Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

***Current Policy Effective Date: 1/1/24**
(See policy history boxes for previous effective dates)

Title: Salivary Testing for Hormone Levels

Description/Background

Salivary tests of various hormones include, but are not limited to estrogen, estradiol, estriol, estrone, progesterone, testosterone, melatonin and dehydroepiandrosterone (DHEA). The tests are noninvasive, may be obtained without a prescription, and are marketed to consumers for home-based testing by pharmacies, laboratories, and through internet sites.

The tests have been proposed as a method for screening, diagnosis or monitoring of menopause, preterm labor, and other conditions.

Regulatory Status

Laboratory tests are regulated under the Clinical Laboratory Improvement Act (CLIA). There are some salivary test kits available via mail order or the Internet that are cleared for marketing by the U.S. Food and Drug Administration.

Medical Policy Statement

Salivary hormone testing of estrogens, progesterone, testosterone, melatonin or DHEA is considered experimental/investigational. Its effectiveness remains unproven in evaluating, diagnosing or monitoring the following conditions:

- Ovulation
- Menopause
- Changes related to aging
- Preterm labor
- Other gonadal dysfunction

Inclusionary and Exclusionary Guidelines

N/A

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

N/A

Other codes (investigational, not medically necessary, etc.):

S3650 S3652

Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.

Rationale

In the 2011 American Association of Clinical Endocrinologists' Medical Guidelines for Clinical Practice for the Diagnosis and Treatment of Menopause, salivary hormone concentrations were addressed. The guidelines noted that studies have revealed large intrasubject variability in salivary sex hormone concentrations. The fluctuations are dependent on numerous variables, including diet, hydration, and circadian rhythm – and that these conditions are difficult to standardize.[1]

In 2012, The North American Menopause Society (NAMS) published a position statement on hormone therapy[2] that stated salivary hormone testing has been proven to be inaccurate and unreliable. The position statement was updated in 2017[3], and continues to affirm: that "…salivary testing for hormone therapy is considered unreliable because of differences in hormone pharmacokinetics and absorption, diurnal variation, and interindividual and intraindividual variability."

In 2012, and reaffirmed in 2020, the American College of Obstetricians and Gynecologists (ACOG)[4] noted:

> "There is no evidence that hormonal levels in saliva are biologically meaningful. In addition, whereas saliva is an ultrafiltrate of the blood and in theory should be amenable to testing for "free" (unbound) concentrations of hormones, salivary testing does not currently offer an accurate or precise method of hormone testing. There are several problems with salivary testing and monitoring of free hormone levels. First, salivary levels do not consistently provide a reasonable representation of endogenous, circulating serum hormones. There is large within-patient variability in salivary hormone concentrations, especially when exogenously administered hormones are given. Salivary hormone levels vary depending on diet, time of testing, and the specific hormone being tested. Second, because the pharmacokinetics of exogenously administered compounded hormones cannot be

known, it is not possible to estimate with reliability how and when to test saliva to obtain a representative result. Third, saliva contains far lower concentrations of hormone than serum and is prone to contamination with blood, infectious agents, and epithelial cells—all of which may affect the level of hormone to be measured."

The most recent ACOG practice bulletin on Prediction and Prevention of Spontaneous Preterm Birth (August 2021)[5] states that there are a variety of tests and monitoring modalities that have been proposed as markers for preterm delivery risk, including salivary hormone concentrations. "…These emerging prediction methods should be considered investigational, and routine adoption into clinical practice is not recommended."

Serum levels are the standard for hormone measurement. Hormone concentrations in saliva vary and may not provide an accurate clinical assessment. Due to their variability, salivary hormone measurements are unreliable and not appropriate for evaluating, diagnosing or monitoring ovulation, menopause, changes related to aging, preterm labor, or other gonadal dysfunction.

Government Regulations
National/Local:

There is no national or local coverage determination.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

N/A

References

1. American Association of Clinical Endocrinologists (AACE). Medical Guidelines for Clinical Practice for the Diagnosis and Treatment of Menopause. Endocrine Practice 2011, Vol. 17, Supp 6. Link no longer available 8/1/23.
2. North American Menopause Society. The 2012 Hormone Therapy Position Statement of the North American Menopause Society. Menopause: The Journal of the North American Menopause Society. Vol. 19, No. 3, pp. 257-271. http://www.menopause.org/docs/default-document-library/psht12.pdf?sfvrsn=2 Accessed 8/1/23.
3. North American Menopause Society. The 2017 hormone therapy position statement of The North American Menopause Society. Vol. 24, No.7, pp 728-753. https://www.menopause.org/docs/default-source/2017/nams-2017-hormone-therapy-position-statement.pdf Accessed 8/1/23.
4. American College of Obstetricians and Gynecologists (ACOG). Compounded Bioidentical Menopausal Hormone Therapy. ACOG Committee Opinion No. 532, August 2012. Reaffirmed 2018, reaffirmed 2020. https://www.acog.org/clinical/clinical-

guidance/committee-opinion/articles/2012/08/compounded-bioidentical-menopausal-hormone-therapy Accessed 8/1/23.
5. American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin Number 234, Prediction and Prevention of Spontaneous Preterm Birth. August 2021. https://www.acog.org/clinical/clinical-guidance/practice-bulletin/articles/2021/08/prediction-and-prevention-of-spontaneous-preterm-birth Accessed 8/1/23.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 8/1/23, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
7/27/05	7/27/05	7/26/05	Joint policy established
7/1/08	7/3/08	7/3/08	Routine maintenance
7/1/10	4/20/10	4/20/10	Routine maintenance
1/1/13	10/16/12	10/16/12	Routine maintenance, title changed from Salivary Testing for Hormonal Levels to Salivary Testing for Hormone Levels
7/1/15	4/24/15	5/8/15	Routine maintenance
7/1/16	4/19/16	4/19/16	Routine maintenance
3/1/17	12/13/16	12/13/16	Routine maintenance
3/1/18	12/12/17	12/12/17	Routine maintenance Updated references
3/1/19	12/11/18		Routine maintenance
3/1/20	12/17/19		Routine maintenance
3/1/21	12/15/20		Routine maintenance
3/1/22	12/14/21		Routine maintenance Ref 5 added
3/1/23	12/20/22		Routine maintenance (jf) Vendor: Avalon
1/1/24	10/17/23		Routine maintenance (jf) Vendor managed: Avalon

Next Review Date: 3th Qtr., 2024

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: SALIVARY TESTING FOR HORMONE LEVELS

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Not covered
BCNA (Medicare Advantage)	See Government Regulations section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.