

## 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:** 3/2020  
**Next CAP Review:** 3/2021  
**Last Review:** 10/2020

#### 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 (Dooley et al., 2001; Khan et al., 2005).

***\*\*\*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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Globally, breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in women. In the United States, breast cancer is the most commonly diagnosed cancer and the second most common cause of cancer death in women. Approximately 1 in 8 women will develop breast cancer in their lifetime (Taghian, El-Ghamry, & Merajver, 2017). Nipple discharge is a common breast complaint (Hussain, Policarpio, & Vincent, 2006). 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. (Jardines, 1996; King, Carter, Bolton, & Fuhrman, 2000; Murad, Contesso, & Mouriesse, 1982). 6.8 percent of women referred to a

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surgeon because of symptoms of a breast disorder have nipple discharge (Golshan, 2017; Santen & Mansel, 2005).

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 (Dooley et al., 2001). Due to the 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 (Khan et al., 2005). However, no definite benefits have been identified for the routine use of cytology in the evaluation of nipple discharge (Simmons et al., 2003). and systematic cytologic examination of all nipple discharge is not cost-effective (Ciatto, Bravetti, & Cariaggi, 1986; Golshan, 2017; Khan et al., 2005).

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 (Kooistra, Wauters, van de Ven, & Strobbe, 2009) and concluded that “Nipple discharge cytology has little complementary diagnostic value”(Golshan, 2017).

Recently, Do Canto et al (2016) proposed that “Recent studies suggest that microRNAs show promise as excellent biomarkers for breast cancer; however there is still a high degree of variability between studies making the findings difficult to interpret. In addition to blood, ductal lavage (DL) and nipple aspirate fluids represent an excellent opportunity for biomarker detection because they can be obtained in a less invasive manner than biopsies and circumvent the limitations of evaluating blood biomarkers with regards to tissue of origin specificity. In this study, we have investigated for the first time, through a real- time PCR array, the expression of 742 miRNAs in the ductal lavage fluid collected from 22 women with unilateral breast tumors. We identified 17 differentially expressed miRNAs between tumor and paired normal samples from patients with ductal breast carcinoma.” And concluded that “our findings suggest that miRNA analysis of breast ductal fluid is feasible and potentially very useful for the detection of breast cancer.”

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

This test is considered a laboratory developed test (LDT); developed, validated and performed by individual laboratories.

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**

Wrensch et al (1992) reported on a prospective study of 2,701 white women at average risk of breast cancer who underwent nipple aspiration and then were followed up for an average of 12 years. The relative risk of cancer in women with cytologic atypia was 4.9 compared to non-yielders of nipple fluid or 2.8 compared to women with normal cytology. In women with cytologic atypia and a family history, the relative risk was 18.1 compared to non-yielders of fluid without family history. After 21 years of follow-up (2001), the relative risks were lower, with a relative risk of 1.4 compared to non-yielders of nipple fluid.

Fabian et al (2000) reported on a group of 480 women without mammographic abnormalities who were considered at high risk of breast cancer and who underwent two random periareolar fine-needle aspirations at 6-month intervals. Risk factors included a family history of breast cancer, a prior history of a precancerous lesion (i.e., atypical hyperplasia or carcinoma in situ), or a prior history of breast cancer. In 21 percent of patients, results of the fine-needle aspiration revealed atypical hyperplasia.

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After 45 months of follow-up, the relative risk of cancer in women with cytologic atypia was 5.0 compared to women without atypical results. The two strongest predictors of cancer development were risk assessment based on the Gail model and the presence of atypical hyperplasia on fine-needle aspiration.

### **Guidelines and Position Statements American Society of Breast Surgeons**

The Official Statement by the American Society of Breast Surgeons (ASBS, 2017) regarding Screening Mammography state that “Current evidence does not support the use of breast scintigraphy (e.g. sestamibi scan), thermography or ductal lavage for screening of average risk women outside of clinical trials.”

### **National Comprehensive Cancer Network**

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology™, breast cancer screening and diagnosis guidelines (NCCN, 2018) 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**

In 2013 the FDA issued a safety warning (FDA, 2013) stating that “a nipple aspirate test is not a replacement for mammography, other breast imaging tests, or breast biopsy, and should not be used by itself to screen for or diagnose breast cancer. The FDA is not aware of any valid scientific data to show that a nipple aspirate test by itself is an effective screening tool for any medical condition including the early detection of breast cancer or other breast disease. The FDA, other public health agencies, and national medical and professional societies agree that mammography is the most effective method for detecting breast cancer in its earliest, most treatable stages. These organizations include the American Cancer Society, the American College of Radiology, the Centers for Disease Control and Prevention, the National Cancer Institute, and the Society for Breast Imaging. The National Comprehensive Cancer Network (NCCN) 2013 guidelines state that the clinical utility of nipple aspiration is still being evaluated and it should not be used as a breast cancer screening technique.”

## **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

### 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)
- 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)

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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.