

## 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 CAP Review:** 3/2021  
**Next CAP Review:** 3/2022  
**Last Review:** 10/2021

#### Description of Procedure or Service

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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, 2020).

**Related Policies:**

Serum Tumor Markers for Malignancies AHS-G2124

Use of Common Genetic Variants to Predict Risk of Non-Familial Breast Cancer AHS-M2126

***\*\*\*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

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

#### Benefits Application

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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

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Not applicable.

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

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Reimbursement is not allowed for 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. Techniques of collecting nipple aspiration fluid, include, but are not limited to, ductal lavage and suction.

#### Policy Guidelines

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Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in women in the United States. Approximately 1 in 8 women will develop breast cancer in their lifetime and breast cancer alone makes up 30% of female cancers (Siegel, Miller, Fuchs, & Jemal, 2021; Siegel, Miller, & Jemal, 2019). Nipple discharge is a common breast complaint.

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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 5-15 percent of pathologic nipple discharge cases, cancer is identified (Golshan, 2018, 2020).

Breast cancer originates in breast epithelium and is associated with progressive molecular and morphologic changes. Women 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, Patuleia, van Gils, van der Wall, & van Diest, 2019).

### *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, Wauters, van de Ven, & Strobbe, 2009).

### *Clinical Utility and Validity*

Hornberger, Chen, Li, Kakad, and Quay (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).

### **State and Federal Regulations, as applicable**

A search for “ductal lavage” and “nipple aspirate” on the FDA website is limited to a consumer update titled “Nipple Aspirate Test is No Substitute for Mammogram.” Additionally, 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). As an LDT, the U. S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use.

### **Guidelines and Recommendations**

#### **American Society of Breast Surgeons (ASBS) (ASBS, 2016, 2019)**

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.

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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) (NCCN, 2021)**

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology™, breast cancer screening and diagnosis guidelines (NCCN, 2019, 2021) state that “current evidence does not support the routine use of ductal lavage as a screening procedure,” and that “ductal lavage is not recommended by the NCCN for breast cancer screening or diagnosis.”

### **Food and Drug Administration (FDA) (FDA, 2017)**

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) (Lee et al., 2017)**

In 2017, the ACR published appropriateness criteria for the evaluation of nipple discharge. These criteria state that “Cytologic examination of nipple discharge has not proven to be effective in differentiating benign from malignant lesions” (Lee et al., 2017).

## **Billing/Coding/Physician Documentation Information**

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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.bcsnc.com](http://www.bcsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable service codes: 88108, 88112*

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**

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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

### Policy Implementation/Update Information

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- 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)

## Epithelial Cell Cytology in Breast Cancer Risk Assessment AHS - G2059

- 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 3<sup>rd</sup> 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 3<sup>rd</sup> 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 3<sup>rd</sup> Quarter 2021 CAB. Updated policy guidelines, references and added Related Policies section. Medical Director review 10/2021. (lpr)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.