

Corporate Medical Policy

Salivary Hormone Tests

File Name: salivary_hormone_tests
Origination: 12/2004
Last CAP Review: 3/2018
Next CAP Review: 3/2019
Last Review: 3/2018

Description of Procedure or Service

Many products of physiology and metabolism are known to be excreted by the body into the saliva. It has been proposed that measurement of these substances may be useful in some cases as an indicator of some disease states. Salivary tests of estrogen, progesterone, androgens, melatonin, cortisol and dehydroepiandrosterone (DHEA) are available to consumers over the Internet. Some of these websites include a questionnaire to allow consumers to determine whether they need saliva testing, and a form to order these tests online. The results of these tests are purportedly used to determine the need for prescriptions of DHEA, vitamins, herbs, phytoestrogens, and other anti-aging regimens.

For many substances the concentrations available in saliva do not correlate well with various disease states, are not as accurate as other testing methods, or have yet to be established as useful tools in the management or detection of disease. In addition, salivary hormone levels may vary according to the time of day, diet or hydration.

Measurement of late-night and/or midnight salivary cortisol is used as a screening test for the initial diagnosis of Cushing's syndrome. If screening tests are positive, confirmatory tests are then performed. Initial testing could include urine cortisol or late night salivary cortisol. Secondary testing may also include one of these tests or a blood test.

******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

BCBSNC will provide coverage for Salivary Hormone Testing for cortisol when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Salivary Hormone Testing for evaluation of estrogens, progesterone, androgens, melatonin or dehydroepiandrosterone (DHEA) 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 Salivary Hormone Tests are covered

Salivary hormone testing by radioimmunoassay for cortisol is considered medically necessary when performed to evaluate suspected endogenous hypercortisolism of Cushing's syndrome (CS) in

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children or adults. The testing should be ordered by a physician and performed in a CLIA (Clinical Laboratory Improvement Amendments) approved laboratory.

When Salivary Hormone Tests are not covered

Salivary testing of cortisol is not covered for any indication other than as specified under "When Covered" above. Salivary cortisol testing for screening, diagnosing, or monitoring any other health condition, or any other indication, is considered investigational.

The following tests are considered investigational (not an all inclusive list):

Salivary Hormone testing of estrogen, progesterone, androgens, melatonin, or dehydroepiandrosterone (DHEA) for the screening, diagnosis, or monitoring of menopause (pre, peri, and post), aging, hormone replacement therapy, transgender hormonal therapy, or any other indication is considered investigational. BCBSNC does not cover investigational services.

Salivary tests of cortisol for the screening, diagnosis, or monitoring of menopause or diseases related to aging, or any other indications (e.g., diagnosis of adrenal insufficiency in preterm infants, diagnosis of bipolar disorder, depression, or eating disorders).

Serial monitoring of estradiol and progesterone levels to detect/predict ovulation during the menstrual cycle.

Serial monitoring of estrin levels as a technique of risk assessment of preterm labor or delivery.

Cordant Health Solutions Comprehensive Oral Fluid Rx Evaluation (CORE) for prescription drug monitoring using oral fluid.

Measurement of diurnal salivary cortisol patterns for prediction of infant birth weight.

Salivary antibody testing (IgA, IgG, IgM) for the diagnosis of Sicca syndrome.

Salivary testing for anti-tissue transglutaminase for the diagnosis of celiac disease.

Salivary testing of biomarkers for the diagnosis of cancers (e.g., breast cancer, head and neck carcinoma, oral pre-cancer and oral squamous cell carcinoma (e.g., CYFRA 21-1, interleukin-8, or mRNAs of dual specificity phosphatase 1 (DUSP1), ornithin decarboxylase antizyme 1 (OAZ1), and S100 calcium-binding protein P (S100P)).

Salivary testing of mutans streptococci for determining the risk of developing dental caries.

Salivary testing of pepsin for the diagnosis of gastro-esophageal reflux disease.

Salivary testing of telomere length for the diagnosis of depression.

Policy Guidelines

The American Association of Clinical Endocrinologists Position Statement on Bioidentical Hormones states: "large intra-subject variability has been shown in salivary sex hormone concentrations. Salivary sex hormone levels fluctuate depending upon numerous variables such as diet, hydration status, and circadian rhythm. These conditions are difficult to standardize".

The American College of Obstetricians and Gynecologists (ACOG), in their Committee Opinion #532, Compounded Bioidentical Menopausal Hormone Therapy, address salivary hormone level testing as not

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meaningful because salivary hormone levels vary within each woman depending on her diet, the time of day, the specific hormone being tested, and other variables (ACOG 2012).

The North American Menopause Society (NAMS) in their position statement has concluded that "the use of salivary hormone testing (which) has been proven to be inaccurate and unreliable."

A National Institutes of Health State-of-the-Science Conference Statement on Management of Menopause-related Symptoms (2005) reached the following conclusions about salivary hormone testing and bioidentical hormones. "Bioidentical hormones, often called "natural" hormones, are treatments with individually compounded recipes of a variety of steroids in various dosage forms, with the composition and dosages based on a person's salivary hormone concentration. These steroids may include estrone, estradiol, estriol, DHEA, progesterone, pregnenolone, and testosterone. There is a paucity of data on the benefits and adverse effects of these compounds."

Cushing's syndrome can be difficult to diagnose and is often a challenge for clinicians because other conditions share the same signs and symptoms. The laboratory investigations of CS are based on the demonstration of excessive cortisol secretion. Cortisol levels normally rise and fall throughout the day. In patients without CS, the levels drop significantly overnight. Several tests have been used extensively, but each of the currently available biochemical tests for the diagnosis of CS has limitations (24-hour urine free cortisol level and low dose dexamethasone suppression test). Late night salivary cortisol test is a simple way to screen for CS and it has been found to have high diagnostic sensitivity and specificity. Major advantages of this method are the reliability, non-invasiveness, and use in ambulatory patients.

The U.S. Food and Drug Administration (FDA) regulates laboratory tests under the Clinical Laboratory Improvement Act (CLIA). The CLIA stipulates that clinical laboratories need to be accredited by the College of American Pathologists Laboratory Accreditation Program.

Although saliva testing kits to evaluate hormone levels during menopause are currently available, these kits are not subject to FDA Approval. Several testing methods for salivary cortisol have been cleared for marketing by the FDA.

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: S3650. S3652

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

From Original Policy Titled: Salivary Hormone Tests for Menopause

Specialty Matched Consultant Advisory Panel 12/2004

Specialty Matched Consultant Advisory Panel 12/13/2006

For Policy Titled: Salivary Hormone Tests

National Institutes of Health (NIH). NIH State-of-the-Science Conference Statement on management of menopause-related symptoms. NIH Consensus State Sci Statements. 2005 Mar 21-23;22(1):1-38. Accessed on April 5, 2013 at <http://consensus.nih.gov/2005/menopausestatement.htm> .

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Viardot A, Huber P, Puder JJ, Zulewski H, Keller U, Müller B. Reproducibility of nighttime salivary cortisol and its use in the diagnosis of hypercortisolism compared with urinary free cortisol and overnight dexamethasone suppression test. *J Clin Endocrinol Metab.* 2005 Oct;90(10):5730-6. Epub 2005 Jul 12. Accessed on November 20, 2008 at <http://jcem.endojournals.org/cgi/content/full/90/10/5730>

Papanicolaou DA, Mullen N, Kyrou I, Nieman LK. Nighttime salivary cortisol: a useful test for the diagnosis of Cushing's syndrome. *J Clin Endocrinol Metab.* 2002 Oct;87(10):4515-21. Accessed on November 20, 2008 at <http://jcem.endojournals.org/cgi/content/full/87/10/4515>

Specialty Matched Consultant Advisory Panel - 12/2008

Specialty Matched Consultant Advisory Panel – 3/21/12

Menopause: The Journal of The North American Menopause Society. The 2012 Hormone Therapy Position Statement of The North American Menopause Society Vol. 19, No. 3, pp. 257/271. Available at: <http://www.menopause.org/docs/default-document-library/psht12.pdf?sfvrsn=2> .Accessed February 26, 2013

American College of Obstetricians and Gynecologists. ACOG Committee Opinion #532, August 2012: Compounded Bioidentical Menopausal Hormone Therapy. Available at: <http://www.acog.org/~media/Committee%20Opinions/Committee%20on%20Gynecologic%20Practice/o532.pdf?dmc=1&ts=20130225T0923233804> . Accessed February 26, 2013

Specialty Matched Consultant Advisory Panel – 3/2013

American Association of Clinical Endocrinologists(AACE). Reproductive Medicine Committee Position Statement on Bioidentical Hormones updated 7/15/2007. Accessed on April 5, 2013 at <https://www.aace.com/files/position-statements/aacebhstatement071507.pdf> .

American Association of Clinical Endocrinologists (AACE). Medical Guidelines for Clinical Practice for the Diagnosis and Treatment of Menopause. Accessed on February 27, 2014 at <https://www.aace.com/files/menopause.pdf> .

Specialty Matched Consultant Advisory Panel – 3/2014

Senior Medical Director review 3/2014

Recommendation Summary. U.S. Preventive Services Task Force. October 2012. <http://www.uspreventiveservicestaskforce.org/Page/Topic/recommendation-summary/menopausal-hormone-therapy-preventive-medication> . Accessed on March 11, 2015

The North American Menopause Society Recommendations for Clinical Care of Midlife Women available at <http://www.menopause.org/docs/default-source/2014/nams-recomm-for-clinical-care.pdf> . Accessed on March 11, 2015.

Specialty Matched Consultant Advisory Panel – 3/2015

Senior Medical Director review 3/2015

Specialty Matched Consultant Advisory Panel – 3/2016

Policy Implementation/Update Information

From Original Policy Titled: Salivary Hormone Tests for Menopause

12/23/2004 Specialty Matched Consultant Advisory Panel review -12/9/2004. Notification of new policy indicating that salivary hormone tests are not covered for the screening, diagnosing or monitoring of menopause. These tests are considered investigational and BCBSNC does not cover investigational services. Notification given 12/23/2004. Effective 3/3/2005.

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1/17/07 Specialty Matched Consultant Advisory Panel review - 12/13/2006. No changes to criteria. Reference source added. (pmo)

For Policy Titled: Salivary Hormone Tests

- 1/12/09 Policy retitled to Salivary Hormone Tests. Policy sections updated to include guidelines for salivary hormone testing for indications other than menopause. Salivary Hormone testing by radioimmunoassay for cortisol is considered medically necessary when performed to evaluate suspected endogenous hypercortisolism of Cushing's syndrome (CS) in children or adults. The testing should be ordered by a physician and performed in a CLIA (Clinical Laboratory Improvement Amendments) approved laboratory. This is the only salivary hormone test that is covered. All other salivary hormone tests are considered investigational and are not covered for any indication. Reference sources added. (pmo)
- 6/22/10 Policy Number(s) removed (amw)
- 1/18/2011 Description section revised. Policy Statement reworded, but intent of policy is unchanged. Specialty Matched Consultant Advisory Panel review 12/16/2010. (adn)
- 4/17/12 No change to policy statement. Specialty Matched Consultant Advisory Panel review 3/21/12. (sk)
- 6/29/12 Removed Related Policy from Description section. (sk)
- 9/4/12 Medical Director review. Replaced the word testosterone with the word androgens in the Description, Policy, and When Salivary Hormone Tests are not covered sections of the Policy. (sk)
- 4/16/13 References added. Specialty Matched Consultant Advisory Panel review 3/20/13. No change to policy statement. (sk)
- 4/29/14 Reference added. Specialty Matched Consultant Advisory Panel review 3/25/14. Senior Medical Director review. No change to policy statement. (sk)
- 4/28/15 References added. Specialty Matched Consultant Advisory Panel review 3/25/15. Senior Medical Director review. (sk)
- 4/29/16 Specialty Matched Consultant Advisory Panel review 3/30/2016. Policy statement unchanged. (an)
- 10/25/16 Statement added to the Not Covered section. Salivary hormone testing related to transgender hormonal therapy is considered investigational. (an)
- 4/28/17 Specialty Matched Consultant Advisory Panel review 3/29/2017. No change to policy statement. (an)
- 4/27/18 Additional investigational tests added to the "When Not Covered" section for clarity. Added code S3652 to Billing/Coding section. Specialty Matched Consultant Advisory Panel review 3/28/2018. No change to policy intent. (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.