

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: April 28, 2025**

**Plan Effective Date: August 8, 2025**

## Description

The plan 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, 0462U, S3650, S3652 |

## References:

1. ACOG, ASRM. Compounded bioidentical menopausal hormone therapy. *Fertility and sterility*. Aug 2012;98(2):308-12. doi:10.1016/j.fertnstert.2012.06.002
2. Nieman, Biller BM, Findling JW, et al. The diagnosis of Cushing's syndrome: an Endocrine Society Clinical Practice Guideline. *The Journal of clinical endocrinology and metabolism*. May 2008;93(5):1526-40. doi:10.1210/jc.2008-0125
3. Nieman LK. Causes and pathophysiology of Cushing's syndrome. Updated September 19, 2024. <https://www.uptodate.com/contents/causes-and-pathophysiology-of-cushing-syndrome>
4. Lacroix A, Feelders RA, Stratakis CA, Nieman LK. Cushing's syndrome. *Lancet (London, England)*. Aug 29 2015;386(9996):913-27. doi:10.1016/s0140-6736(14)61375-1
5. Quddusi S, Browne P, Toivola B, Hirsch IB. Cushing syndrome due to surreptitious glucocorticoid administration. *Archives of internal medicine*. Feb 09 1998;158(3):294-6. doi:10.1001/archinte.158.3.294
6. Wood P. Salivary steroid assays - research or routine? *Annals of clinical biochemistry*. May 2009;46(Pt 3):183-96. doi:10.1258/acb.2008.008208
7. Conaway E. Bioidentical hormones: an evidence-based review for primary care providers. *The Journal of the American Osteopathic Association*. Mar 2011;111(3):153-64.

8. Flyckt RL, Liu J, Frasure H, Wekselman K, Buch A, Kingsberg SA. Comparison of salivary versus serum testosterone levels in postmenopausal women receiving transdermal testosterone supplementation versus placebo. *Menopause (New York, NY)*. Jul-Aug 2009;16(4):680-8. doi:10.1097/gme.0b013e318199d5c4
9. Lewis JG, McGill H, Patton VM, Elder PA. Caution on the use of saliva measurements to monitor absorption of progesterone from transdermal creams in postmenopausal women. *Maturitas*. Jan 30 2002;41(1):1-6. doi:10.1016/s0378-5122(01)00250-x
10. Hardiman P, Thomas M, Osgood V, Vlassopoulou V, Ginsburg J. Are estrogen assays essential for monitoring gonadotropin stimulant therapy? *Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology*. Dec 1990;4(4):261-9. doi:10.3109/09513599009024980
11. Klee GG, Heser DW. Techniques to measure testosterone in the elderly. *Mayo Clinic proceedings*. Jan 2000;75 Suppl:S19-25. doi:10.1016/S0025-6196(19)30637-8
12. Meulenbergh PM, Ross HA, Swinkels LM, Benraad TJ. The effect of oral contraceptives on plasma-free and salivary cortisol and cortisone. *Clinica chimica acta; international journal of clinical chemistry*. Jun 15 1987;165(2-3):379-85. doi:10.1016/0009-8981(87)90183-5
13. Wren BG, McFarland K, Edwards L, et al. Effect of sequential transdermal progesterone cream on endometrium, bleeding pattern, and plasma progesterone and salivary progesterone levels in postmenopausal women. *Climacteric : the journal of the International Menopause Society*. Sep 2000;3(3):155-60. doi:10.1080/13697130008500109
14. Martin K, Barbieri R. Menopausal hormone therapy: Benefits and risks. UpToDate. Updated August 31. <https://www.uptodate.com/contents/menopausal-hormone-therapy-benefits-and-risks>
15. Taylor HS, Manson JE. Update in hormone therapy use in menopause. *The Journal of clinical endocrinology and metabolism*. Feb 2011;96(2):255-64. doi:10.1210/jc.2010-0536
16. Genova Diagnostics. Menopause™ The Original Genova Salivary Sex-Hormone Test. <https://www.gdx.net/core/sample-reports/Menopause-Sample-Report.pdf>
17. Genova Diagnostics. Hormonal Health. <https://www.gdx.net/hormonal-health>
18. Nieman LK. Measurement of cortisol in serum and saliva. UpToDate. Updated September 29. <https://www.uptodate.com/contents/measurement-of-cortisol-in-serum-and-saliva>
19. Nieman LK. Establishing the diagnosis of Cushing's syndrome. Updated June 28. <https://www.uptodate.com/contents/establishing-the-diagnosis-of-cushing-syndrome>
20. Fleseriu M, Hamrahian AH, Hoffman AR, Kelly DF, Katznelson L. AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY DISEASE STATE CLINICAL REVIEW: DIAGNOSIS OF RECURRENCE IN CUSHING DISEASE. *Endocr Pract*. Dec 2016;22(12):1436-1448. doi:10.4158/ep161512.Dscr
21. ZRTLAB. LCMS Saliva Steroid & Steroid Synthesis Inhibitor Profile. <https://www.zrtlab.com/media/2405/lcms-saliva-steroid-profile-pds.pdf>
22. UnikeyHealth. Salivary Hormone Test. <https://unikeyhealth.com/products/salivary-hormone-test>

23. Genova. Rhythm™. <https://www.gdx.net/product/rhythm-hormone-test-saliva>
24. Genova. Menopause Plus™ <https://www.gdx.net/core/sample-reports/Menopause-Plus-Sample-Report.pdf>
25. Genova. Comprehensive Melatonin Profile.  
<https://www.gdx.net/product/comprehensive-melatonin-test-saliva>
26. Genova. Adrenocortex Stress Profile.  
<https://www.gdx.net/product/adrenocortex-stress-hormone-test-saliva>
27. Spence K, McKeever E, Graham U, et al. Salivary cortisol determination using the Roche generation II assay. 2018; <https://www.endocrine-abstracts.org/ea/0059/ea0059p007>
28. Wurtman. Multiple Sclerosis, Melatonin, and Neurobehavioral Diseases. *Frontiers in endocrinology*. 2017;8:280. doi:10.3389/fendo.2017.00280
29. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *Jama*. Jul 17 2002;288(3):321-33. doi:10.1001/jama.288.3.321
30. Schiffer L, Adaway JE, Arlt W, Keevil BG. A liquid chromatography-tandem mass spectrometry assay for the profiling of classical and 11-oxygenated androgens in saliva. *Annals of clinical biochemistry*. Sep 2019;56(5):564-573. doi:10.1177/0004563219847498
31. El-Farhan N, Rees DA, Evans C. Measuring cortisol in serum, urine and saliva - are our assays good enough? *Annals of clinical biochemistry*. May 2017;54(3):308-322. doi:10.1177/0004563216687335
32. Li XS, Li S, Kellermann G. 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*. Feb 1 2018;178:464-472. doi:10.1016/j.talanta.2017.09.062
33. Hinojosa-Amaya JM, Varlamov EV, McCartney S, Fleseriu M. Hypercortisolemia Recurrence in Cushing's Disease; a Diagnostic Challenge. *Frontiers in endocrinology*. 2019;10:740. doi:10.3389/fendo.2019.00740
34. Nunes ML, Vattaut S, Corcuff JB, et al. Late-night salivary cortisol for diagnosis of overt and subclinical Cushing's syndrome in hospitalized and ambulatory patients. *The Journal of clinical endocrinology and metabolism*. Feb 2009;94(2):456-62. doi:10.1210/jc.2008-1542
35. Ueland GÅ, Kellmann R, Jørstad Davidsen M, et al. Bedtime Salivary Cortisol as a Screening Test for Cushing Syndrome in Children. *Journal of the Endocrine Society*. 2021;5(5)doi:10.1210/jendso/bvab033
36. Sakkas D, Howles CM, Atkinson L, et al. A multi-centre international study of salivary hormone oestradiol and progesterone measurements in ART monitoring. *Reprod Biomed Online*. Oct 24 2020;doi:10.1016/j.rbmo.2020.10.012
37. Doi SA, Clark J, Russell AW. Concordance of the late night salivary cortisol in patients with Cushing's syndrome and elevated urine-free cortisol. *Endocrine*. Apr 2013;43(2):327-33. doi:10.1007/s12020-012-9855-0
38. Antonelli G, Ceccato F, Artusi C, Marinova M, Plebani M. Salivary cortisol and cortisone by LC-MS/MS: validation, reference intervals and diagnostic accuracy in Cushing's syndrome. *Clinica chimica acta; international journal of clinical chemistry*. Dec 7 2015;451(Pt B):247-51. doi:10.1016/j.cca.2015.10.004

39. Crewther BT, Obminski Z, Orysiak J, Al-Dujaili EAS. 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*. Jan 2018;32(1)doi:10.1002/jcla.22197
40. Valassi E, Franz H, Brue T, et al. Diagnostic tests for Cushing's syndrome differ from published guidelines: data from ERCUSYN. *Eur J Endocrinol*. May 2017;176(5):613-624. doi:10.1530/eje-16-0967
41. Oldenburg M, Jensen HJ. Saliva cortisol level as a strain parameter for crews aboard merchant ships. *Chronobiol Int*. Jul 2019;36(7):1005-1012. doi:10.1080/07420528.2019.1604540
42. Kim YJ, Kim JH, Hong AR, et al. Stimulated Salivary Cortisol as a Noninvasive Diagnostic Tool for Adrenal Insufficiency. *Endocrinol Metab (Seoul)*. Sep 2020;35(3):628-635. doi:10.3803/EnM.2020.707
43. Kvam Hellan K, Lyngstad M, Methlie P, Løvås K, Husebye ES, Ueland GÅ. Utility of Salivary Cortisol and Cortisone in the Diagnostics of Adrenal Insufficiency. *The Journal of Clinical Endocrinology & Metabolism*. 2024:dgae486. doi:10.1210/clinem/dgae486
44. Goodman NF, Cobin RH, Ginzburg SB, Katz IA, Woode DE. American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the diagnosis and treatment of menopause. *Endocr Pract*. Nov-Dec 2011;17 Suppl 6:1-25. doi:https://doi.org/10.4158/EP.17.S6.1
45. Cobin RH, Goodman NF. American Association of Clinical Endocrinologists and American College of Endocrinology Position Statement on Menopause;2017 Update. *Endocrine Practice*. 2017;23(7):869-881. doi:10.4158/EP171828.PS
46. ACOG AJP, Belinda Yaeger, ASRM. Compounded Bioidentical Menopausal Hormone Therapy. <https://www.acog.org/-/media/project/acog/acogorg/clinical/files/clinical-consensus/articles/2023/11/compounded-bioidentical-menopausal-hormone-therapy.pdf>
47. NAMS. The 2012 hormone therapy position statement of: The North American Menopause Society. *Menopause (New York, NY)*. Mar 2012;19(3):257-71. doi:10.1097/gme.0b013e31824b970a
48. NAMS. The 2022 hormone therapy position statement of The North American Menopause Society. *Menopause: The Journal of the North American Menopause Society*. 2022;doi:10.1097/GME.0000000000002028
49. Santoro N, Braunstein GD, Butts CL, Martin KA, McDermott M, Pinkerton JV. Compounded Bioidentical Hormones in Endocrinology Practice: An Endocrine Society Scientific Statement. *The Journal of clinical endocrinology and metabolism*. Apr 2016;101(4):1318-43. doi:10.1210/jc.2016-1271
50. Nieman. Cushing's syndrome: update on signs, symptoms and biochemical screening. *Eur J Endocrinol*. Oct 2015;173(4):M33-8. doi:10.1530/eje-15-0464

## Policy Update History:

| Approval Date | Effective Date: Summary of Changes                                                                                                                                                                                             |
|---------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 04/28/2025    | 08/08/2025; Document updated with literature review. Reimbursement information unchanged. Removed the following codes: 82626, 82627, 82670, 82671, 82672, 82677, 82679, 82681, 84144, 84402, 84403, 84410. References revised. |
| 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                                                                                                                                                                                                         |