

If a conflict arises between a Clinical Payment and Coding Policy 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. Blue Cross and Blue Shield of New Mexico may use reasonable discretion interpreting and applying this policy to services being delivered in a particular case. BCBSNM 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 approved code sets. Claims should be coded appropriately according to industry standard coding guidelines including, but not limited to: Uniform Billing Editor, American Medical Association, Current Procedural Terminology, CPT® Assistant, Healthcare Common Procedure Coding System, ICD-10 CM and PCS, National Drug Codes, Diagnosis Related Group guidelines, Centers for Medicare and Medicaid Services National Correct Coding Initiative 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

Approval Date: October 30, 2024

Plan Effective Date: January 15, 2025

Description

BCBSNM 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

1. For the diagnosis of Cushing syndrome, late night salivary cortisol testing **may be reimbursable**.
2. 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, salivary hormone testing **is not reimbursable**.

Procedure Codes

The following is not an all-encompassing code list. The inclusion of a code does not guarantee it is a covered service or eligible for reimbursement.

Codes
82530, 82533, 82626, 82627, 82670, 82671, 82672, 82677, 82679, 82681, 84144, 84402, 84403, 84410, 0462U, S3650, S3652

References

ACOG, & ASRM. (2012). Compounded bioidentical menopausal hormone therapy. *Fertil Steril*, 98(2), 308-312. <https://doi.org/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. <https://doi.org/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. <https://pubmed.ncbi.nlm.nih.gov/21464264/>

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). <https://doi.org/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. <https://doi.org/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. <https://doi.org/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. <https://doi.org/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. <https://doi.org/10.1097/gme.0b013e318199d5c4>
- Genova. (2022a). Adrenocortex Stress Profile. <https://www.gdx.net/product/adrenocortex-stress-hormone-test-saliva>
- Genova. (2022b). Comprehensive Melatonin Profile. <https://www.gdx.net/core/sample-reports/Melatonin-Sample-Report.pdf>
- Genova. (2022c). Menopause Plus™ <https://www.gdx.net/core/sample-reports/Menopause-Plus-Sample-Report.pdf>
- Genova. (2022d). Rhythm™. <https://www.gdx.net/core/sample-reports/Rhythm-Sample-Report.pdf>
- Genova_Diagnostics. (2020). *Menopause™ The Original Genova Salivary Sex-Hormone Test*. <https://www.gdx.net/core/sample-reports/Menopause-Sample-Report.pdf>
- 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. <https://doi.org/10.4158/EP.17.S6.1>
- 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. <https://doi.org/10.3109/09513599009024980>
- 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. <https://doi.org/10.3389/fendo.2019.00740>

- Kim, Y. J., Kim, J. H., Hong, A. R., Park, K. S., Kim, S. W., Shin, C. S., & Kim, S. Y. (2020). Stimulated Salivary Cortisol as a Noninvasive Diagnostic Tool for Adrenal Insufficiency. *Endocrinol Metab (Seoul)*, 35(3), 628-635. <https://doi.org/10.3803/EnM.2020.707>
- Klee, G. G., & Hesser, D. W. (2000). Techniques to measure testosterone in the elderly. *Mayo Clin Proc*, 75 Suppl, S19-25. [https://doi.org/10.1016/S0025-6196\(19\)30637-8](https://doi.org/10.1016/S0025-6196(19)30637-8)
- Lacroix, A., Feelders, R. A., Stratakis, C. A., & Nieman, L. K. (2015). Cushing's syndrome. *Lancet*, 386(9996), 913-927. [https://doi.org/10.1016/s0140-6736\(14\)61375-1](https://doi.org/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. [https://doi.org/10.1016/s0378-5122\(01\)00250-x](https://doi.org/10.1016/s0378-5122(01)00250-x)
- 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. <https://doi.org/10.1016/j.talanta.2017.09.062>
- Martin, K., & Barbieri, R. (2022, August 31). *Menopausal hormone therapy: Benefits and risks*. UpToDate. <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. [https://doi.org/10.1016/0009-8981\(87\)90183-5](https://doi.org/10.1016/0009-8981(87)90183-5)
- NAMS. (2012). The 2012 hormone therapy position statement of: The North American Menopause Society. *Menopause*, 19(3), 257-271. <https://doi.org/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. <https://doi.org/10.1097/GME.0000000000000921>
- Nieman. (2015). Cushing's syndrome: update on signs, symptoms and biochemical screening. *Eur J Endocrinol*, 173(4), M33-38. <https://doi.org/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. <https://doi.org/10.1210/jc.2008-0125>

Nieman, L. K. (2019, September 29). *Measurement of cortisol in serum and saliva*. UpToDate. <https://www.uptodate.com/contents/measurement-of-cortisol-in-serum-and-saliva>

Nieman, L. K. (2022a, November 12). *Causes and pathophysiology of Cushing's syndrome*. <https://www.uptodate.com/contents/causes-and-pathophysiology-of-cushings-syndrome>

Nieman, L. K. (2022b, May 29). *Establishing the diagnosis of Cushing's syndrome*. <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., Valli, N., Letenneur, L., & 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. <https://doi.org/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. <https://doi.org/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. <https://doi.org/10.1001/archinte.158.3.294>

Rossouw, J. E., Anderson, G. L., Prentice, R. L., LaCroix, A. Z., Kooperberg, C., Stefanick, M. L., Jackson, R. D., Beresford, S. A., Howard, B. V., Johnson, K. C., Kotchen, J. M., & 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. <https://jamanetwork.com/journals/jama/fullarticle/195120>

Sakkas, D., Howles, C. M., Atkinson, L., Borini, A., Bosch, E. A., Bryce, C., Cattoli, M., Copperman, A. B., de Bantel, A. F., French, B., Gerris, J., Granger, S. W., Grzegorzczk-Martin, V., Lee, J. A., Levy, M. J., Matin, M. J., Somers, S., Widra, E. A., & Alper, M. M. (2020). A multi-centre international study of salivary hormone oestradiol and progesterone measurements in ART monitoring. *Reprod Biomed Online*. <https://doi.org/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. <https://doi.org/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. <https://doi.org/10.1177/0004563219847498>

- Spence, K., McKeever, E., Graham, U., Irwin, S., Neely, J., McAlister, C., Courtney, H., Hunter, S., Mullan, K., McCance, D., & 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. <https://doi.org/10.1210/jc.2010-0536>
- Ueland, G. Å., Kellmann, R., Jørstad Davidsen, M., Viste, K., Husebye, E. S., Almås, B., Storr, H. L., Sagen, J. V., Mellgren, G., Júlíusson, P. B., & Methlie, P. (2021). Bedtime Salivary Cortisol as a Screening Test for Cushing Syndrome in Children. *Journal of the Endocrine Society*, 5(5). <https://doi.org/10.1210/jendso/bvab033>
- UnikeyHealth. (2022). *Salivary Hormone Test*. <https://unikeyhealth.com/products/salivary-hormone-test>
- Valassi, E., Franz, H., Brue, T., Feelders, R. A., Netea-Maier, R., Tsagarakis, S., Webb, S. M., Yaneva, M., Reincke, M., Droste, M., Komerduş, I., Maiter, D., Kastelan, D., Chanson, P., Pfeifer, M., Strasburger, C. J., Toth, M., Chabre, O., Tabarin, A., . . . Trainer, P. J. (2017). Diagnostic tests for Cushing's syndrome differ from published guidelines: data from ERCUSYN. *Eur J Endocrinol*, 176(5), 613-624. <https://doi.org/10.1530/eje-16-0967>
- Wood, P. (2009). Salivary steroid assays - research or routine? *Ann Clin Biochem*, 46(Pt 3), 183-196. <https://doi.org/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. <https://doi.org/10.1080/13697130008500109>
- Wurtman. (2017). Multiple Sclerosis, Melatonin, and Neurobehavioral Diseases. *Front Endocrinol (Lausanne)*, 8, 280. <https://doi.org/10.3389/fendo.2017.00280>
- ZRTLAB. (2019). LCMS Saliva Steroid & Steroid Synthesis Inhibitor Profile. <https://www.zrtlab.com/media/2405/lcms-saliva-steroid-profile-pds.pdf>

Policy Update History

Approval Date	Effective Date: Summary of Changes
10/30/2024	01/15/2025: Added code 0462U. No other changes.
06/15/2023	06/15/2023: Document updated with literature review. Reimbursement information revised for clarity. References

	updated; some revised, others removed.
11/1/2022	11/01/2022: New policy