Corporate Medical Policy

Oral Screening Lesion Identification Systems and Genetic Screening AHS – G2113 “Notification”

**Effective Date October 15, 2019**

**Description of Procedure or Service**

Oral cancer is defined as cancer occurring in the oral cavity between the vermilion border of the lips and the junction of the hard and soft palates or the posterior one third of the tongue. Squamous cell carcinoma is the most common (Gross, Lee, Okuno, & Rao, 2017).

Oral Screening and Lesion Identification Systems are adjunctive screening tests to identify malignancy in the lips, oral cavity or oropharynx (Fuller et al., 2015).

***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**

Oral screening lesion identification systems and genetic screening is considered investigational. BCBSNC does not provide coverage for investigational 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 Oral Screening Lesion Identification Systems and Genetic Screening is covered**

Not applicable.

**When Oral Screening Lesion Identification Systems and Genetic Screening is not covered**

Oral screening, lesion identification systems and genetic testing are not covered for any use, including, but not limited to, the following:

- OraRisk® HPV Salivary Diagnostic Test (OralDNA labs, Brentwood, TN)
- MOP™ testing
- SaliMark OSCC® (PeriRx)
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Policy Guidelines

The American Cancer Society estimates the 2016 incidence of oral cancer to be 48,330 cases with approximately 9,570 deaths. OSCC is the most common form of oral cavity cancer (Scully & Porter, 2000). Many are preceded by potentially malignant disorders (PMD), a heterogeneous group of conditions including erythroplakia, non-homogeneous leukoplakia, erosive lichen planus, oral submucous fibrosis and actinic keratosis (Warnakulasuriya, Johnson, & van der Waal, 2007). The early detection and excision of PMD can prevent malignant transformation (Paul Brocklehurst, 2017; van der Waal, 2009; Warnakulasuriya et al., 2007).

Diagnosing and treating dermatologic lesions of the mouth and gums is challenging for most clinicians because of the wide variety of disease processes that can present with similar appearing lesions and the fact that most clinicians receive inadequate training in mouth diseases. (Goldstein & Goldstein, 2017) A number of index tests have been proposed as adjucnts to a conventional oral examination (COE) to improve diagnostic test accuracy (Fedele, 2009; Lingen, Kalmar, Karrison, & Speight, 2008; Patton, Epstein, & Kerr, 2008; Rethman et al., 2010; Seoane Leston & Diz Dios, 2010). Table from (Macey et al., 2015) – see Appendix.

None of the adjunctive tests can be recommended as a replacement for the currently used standard of COE followed by a scalpel biopsy and histological assessment (Fuller et al., 2015; Macey et al., 2015; Richards, 2015).

Clinical Validity and Utility

Patton et al (2008) conducted a systematic review to evaluate the effectiveness of adjunctive techniques including toluidine blue, ViziLite Plus with toluidine blue, ViziLite, VELscope, MicroLux/DL, Orascoptic DK and OralCDx brush biopsy. A total of 23 studies met the inclusion criteria. The authors concluded that there is insufficient evidence to support or refute the use of visually based examination adjuncts. The review concluded that, given the lack of effectiveness data in general dental practice settings, clinicians must rely on a thorough oral mucosal examination supported by specialty referral and/or tissue biopsy for oral premalignant and malignant lesions.

According to Huber (2012), several products like OralCDx Brush Test, ViziLite Plus with TBlue, Microlux, VELscope Vx, Sapphire Plus, Identafi, and the DOE Oral Exam System have been proposed as an adjunctive aid for identifying oral premalignant and malignant lesions (OPMLs). The author noted that studies evaluating the efficacy and utility of these products to screen for OPMLs are limited and conflicting.

Rashid and Warnakulasuriya (2015) studied the effectiveness of chemi-luminescence (CL) and tissue auto-fluorescence (AF) devices as adjuncts in the detection of oral cancer (OC) and oral potentially malignant disorders (OPMD). The authors performed a systematic review of the published literature to evaluate the effectiveness of the ViziLite and ViziLite Plus with TB, MicroLux/DL and the VELscope as aids in the detection of OC and OPMDs. Twenty-five primary studies published between 2004 and 2013 satisfied the criteria for selection – 13 utilized chemiluminescence and 12 tissue autofluorescence. The authors concluded that there is limited evidence for their use in primary care, and these tools are better suited to specialist clinics in which there is a higher prevalence of disease and where experienced clinicians may better discriminate between benign and malignant lesions.

Nagi et al (2016) conducted a systematic review to evaluate the effectiveness of adjunctive devices that utilize the principles of chemiluminescence and tissue autofluorescence in the detection of oral squamous cell carcinoma (OSCC) and oral potentially malignant disorders (OPMD). Twenty primary studies published satisfied the criteria for selection - 10 utilized chemiluminescence and 10 tissue autofluorescence. The authors concluded that more clinical trials in future should be conducted to establish optical imaging as an efficacious adjunct tool in early diagnosis of OSCC and OPMD.
Vila et al (2012) evaluated the accuracy of high-resolution microendoscopic (HRME) images to discriminate between cancerous and benign mucosa. The authors concluded that “with further refinement, HRME and other optical imaging methods have the potential to enhance the rational selection of initial margins, and decrease operative time and expense by limiting the use of frozen section analysis.” Although HRME is a promising tool, the authors caution that there are several limitations which highlight areas for further development.

Applicable Federal Regulations
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

Practice Guidelines and Position Statements

American Dental Association (ADA)
In 2010, the ADA released evidence-based clinical recommendations for screening for oral squamous cell carcinomas and the use of adjunctive screening aids to visualize and detect potentially malignant and malignant oral lesions (Rethman et al, 2010). The guideline evaluated adjunctive screening aids based on tissue reflectance (i.e., ViziLite Plus, MicroLux/DL, Orascoptic DK), autofluorescence (i.e., VELscope) and combination of autofluorescence and tissue reflectance (i.e., TRIMIRA Identafi). The authors noted that “overall, visualization aids may affect a lesion's appearance in terms of brightness, texture and delineation of margins and in patients with previously detected lesions, but they have not been shown to enhance the practitioner's ability to identify potentially malignant lesions specifically or to identify lesions not visible under normal operatory lighting. Furthermore, there is insufficient evidence that these devices improve patient compliance or aid in patient education” The guidelines include the following conclusions:

- “There is insufficient evidence that commercial devices based on autofluorescence enhance visual detection of potentially malignant lesions beyond that achieved through a conventional visual and tactile examination.”
- “There is insufficient evidence that commercial devices based on tissue reflectance enhance visual detection of potentially malignant lesions beyond that achieved through a conventional visual and tactile examination.”

US Preventive Services Task Force (USPSTF)
In 2013, the USPSTF published final recommendations for screening of oral cancer. The recommendation stated that “the current evidence is insufficient to assess the balance of benefits and harms of screening for oral cancer in asymptomatic adults.” The USPSTF also noted that “additional tests proposed as adjuncts to the oral cancer screening examination include toluidine blue dye staining, chemiluminescent and autofluorescent lighting devices, and brush cytology. These screening and adjunct tests have not been adequately tested in primary care nondental settings.”

National Comprehensive Cancer Network (NCCN)
NCCN’s 2017 clinical practice guidelines on head and neck cancers does not mention the use of adjunctive screening aids based on autofluorescence or tissue reflectance as a management tool.

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.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 82397, 87623, 87624, 87625

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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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An Independent Licensee of the Blue Cross and Blue Shield Association

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[http://doi.org/10.1245/s10434-012-2351-1](http://doi.org/10.1245/s10434-012-2351-1)

doi:10.1111/j.1600-0714.2007.00582.x

**Policy Implementation/Update Information**

1/1/19  
New policy developed. Oral screening lesion identification systems and genetic screening is considered investigational. BCBSNC does not provide coverage for investigational services or procedures. Medical Director review 1/1/2019. Policy noticed 1/1/2019 for effective date 4/1/2019. (an)

8/13/19  
Reviewed by Avalon 2nd Quarter CAB. Added SaliMark OSCC® (PeriRx) test to the Non Covered list. In the When Not Covered section, the investigational statement is revised to read “Oral screening, lesion identification systems and genetic testing are *not covered* for any use…” Code 81599 to Billing/Coding section. Medical Director review 8/2019. Policy noticed 8/13/2019 for effective date 10/15/2019. (an)

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.
### APPENDIX

Table from (Macey et al., 2015)

<table>
<thead>
<tr>
<th>Test</th>
<th>Characteristics</th>
<th>Classification of response</th>
<th>Other information</th>
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<tbody>
<tr>
<td>Conventional oral examination (COE)</td>
<td>A standard visual and tactile examination of the oral mucosa under normal (incandescent) light.</td>
<td>The presence of an oral mucosal abnormality with a suspicion of malignancy or potential malignancy is classified as a positive test result; the presence of oral mucosal abnormality without a suspicion of malignancy or potential malignancy is classified as a negative test result.</td>
<td>Traditionally used as a oral cancer screen rather than diagnosis, but its utility is debated (Lingen 2008).</td>
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<td>Vital staining (e.g. toluidine blue, tolonium chloride)</td>
<td>Vital staining refers to the use of dyes such as toluidine blue or tolonium chloride to stain oral mucosa tissues for PMD or malignancy (Leston 2010; Lingen 2008; Patton 2008). The procedure is as follows: Pre-rinse with acetic acid, Rinse with water, Apply toluidine blue, Post rinse with acetic acid, Rinse with water.</td>
<td>The result of the test is classified as positive if tissue is stained and negative if no tissue is stained, or equivocal if no definitive result can be obtained.</td>
<td>Advantages: ability to define areas that could be malignant or abnormal but cannot be seen; assess the extent of the PMD for excision. Disadvantages: benign inflammatory lesions are subject to stain; possibility</td>
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<td>Brush cytology (e.g. OralCDx brush biopsy)</td>
<td>Brush cytology refers to the microscopic assessment and interpretation of cell samples from PMD that are flaked off from the oral mucosa by the brushing, smearing, scraping or lavage to collect cell samples, which are then sealed on glass slides. They are then analysed using an imaging system that assesses the sampled cells (Leston 2010; Lingen 2008; Patton 2008).</td>
<td>Following analysis, cytopathologists classify test results as positive, atypical or negative.</td>
<td>Advantages: include the ability to collect information from, and detect large or multiple lesions and to access &quot;the basement membrane collecting cells from all three epithelial layers of the oral mucosa. The liquid-based cytology reduces the problems relating to sampling and fixation and presents a better cytological morphology&quot; (Divani 2009). Disadvantages: smaller or less obvious lesions may be overlooked; difficulties in detecting lesions when there is necrosis or coagulated blood; inadequate training of operators (Divani 2009); cells are potentially seen out of context.</td>
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<td>Light-based detection (chemiluminescence e.g. ViziLite, Microlux DL; VELscope, Identafi 2000; tissue fluorescence spectroscopy)</td>
<td>Light-based systems to identify malignant and potentially malignant lesions and to highlight their presence through tissue reflectance (Leston 2010; Lingen 2008; Patton 2008) e.g. using Microlux DL, the procedure is as follows (Lingen 2008). Pre-rinse with acetic acid, Use blue-light source to visually assess the oral cavity. ViziLite Plus also provides a toluidine chloride solution (toluidine blue) to aid in the marking of the lesion for biopsy once the light source is removed.</td>
<td>The result of the test is classed as negative if the appearance of the epithelium is lightly bluish white and positive if the appearance of the epithelium is distinctly white (acetowhite).</td>
<td>Advantages: simple to use; non-invasive; do not require consumable reagents; provide real-time results; can be performed by a wide range of operators after a short training period. Disadvantages: the necessity of a dark environment; high initial set up (for VELscope) or recurrent costs (for ViziLite in low-income countries); lack of permanent record unless photographed; inability to objectively measure visualisation results.</td>
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<td>Blood and saliva analysis</td>
<td>These novel technologies are at an early stage of development and evaluation. Analysis of blood or saliva samples which tests for the presence of biomarkers of PMD and oral cancer (Brinkmann 2011; Lee 2009; Li 2006). Cut-off probabilities vary widely and are dependent on the individual biomarker or combination of biomarkers examined.</td>
<td>Advantages: non-invasive (saliva tests) or minimally invasive (blood tests). Disadvantages: there is a tendency for the estimated diagnostic accuracy of new health technologies to decline over time as evidence from independent evaluations accumulate (Wyatt 1995). This bias, which can be substantial, has been demonstrated in other domains, e.g. acute abdominal pain (Liu 2006) and clinical decision support systems (Garg 2005). Promising biomarker tests in several clinical areas were eventually shown to be disappointing (Buchen 2011). It remains to be seen whether this is the case with oral cancer and PMDs.</td>
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