



**BlueCross BlueShield  
of Oklahoma**

If a conflict arises between a Clinical Payment and Coding Policy (“CPCP”) and any plan document under which a member is entitled to Covered Services, the plan document will govern. If a conflict arises between a CPCP and any provider contract pursuant to which a provider participates in and/or provides Covered Services to eligible member(s) and/or plans, the provider contract will govern. “Plan documents” include, but are not limited to, Certificates of Health Care Benefits, benefit booklets, Summary Plan Descriptions, and other coverage documents. BCBSOK may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSOK has full and final discretionary authority for their interpretation and application to the extent provided under any applicable plan documents.

Providers are responsible for submission of accurate documentation of services performed. Providers are expected to submit claims for services rendered using valid code combinations from Health Insurance Portability and Accountability Act (“HIPAA”) approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing (“UB”) Editor, American Medical Association (“AMA”), Current Procedural Terminology (“CPT®”), CPT® Assistant, Healthcare Common Procedure Coding System (“HCPCS”), ICD-10 CM and PCS, National Drug Codes (“NDC”), Diagnosis Related Group (“DRG”) guidelines, Centers for Medicare and Medicaid Services (“CMS”) National Correct Coding Initiative (“NCCI”) Policy Manual, CCI table edits and other CMS guidelines.

Claims are subject to the code edit protocols for services/procedures billed. Claim submissions are subject to claim review including but not limited to, any terms of benefit coverage, provider contract language, medical policies, clinical payment and coding policies as well as coding software logic. Upon request, the provider is urged to submit any additional documentation.

## Salivary Hormone Testing

**Policy Number: CPCPLAB034**

**Version 1.0**

**Plan Effective Date: Nov. 1, 2022**

### Description

BCBSOK has implemented certain lab management reimbursement criteria. Not all requirements apply to each product. Providers are urged to review Plan documents for eligible coverage for services rendered.

### Reimbursement Information:

Late Night Salivary Cortisol testing **is reimbursable** for diagnosing Cushing’s Syndrome.

Salivary hormone testing for the screening, diagnosis, and/or monitoring of menopause, infertility, endometriosis, polycystic ovary disease (PCOS), premenstrual syndrome, osteoporosis, sexual dysfunction, seasonal affective disorder, depression, multiple sclerosis, sleep disorders, or diseases related to aging **is not reimbursable**. Salivary hormone tests include but are not limited to the following:

- a. Estrogen, including estrone (E1), estradiol (E2), and estriol (E3)
- b. Melatonin
- c. Progesterone

- d. Testosterone
- e. DHEA
- f. Cortisol

## Procedure Codes

Codes
82530, 82533, 82626, 82627, 82670, 82671, 82672, 82677, 82679, 82681, 84144, 84402, 84403, 84410, S3650, S3652

## References:

ACOG, & ASRM. (2012). Compounded bioidentical menopausal hormone therapy. *Fertil Steril*, 98(2), 308-312. doi:10.1016/j.fertnstert.2012.06.002

Antonelli, G., Ceccato, F., Artusi, C., Marinova, M., & Plebani, M. (2015). Salivary cortisol and cortisone by LC-MS/MS: validation, reference intervals and diagnostic accuracy in Cushing's syndrome. *Clin Chim Acta*, 451(Pt B), 247-251. doi:10.1016/j.cca.2015.10.004

Conaway, E. (2011). Bioidentical hormones: an evidence-based review for primary care providers. *J Am Osteopath Assoc*, 111(3), 153-164.

Crewther, B. T., Obminski, Z., Orysiak, J., & Al-Dujaili, E. A. S. (2018). The utility of salivary testosterone and cortisol concentration measures for assessing the stress responses of junior athletes during a sporting competition. *J Clin Lab Anal*, 32(1). doi:10.1002/jcla.22197

Doi, S. A., Clark, J., & Russell, A. W. (2013). Concordance of the late night salivary cortisol in patients with Cushing's syndrome and elevated urine-free cortisol. *Endocrine*, 43(2), 327-333. doi:10.1007/s12020-012-9855-0

El-Farhan, N., Rees, D. A., & Evans, C. (2017). Measuring cortisol in serum, urine and saliva - are our assays good enough? *Ann Clin Biochem*, 54(3), 308-322. doi:10.1177/0004563216687335

Fleseriu, M., Hamrahian, A. H., Hoffman, A. R., Kelly, D. F., & Katznelson, L. (2016). American Association Of Clinical Endocrinologists And American College Of Endocrinology Disease State Clinical Review: Diagnosis Of Recurrence In Cushing Disease. *Endocr Pract*, 22(12), 1436-1448. doi:10.4158/ep161512.Dscr

Flyckt, R. L., Liu, J., Frasure, H., Wekselman, K., Buch, A., & Kingsberg, S. A. (2009). Comparison of salivary versus serum testosterone levels in postmenopausal women receiving transdermal testosterone supplementation versus placebo. *Menopause*, 16(4), 680-688. doi:10.1097/gme.0b013e318199d5c4

Genova. (2019a). Comprehensive Melatonin Profile. Retrieved from <https://www.gdx.net/product/comprehensive-melatonin-test-saliva>

Genova. (2019b). Rhythm™. Retrieved from <https://www.gdx.net/product/rhythm-hormone-test-saliva>

Genova\_Diagnostics. (2020). Menopause™ The Original Genova Salivary Sex-Hormone Test. Retrieved from <https://www.gdx.net/product/menopause-hormone-test-saliva>

Goodman, N. F., Cobin, R. H., Ginzburg, S. B., Katz, I. A., & Woode, D. E. (2011). American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the diagnosis and treatment of menopause. *Endocr Pract*, 17 Suppl 6, 1-25.

Hardiman, P., Thomas, M., Osgood, V., Vlassopoulou, V., & Ginsburg, J. (1990). Are estrogen assays essential for monitoring gonadotropin stimulant therapy? *Gynecol Endocrinol*, 4(4), 261-269.

Hinojosa-Amaya, J. M., Varlamov, E. V., McCartney, S., & Fleseriu, M. (2019). Hypercortisolemia Recurrence in Cushing's Disease; a Diagnostic Challenge. *Front Endocrinol (Lausanne)*, 10, 740. doi:10.3389/fendo.2019.00740

Klee, G. G., & Heser, D. W. (2000). Techniques to measure testosterone in the elderly. *Mayo Clin Proc*, 75 Suppl, S19-25.

Lacroix, A., Feelders, R. A., Stratakis, C. A., & Nieman, L. K. (2015). Cushing's syndrome. *Lancet*, 386(9996), 913-927. doi:10.1016/s0140-6736(14)61375-1

Lewis, J. G., McGill, H., Patton, V. M., & Elder, P. A. (2002). Caution on the use of saliva measurements to monitor absorption of progesterone from transdermal creams in postmenopausal women. *Maturitas*, 41(1), 1-6.

Li, X. S., Li, S., & Kellermann, G. (2018). Simultaneous determination of three estrogens in human saliva without derivatization or liquid-liquid extraction for routine testing via miniaturized solid phase extraction with LC-MS/MS detection. *Talanta*, 178, 464-472. doi:10.1016/j.talanta.2017.09.062

Martin, K., & Barbieri, R. (2020, August 31). Menopausal hormone therapy: Benefits and risks. UpToDate. Retrieved from <https://www.uptodate.com/contents/menopausal-hormone-therapy-benefits-and-risks>

Meulenberg, P. M., Ross, H. A., Swinkels, L. M., & Benraad, T. J. (1987). The effect of oral contraceptives on plasma-free and salivary cortisol and cortisone. *Clin Chim Acta*, 165(2-3), 379-385.

NAMS. (2012). The 2012 hormone therapy position statement of: The North American Menopause Society. *Menopause*, 19(3), 257-271. doi:10.1097/gme.0b013e31824b970a

NAMS. (2017). The 2017 hormone therapy position statement of The North American Menopause Society. *Menopause: The Journal of the North American Menopause Society*, 24(7), 728-753. doi:10.1097/GME.0000000000000921

Nieman. (2015). Cushing's syndrome: update on signs, symptoms and biochemical screening. *Eur J Endocrinol*, 173(4), M33-38. doi:10.1530/eje-15-0464

Nieman, Biller, B. M., Findling, J. W., Newell-Price, J., Savage, M. O., Stewart, P. M., & Montori, V. M. (2008). The diagnosis of Cushing's syndrome: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*, 93(5), 1526-1540. doi:10.1210/jc.2008-0125

Nieman, L. K. (2019a, November 12). Causes and pathophysiology of Cushing's syndrome. UpToDate. Retrieved from <https://www.uptodate.com/contents/causes-and-pathophysiology-of-cushings-syndrome>

- Nieman, L. K. (2019b, September 29). Measurement of cortisol in serum and saliva. Retrieved from <https://www.uptodate.com/contents/measurement-of-cortisol-in-serum-and-saliva>
- Nieman, L. K. (2020, May 29). Establishing the diagnosis of Cushing's syndrome. UpToDate. Retrieved from <https://www.uptodate.com/contents/establishing-the-diagnosis-of-cushings-syndrome>
- Nunes, M. L., Vattaut, S., Corcuff, J. B., Rault, A., Loiseau, H., Gatta, B., . . . Tabarin, A. (2009). Late-night salivary cortisol for diagnosis of overt and subclinical Cushing's syndrome in hospitalized and ambulatory patients. *J Clin Endocrinol Metab*, 94(2), 456-462. doi:10.1210/jc.2008-1542
- Oldenburg, M., & Jensen, H. J. (2019). Saliva cortisol level as a strain parameter for crews aboard merchant ships. *Chronobiol Int*, 36(7), 1005-1012. doi:10.1080/07420528.2019.1604540
- Quddusi, S., Browne, P., Toivola, B., & Hirsch, I. B. (1998). Cushing syndrome due to surreptitious glucocorticoid administration. *Arch Intern Med*, 158(3), 294-296.
- Rossouw, J. E., Anderson, G. L., Prentice, R. L., LaCroix, A. Z., Kooperberg, C., Stefanick, M. L., . . . Ockene, J. (2002). Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *Jama*, 288(3), 321-333.
- Rubio-Tapia, A., Hill, I. D., Kelly, C. P., Calderwood, A. H., & Murray, J. A. (2013). ACG clinical guidelines: diagnosis and management of celiac disease. *Am J Gastroenterol*, 108(5), 656-676; quiz 677. doi:10.1038/ajg.2013.79
- Sakkas, D., Howles, C. M., Atkinson, L., Borini, A., Bosch, E. A., Bryce, C., . . . Alper, M. M. (2020). A multi-centre international study of salivary hormone oestradiol and progesterone measurements in ART monitoring. *Reprod Biomed Online*. doi:10.1016/j.rbmo.2020.10.012
- Santoro, N., Braunstein, G. D., Butts, C. L., Martin, K. A., McDermott, M., & Pinkerton, J. V. (2016). Compounded Bioidentical Hormones in Endocrinology Practice: An Endocrine Society Scientific Statement. *J Clin Endocrinol Metab*, 101(4), 1318-1343. doi:10.1210/jc.2016-1271
- Schiffer, L., Adaway, J. E., Arlt, W., & Keevil, B. G. (2019). A liquid chromatography-tandem mass spectrometry assay for the profiling of classical and 11-oxygenated androgens in saliva. *Ann Clin Biochem*, 56(5), 564-573. doi:10.1177/0004563219847498
- Spence, K., McKeever, E., Graham, U., Irwin, S., Neely, J., McAlister, C., . . . McDonnell, M. (2018). Salivary cortisol determination using the Roche generation II assay. <https://www.endocrine-abstracts.org/ea/0059/ea0059p007>
- Taylor, H. S., & Manson, J. E. (2011). Update in hormone therapy use in menopause. *J Clin Endocrinol Metab*, 96(2), 255-264. doi:10.1210/jc.2010-0536
- UniKey. (2018). Retrieved from <https://unikeyhealth.com>
- Valassi, E., Franz, H., Brue, T., Feelders, R. A., Netea-Maier, R., Tsagarakis, S., . . . Trainer, P. J. (2017). Diagnostic tests for Cushing's syndrome differ from published guidelines: data from ERCUSYN. *Eur J Endocrinol*, 176(5), 613-624. doi:10.1530/eje-16-0967

Wood, P. (2009). Salivary steroid assays - research or routine? *Ann Clin Biochem*, 46(Pt 3), 183-196. doi:10.1258/acb.2008.008208

Wren, B. G., McFarland, K., Edwards, L., O'Shea, P., Sufi, S., Gross, B., & Eden, J. A. (2000). Effect of sequential transdermal progesterone cream on endometrium, bleeding pattern, and plasma progesterone and salivary progesterone levels in postmenopausal women. *Climacteric*, 3(3), 155-160.

Wurtman. (2017). Multiple Sclerosis, Melatonin, and Neurobehavioral Diseases. *Front Endocrinol (Lausanne)*, 8, 280. doi:10.3389/fendo.2017.00280

Wurtman, R. (2019, April 30). Physiology and available preparations of melatonin. Retrieved from <https://www.uptodate.com/contents/physiology-and-available-preparations-of-melatonin>

ZRTLAB. (2018). Retrieved from <https://www.zrtlab.com>

### Policy Update History:

11/1/2022	New policy
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