate device. The newer device has been described by the manufacturer as “a high spatial resolution, small field-of-view PET imaging system specifically developed for close-range, spot, ie, limited field, imaging.”

In 2013, Naviscan was acquired by Compañía Mexicana de Radiología SA, which currently markets the Naviscan Solo II™ Breast PET Scanner in the United States (CMR Naviscan). FDA product code: KPS.

IV. RATIONALE

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Positron Emission Mammography

Summary of Evidence

For individuals who are being screened for breast cancer the evidence includes a retrospective study. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. It has not been demonstrated that PEM provides better diagnostic accuracy than the relevant comparators nor has PEM been shown to provide clinical utility. In addition, without demonstrated advantages in clinical utility, the relatively high radiation dosage associated with PEM does not favor its use given that alternative tests deliver lower doses. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with clinically localized breast cancer undergoing presurgical evaluation, the evidence includes prospective studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. It has not been

demonstrated that PEM provides better diagnostic accuracy than the relevant comparators nor has PEM been shown to provide clinical utility. In addition, without demonstrated advantages in clinical utility, the relatively high radiation dosage associated with PEM does not favor its use given that alternative tests deliver lower doses. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with a suspicious breast lesion on conventional breast cancer evaluation, the evidence includes prospective studies as well as a meta-analysis. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, and resource utilization. It has not been demonstrated that PEM provides better diagnostic accuracy than the relevant comparators nor has PEM been shown to provide clinical utility. In addition, without demonstrated advantages in clinical utility, the relatively high radiation dosage associated with PEM does not favor its use given that alternative tests deliver lower doses. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network

The 2021 NCCN Clinical Practice Guideline for Breast Cancer Screening and Diagnosis states: "While there is emerging evidence that molecular imaging (breast-specific gamma imaging, sestamibi scan, or positron emission mammography) as a screening procedures may improve detection, whole-body effective radiation dose with these tests is substantially higher than that of a mammography.

American College of Radiology

The ACR appropriateness criteria palpable breast masses mentions "there is little role for advanced technologies such as MRI, positron emission mammography or molecular breast imaging in the evaluation of a palpable mass."

In 2017, the American College of Radiology has included positron emission mammography (PEM) in its criteria on breast screening. PEM was rated as "usually not appropriate" for screening women at average- or high-risk for breast cancer. The College has also assigned a relative radiation level (effective dose) of 10 to 30 mSv to PEM and stated that PEM is limited "by radiation dose and lack of evidence in large screening population."

V. DEFINITIONS

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N/A

VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits, and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members

and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

VII. DISCLAIMER

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Capital Blue Cross' medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Investigational when used to report Positron Emission Mammography (PEM); therefore, not covered:

Procedure Codes								
78999								

IX. REFERENCES

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X. POLICY HISTORY

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MP 5.008	**09/16/2020 Consensus Review.** No change to policy Statement. Coding reviewed, no changes; Product Variation Statement updated; References reviewed, updated.
	01/15/2021 Administrative Update. Note on preventive mammography updated to reflect the appropriate document.
	12/02/2021 Major Review. Removed criteria for mammogram, continues to be covered service. Update to background, rationale, coding, and references to reflect this change.
	10/20/2022 Consensus Review. Policy statement unchanged. References updated.

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	04/07/2023 Consensus Review. Policy statement unchanged. References updated.
	04/10/2024 Consensus Review. No change to policy statement. References updated. Coding reviewed with no coding changes.

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