Corporate Medical Policy

Epithelial Cell Cytology in Breast Cancer Risk Assessment AHS - G2059

File Name: epithelial_cell_cytology_in_breast_cancer_risk_assessment
Origination: 1/2019
Last Review: 10/2023

Description of Procedure or Service

Nipple aspiration and/or ductal lavage are non-invasive techniques to obtain epithelial cells for cytological examination to aid in the evaluation of nipple discharge for breast cancer risk (Golshan, 2022). Fine needle aspiration (FNA) is another approach that can be used in the initial diagnosis of a suspicious breast mass, although core biopsy is superior in sensitivity, specificity, and correct histological grading (Moy et al., 2017)

Related Policies:
AHS-G2124 Serum Tumor Markers for Malignancies
AHS-M2126 Use of Common Genetic Variants to Predict Risk of Non-Familial Breast Cancer

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

Epithelial cell cytology in breast cancer risk assessment is not covered.
BCBSNC will not reimburse for non-covered services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Epithelial Cell Cytology in Breast Cancer Risk Assessment is covered

Not applicable.

When Epithelial Cell Cytology in Breast Cancer Risk Assessment is not covered

Reimbursement is not allowed for cytologic analysis of epithelial cells to assess breast cancer risk and manage patients at high risk of breast cancer.

Policy Guidelines

Breast cancer is the most frequently diagnosed cancer and is a leading cause of cancer death in the United States. Nipple discharge is a common breast complaint. Most nipple discharge is of benign origin, however, it is necessary to differentiate patients with benign nipple discharge from those who have an underlying pathology. In approximately five to 15 percent of pathologic nipple discharge cases, cancer is identified (Golshan, 2022).

Breast cancer originates in breast epithelium and is associated with progressive molecular and morphologic changes. Individuals with atypical breast ductal epithelial cells have an increased relative risk of breast cancer. Cytological evaluation of epithelial cells in nipple discharge has potential to be a diagnostic aid. Due to the scant cellularity of specimens obtained by expression or aspiration of nipple discharge, ductal lavage was developed to enhance the ease and efficiency of collecting breast epithelial cells for cytologic analysis. The analysis of breast-specific liquid biopsies, such as nipple aspirate fluid, has potential to be used as a biomarker profiling technique for monitoring breast health (Shaheed et al., 2018). Researchers report that the measurement of nipple aspirate fluid, including miRNA, pathological nipple discharge, and breast ductal fluids, may help to improve early detection and management of breast cancer (Moelans, et al., 2019).

Fine needle aspiration (FNA) is a biopsy option for a suspicious palpable breast mass. FNA is a rapid diagnosis technique, but it is not as accurate as core needle biopsy. FNA cannot differentiate in situ and invasive cancer and has higher rates of negative results and insufficient samples than core needle biopsy. The success of FNA results also varies with the operator and cytopathologist (Joe & Esserman, 2023).

Analytic Validity

In a retrospective study of 618 patients with nipple discharge over a 14-year period, the sensitivity and specificity of cytology were 17 and 66 percent, respectively; the authors concluded that "nipple discharge cytology has little complementary diagnostic value" (Kooistra, et al., 2009).

Clinical Utility and Validity

Hornberger, et al., (2015) performed a meta-analysis on the use of nipple aspirate fluid (NAF) in identifying breast cancer based on proliferative epithelial disease (PED). The authors reviewed 16 articles, 20808 unique aspirations, and 17378 subjects. Among cancer-free patients, 51.5% aspirations contained fluid, of which 27.7% showed a PED on cytology. Of the two prospective studies of 7850 women, patients with abnormal cytology showed a 2.1-fold higher risk of developing breast cancer compared to those without fluid (Hornberger et al., 2015).

Chatterton et al. (2016) measured sex steroid levels in nipple aspirate fluid; hormones were measured in samples from 160 breast cancer cases and 157 controls. Results showed a significantly higher concentration of dehydroepiandrosterone (DHEA) in the nipple aspirate fluid of patients with breast cancer compared to controls; further, DHEA levels were highly correlated with estradiol levels, indicating "a potentially important role of this steroid in breast cancer risk" (Chatterton et al., 2016).

Kamalı and Kamalı (2022) studied the usefulness of testing methods in surgical decision making. The study included 141 patients with pathological nipple discharge who were planning to undergo surgery. The diagnostic efficiency of ductal lavage cytology was compared to that of ultrasonography, mammography, magnetic resonance imaging, and ductography. The sensitivity of ductal lavage cytology was 70.5% and the specificity was 94.1%. The authors conclude that "negative cytology does not exclude the possibility of malignancy, and positive results do not help in the differential diagnosis" (Kamalı & Kamalı, 2022).

Applicable State and Federal Regulations

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

Guidelines and Recommendations

American Society of Breast Surgeons (ASBS)

The Official Statement by the American Society of Breast Surgeons (ASBS, 2019) regarding Screening Mammography does not mention ductal lavage at all in their statement.

In 2016, the ASBS published a consensus guideline on the concordance assessment of image-guided breast biopsies and the management of borderline or high-risk lesions. These guideline state that "The decision to excise a papillary lesion without atypia needs to be individualized based on risk, including such criteria as size; symptomatology, including palpability and presence of nipple discharge; and breast cancer risk factors" (ASBS, 2016). This is the only mention of nipple discharge in the document.

National Comprehensive Cancer Network (NCCN)

National Comprehensive Cancer Network Clinical Practice Guidelines in breast cancer screening and diagnosis (NCCN, 2023) state that "thermography and ductal lavage are not recommended by the NCCN panel for breast cancer screening or diagnosis." The NCCN also notes that "the FDA has issued a safety alert stating that ductal lavage should not be a replacement for mammograms" (NCCN, 2023).

Food and Drug Administration (FDA)

In 2017 the FDA issued a safety warning (FDA, 2017) stating that "…the FDA is unaware of any valid scientific data to show that a nipple aspirate test, when used on its own, is an effective screening tool for any medical condition, including the detection of breast cancer or other breast disease."

American College of Radiology (ACR)

The 2022 ACR appropriateness criteria for the evaluation of nipple discharge do not mention cytology. The ACR states that "image-guided FNA and core biopsy are not required for the evaluation of physiologic nipple discharge." The ACR also notes "although some institutions demonstrate good results using FNA, larger series have shown that core biopsy is superior to FNA in terms of sensitivity, specificity, and correct histologic grading of a lesion (Sanford et al., 2022).

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 88108, 88112, 88172, 88173, 88177

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

ASBS. (2016). Consensus Guideline on Concordance Assessment of Image-Guided Breast Biopsies and Management of Borderline or High-Risk Lesions. https://www.breastsurgeons.org/docs/statements/Consensus-Guideline-on-Concordance-Assessment-of-Image-Guided-Breast-Biopsies.pdf

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NCCN. (2023, June 19). *NCCN Clinical Practice Guidelines in Oncology*; *Breast Cancer Screening and Diagnosis* V1.2023. National Comprehensive Cancer Network https://www.nccn.org/professionals/physician_gls/pdf/breast-screening.pdf.

Sanford, M. F., Slanetz, P. J., Lewin, A. A., Baskies, A. M., Bozzuto, L., Branton, S. A., Hayward, J. H., Le-Petross, H. T., Newell, M. S., Scheel, J. R., Sharpe, R. E., Jr., Ulaner, G. A., Weinstein, S. P., & Moy, L. (2022). ACR Appropriateness Criteria® Evaluation of Nipple Discharge: 2022 Update. *J Am Coll Radiol*, *19*(11s), S304-s318. https://doi.org/10.1016/j.jacr.2022.09.020

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Medical Director review 11/2019

Specialty Matched Consultant Advisory Panel 3/2020

Medical Director review 3/2020

Medical Director review 10/2020

Specialty Matched Consultant Advisory Panel 3/2021

Medical Director review 3/2021

Medical Director review 10/2021

Medical Director review 11/2022

Medical Director review 10/2023

Policy Implementation/Update Information

1/1/2019	New policy developed. Cytologic analysis of epithelial cells from nipple aspirations as a technique to assess breast cancer risk and manage patients at high risk of breast cancer is considered **investigational**. Techniques of collecting nipple aspiration fluid, include, but are not limited to, ductal lavage and suction. Medical Director review 1/1/2019. Policy noticed 1/1/2019 for effective date 4/1/2019. (lpr)
8/13/19	In the "When Epithelial Cell Cytology in Breast Cancer Risk Assessment is not covered" section, the investigational statement is revised to read: Cytologic analysis of epithelial cells from nipple aspirations as a technique to assess breast cancer risk and manage patients at high risk of breast cancer is not covered. Policy noticed 8/13/19 for effective date 10/15/2019. (an)
10/29/19	Wording in the Policy, When Covered, and/or Not Covered section(s) changed from Medical Necessity to Reimbursement language, where needed. (gm)
12/10/19	Reviewed by Avalon 3rd Quarter 2019 CAB. No change to policy intent. Coding table removed from Billing/Coding section. Medical Director review 11/2019. (lpr)
4/14/20	Specialty Matched Consultant Advisory Panel review 3/18/2020. No change to policy statement. (lpr)
11/10/20	Reviewed by Avalon 3rd Quarter 2020 CAB. Added CPT code 88108 to Billing/Coding section. Medical Director review 10/2020. (lpr)
11/2/21	Specialty Matched Consultant Advisory Panel review 3/17/21. No change to policy statement. (lpr)
11/16/21	Reviewed by Avalon 3rd Quarter 2021 CAB. Updated policy guidelines, references and added Related Policies section. Medical Director review 10/2021. (lpr)
12/13/22	Reviewed by Avalon 3rd Quarter 2022 CAB. References updated. Medical Director review 11/2022. No change to policy statement. (lpr)
12/5/23	Reviewed by Avalon 3rd Quarter 2023 CAB. Medical Director review 10/2023. Edited non-coverage statement for clarity. References added. Updated description and policy guidelines sections. Added CPT codes 88172, 88173, 88177 to Billing/Coding section. (lpr)