



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. BCBSNM 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 (“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.

## ANA/ENA Testing

**Policy Number: CPCPLAB011**

**Version 1.0**

**Enterprise Medical Policy Committee Approval Date: 1/25/2022**

**Plan Effective Date: May 1, 2022**

## 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. Testing for antinuclear antibodies (ANA) **may be reimbursable** for individuals in whom the clinical suspicion of autoimmune diseases is high based on signs, symptoms, and other factors.
2. ENA panel testing of specific autoantibodies such as nRNP, SS-A, SS-B, Sm, RNP, Sc170, or Jo1 **may be reimbursable** in patients with abnormal, raised antibody titer or abnormal

immunological findings in serum and clinical correlation with the appropriate autoimmune disorder.

3. Testing of dsDNA **may be reimbursable** up to four (4) times per year after an initial positive ANA test, and clinical correlation.
4. Testing of specific antibodies when ANA test is negative or low positive **may be reimbursable** only in the following situations:
  - a. Testing for Anti-Jo-1 in unique clinical subset of myositis
  - b. Testing for Anti-SSA in the setting of lupus or Sjögren’s syndrome
5. Monitoring of disease with ANA testing or ANA titers **is not reimbursable**
6. ANA and/or ENA testing of individuals with nonspecific symptoms including, but not limited to, fatigue and musculoskeletal pain if not present with other symptoms suggestive of SLE, **is not reimbursable**.
7. Testing of ANA and/or ENA **is not reimbursable** in individuals during wellness visits or general encounters without abnormal findings.
8. Testing of specific antibodies in the absence of a positive ANA test **is not reimbursable** in all other situations.
9. The use of cell-bound complement activation products (e.g., AVISE Lupus) **is not reimbursable** for the diagnosis of systemic lupus erythematosus (SLE).
10. Any other serum biomarker panel testing with proprietary algorithms and/or index scores for the diagnosis of systemic lupus erythematosus or connective tissue diseases (e.g., Avise CTD) **is not reimbursable** for all applications.

## Procedure Codes

Codes
81599, 86038, 86039, 86225, 86325, 0039U, 0062U

## References:

AAP. (2019). American Academy of Pediatrics – Section on Rheumatology. Retrieved from <http://www.choosingwisely.org/clinician-lists/aap-sorh-ana-and-other-autoantibody-testing-without-specific-signs-of-autoimmune-disease/>

ACR. (1997). 1997 Update of the 1982 American College of Rheumatology Revised Criteria for Classification of Systemic Lupus Erythematosus. Retrieved from <https://www.rheumatology.org/Portals/0/Files/1997%20Update%20of%201982%20Revised.pdf>

ACR. (2015). Position Statement on Methodology of Testing for Antinuclear Antibodies. Retrieved from <https://www.rheumatology.org/Portals/0/Files/Methodology%20of%20Testing%20Antinuclear%20Antibodies%20Position%20Statement.pdf>

ACR. (2019). Position Statements. Retrieved from <https://www.rheumatology.org/Practice-Quality/Administrative-Support/Position-Statements>

Aggarwal, A. (2014). Role of autoantibody testing. *Best Pract Res Clin Rheumatol*, 28(6), 907-920. doi:10.1016/j.berh.2015.04.010

Aringer, M., Costenbader, K., Daikh, D., Brinks, R., Mosca, M., Ramsey-Goldman, R., . . . Johnson, S. R. (2019). 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. *Ann Rheum Dis*, 78(9), 1151-1159. doi:10.1136/annrheumdis-2018-214819

AVISE. (2020). AVISE Testing Exclusively from Exagen Inc. . Retrieved from <https://avisetest.com/provider/>

Bhana, S. (2019). Antinuclear Antibodies (ANA). ACR. Retrieved from <https://www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Antinuclear-Antibodies-ANA#:~:text=The%20antibodies%20that%20target%20%E2%80%9Cnormal,can%20indicate%20a%20autoimmune%20disease.>

Bloch, D. (2019). Measurement and clinical significance of antinuclear antibodies - UpToDate. UpToDate. Retrieved from [https://www.uptodate.com/contents/measurement-and-clinical-significance-of-antinuclear-antibodies?source=history\\_widget](https://www.uptodate.com/contents/measurement-and-clinical-significance-of-antinuclear-antibodies?source=history_widget)

Bloch, D. (2020, 4/20/20). Antibodies to double-stranded (ds)DNA, Sm, and U1 RNP. UpToDate. Retrieved from <https://www.uptodate.com/contents/antibodies-to-double-stranded-ds-dna-sm-and-u1-rnp>

BSR. (2018). Recommendations 2018. Retrieved from <http://www.choosingwisely.co.uk/i-am-a-clinician/recommendations/#1528717503996-57a4ac0d-2345>

CDC. (2018, 10/17/2018). Systemic Lupus Erythematosus (SLE). Retrieved from <https://www.cdc.gov/lupus/facts/detailed.html#diagnose>

Chan, E. K., Damoiseaux, J., Carballo, O. G., Conrad, K., de Melo Cruvinel, W., Francescantonio, P. L., . . . Andrade, L. E. (2015). Report of the First International Consensus on Standardized Nomenclature of Antinuclear Antibody HEp-2 Cell Patterns 2014-2015. *Front Immunol*, 6, 412. doi:10.3389/fimmu.2015.00412

Chan, E. K., Damoiseaux, J., de Melo Cruvinel, W., Carballo, O. G., Conrad, K., Francescantonio, P. L., . . . Andrade, L. E. (2016). Report on the second International Consensus on ANA Pattern (ICAP) workshop in Dresden 2015. *Lupus*, 25(8), 797-804. doi:10.1177/0961203316640920

Clarke, A. E., Weinstein, A., Piscitello, A., Heer, A., Chandra, T., Doshi, S., . . . Powell, T. (2020). Evaluation of the Economic Benefit of Earlier Systemic Lupus Erythematosus (SLE) Diagnosis Using a Multivariate Assay Panel (MAP). *ACR Open Rheumatology*, n/a(n/a). doi:<https://doi.org/10.1002/acr2.11177>

CRA. (2019). Five Things Physicians and Patients Should Question. Retrieved from <https://choosingwiselycanada.org/rheumatology/>

Damoiseaux, J., Andrade, L. E., Fritzler, M. J., & Shoenfeld, Y. (2015). Autoantibodies 2015: From diagnostic biomarkers toward prediction, prognosis and prevention. *Autoimmun Rev*, 14(6), 555-563. doi:10.1016/j.autrev.2015.01.017

Dervieux, T., Conklin, J., Ligayon, J. A., Wolover, L., O'Malley, T., Alexander, R. V., . . . Ibarra, C. A. (2017). Validation of a multi-analyte panel with cell-bound complement activation products for systemic lupus erythematosus. *J Immunol Methods*, 446, 54-59. doi:10.1016/j.jim.2017.04.001

Durcan, L., O'Dwyer, T., & Petri, M. (2019). Management strategies and future directions for systemic lupus erythematosus in adults. *Lancet*, 393(10188), 2332-2343. doi:10.1016/s0140-6736(19)30237-5

ESPGHAN. (2019). 2019 Diagnosis and Management of Paediatric Autoimmune Hepatitis. Retrieved from [https://www.espghan.org/knowledge-center/publications/Clinical-Advice-Guides/2019\\_Diagnosis\\_and\\_Management\\_of\\_Paediatric\\_Autoimmune\\_Hepatitis](https://www.espghan.org/knowledge-center/publications/Clinical-Advice-Guides/2019_Diagnosis_and_Management_of_Paediatric_Autoimmune_Hepatitis)

Exagen. (2020). AVISE Lupus. Retrieved from <https://exagen.com/tests/lupus/>

Fava, A., & Petri, M. (2019). Systemic lupus erythematosus: Diagnosis and clinical management. *J Autoimmun*, 96, 1-13. doi:10.1016/j.jaut.2018.11.001

Finzel, S., Schaffer, S., Rizzi, M., & Voll, R. E. (2018). [Pathogenesis of systemic lupus erythematosus]. *Z Rheumatol*, 77(9), 789-798. doi:10.1007/s00393-018-0541-3

Gordon, C., Amissah-Arthur, M.-B., Gayed, M., Brown, S., Bruce, I. N., D'Cruz, D., . . . Guidelines Working, G. (2018). The British Society for Rheumatology guideline for the management of systemic lupus erythematosus in adults. *Rheumatology*, 57(1), e1-e45. doi:10.1093/rheumatology/kex286

Hargraves, M. M., Richmond, H., & Morton, R. (1948). Presentation of two bone marrow elements; the tart cell and the L.E. cell. *Proc Staff Meet Mayo Clin*, 23(2), 25-28. Retrieved from <http://dx.doi.org/>

Hochberg, M. C. (1997). Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum*, 40(9), 1725. doi:10.1002/art.1780400928

ImmunArray. (2016). What is SLE-key? Retrieved from <http://sle-key.com/what-is-sle-key/>

ImmunArray. (2017). Using the SLE-key® Rule-Out Test in Clinical Practice. Retrieved from <http://sle-key.com/wp-content/uploads/2017/05/Using-the-SLE-key-Rule-Out-Test-in-Clinical-Practice.pdf>

Keeling, S. O., Alabdurubalnabi, Z., Avina-Zubieta, A., Barr, S., Bergeron, L., Bernatsky, S., . . . Santesso, N. (2018). Canadian Rheumatology Association Recommendations for the Assessment and Monitoring of Systemic Lupus Erythematosus. *J Rheumatol*, 45(10), 1426-1439. doi:10.3899/jrheum.171459

Kim, J., Lee, W., Kim, G. T., Kim, H. S., Ock, S., Kim, I. S., & Jeong, S. (2019). Diagnostic utility of automated indirect immunofluorescence compared to manual indirect immunofluorescence for

anti-nuclear antibodies in patients with systemic rheumatic diseases: A systematic review and meta-analysis. *Semin Arthritis Rheum*, 48(4), 728-735. doi:10.1016/j.semarthrit.2018.03.015

Knobler, R., Moinzadeh, P., Hunzelmann, N., Kreuter, A., Cozzio, A., Mouthon, L., . . . Krieg, T. (2017). European Dermatology Forum S1-guideline on the diagnosis and treatment of sclerosing diseases of the skin, Part 1: localized scleroderma, systemic sclerosis and overlap syndromes. *Journal of the European Academy of Dermatology and Venereology*, 31(9), 1401-1424. doi:10.1111/jdv.14458

LFA. (2019, 05/01/2019). Lupus Foundation of America Survey: More than Half of Americans Lack Awareness, Understanding of Lupus. Retrieved from <https://www.lupus.org/news/lupus-foundation-of-america-survey-more-than-half-of-americans-lack-awareness-understanding-of-lupus#>

Liang, E., Taylor, M., & McMahon, M. (2020). Utility of the AVISE Connective Tissue Disease test in predicting lupus diagnosis and progression. *Lupus Science & Medicine*, 7(1), e000345. doi:10.1136/lupus-2019-000345

Mieli-Vergani, G., Vergani, D., Baumann, U., Czubkowski, P., Debray, D., Dezsofi, A., . . . Hadzic, N. (2018). Diagnosis and Management of Pediatric Autoimmune Liver Disease: ESPGHAN Hepatology Committee Position Statement. *J Pediatr Gastroenterol Nutr*, 66(2), 345-360. doi:10.1097/mpg.0000000000001801

Mosca, M., Costenbader, K. H., Johnson, S. R., Lorenzoni, V., Sebastiani, G. D., Hoyer, B. F., . . . Touma, Z. (2019). Brief Report: How Do Patients With Newly Diagnosed Systemic Lupus Erythematosus Present? A Multicenter Cohort of Early Systemic Lupus Erythematosus to Inform the Development of New Classification Criteria. *Arthritis Rheumatol*, 71(1), 91-98. doi:10.1002/art.40674

Mossell, J., Goldman, J. A., Barken, D., & Alexander, R. V. (2016). The Avise Lupus Test and Cell-bound Complement Activation Products Aid the Diagnosis of Systemic Lupus Erythematosus. *Open Rheumatol J*, 10, 71-80. doi:10.2174/1874312901610010071

Oglesby, A., Korves, C., Laliberté, F., Dennis, G., Rao, S., Suthoff, E. D., . . . Duh, M. S. (2014). Impact of early versus late systemic lupus erythematosus diagnosis on clinical and economic outcomes. *Appl Health Econ Health Policy*, 12(2), 179-190. doi:10.1007/s40258-014-0085-x

Petri, M., Orbai, A. M., Alarcón, G. S., Gordon, C., Merrill, J. T., Fortin, P. R., . . . Magder, L. S. (2012). Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum*, 64(8), 2677-2686. doi:10.1002/art.34473

Putterman, C., Furie, R., Ramsey-Goldman, R., Askanase, A., Buyon, J., Kalunian, K., . . . Dervieux, T. (2014). Cell-bound complement activation products in systemic lupus erythematosus: comparison with anti-double-stranded DNA and standard complement measurements. *Lupus Sci Med*, 1(1), e000056. doi:10.1136/lupus-2014-000056

Ramsey-Goldman, R., Alexander, R. V., Massarotti, E. M., Wallace, D. J., Narain, S., Arriens, C., . . . Weinstein, A. (2020). Complement Activation in Patients With Probable Systemic Lupus Erythematosus and Ability to Predict Progression to American College of Rheumatology-

Classified Systemic Lupus Erythematosus. *Arthritis Rheumatol*, 72(1), 78-88.  
doi:10.1002/art.41093

Rees, F., Doherty, M., Grainge, M. J., Lanyon, P., & Zhang, W. (2017). The worldwide incidence and prevalence of systemic lupus erythematosus: a systematic review of epidemiological studies. *Rheumatology (Oxford)*, 56(11), 1945-1961. doi:10.1093/rheumatology/kex260

Rouster-Stevens, K. A., Ardoin, S. P., Cooper, A. M., Becker, M. L., Dragone, L. L., Huttenlocher, A., . . . Ferguson, P. J. (2014). Choosing Wisely: the American College of Rheumatology's Top 5 for pediatric rheumatology. *Arthritis Care Res (Hoboken)*, 66(5), 649-657. doi:10.1002/acr.22238

Satoh, M., Chan, E. K., Sobel, E. S., Kimpel, D. L., Yamasaki, Y., Narain, S., . . . Reeves, W. H. (2007). Clinical implication of autoantibodies in patients with systemic rheumatic diseases. *Expert Rev Clin Immunol*, 3(5), 721-738. doi:10.1586/1744666x.3.5.721

Selmi, C., Ceribelli, A., Generali, E., Scire, C. A., Alborghetti, F., Colloredo, G., . . . Meroni, P. L. (2016). Serum antinuclear and extractable nuclear antigen antibody prevalence and associated morbidity and mortality in the general population over 15 years. *Autoimmun Rev*, 15(2), 162-166. doi:10.1016/j.autrev.2015.10.007

Simon, T. A., Kawabata, H., Ray, N., Baheti, A., Suissa, S., & Esdaile, J. M. (2017). Prevalence of Co-existing Autoimmune Disease in Rheumatoid Arthritis: A Cross-Sectional Study. *Adv Ther*, 34(11), 2481-2490. doi:10.1007/s12325-017-0627-3

Sirotti, S., Generali, E., Ceribelli, A., Isailovic, N., De Santis, M., & Selmi, C. (2017). Personalized medicine in rheumatology: the paradigm of serum autoantibodies. *Auto Immun Highlights*, 8(1), 10. doi:10.1007/s13317-017-0098-1

Suurmond, J., & Diamond, B. (2015). Autoantibodies in systemic autoimmune diseases: specificity and pathogenicity. *J Clin Invest*, 125(6), 2194-2202. doi:10.1172/jci78084

Tan, E. M. (1989). Antinuclear antibodies: diagnostic markers for autoimmune diseases and probes for cell biology. *Adv Immunol*, 44, 93-151. Retrieved from <http://dx.doi.org/>

Tebo, A. E. (2017). Recent Approaches To Optimize Laboratory Assessment of Antinuclear Antibodies. *Clin Vaccine Immunol*, 24(12). doi:10.1128/cvi.00270-17

Thong, B., & Olsen, N. J. (2017). Systemic lupus erythematosus diagnosis and management. *Rheumatology (Oxford)*, 56(suppl\_1), i3-i13. doi:10.1093/rheumatology/kew401

Tipu, H., & Bashir, M. (2018). Determination Of Specificity And Pattern Of Antinuclear Antibodies (ana) In Systemic Rheumatic Disease Patients Positive For Ana Testing. *Journal of College of Physicians And Surgeons Pakistan*, 28, 40-43. doi:10.29271/jcpsp.2018.01.40

Tonutti, E., Bizzaro, N., Morozzi, G., Radice, A., Cinquanta, L., Villalta, D., . . . Bagnasco, M. (2016). The ANA-reflex test as a model for improving clinical appropriateness in autoimmune diagnostics. *Auto Immun Highlights*, 7(1). doi:10.1007/s13317-016-0080-3

van der Pol, P., Bakker-Jonges, L. E., Kuijpers, J., & Schreurs, M. W. J. (2018). Analytical and clinical comparison of two fully automated immunoassay systems for the detection of

autoantibodies to extractable nuclear antigens. *Clin Chim Acta*, 476, 154-159.  
doi:10.1016/j.cca.2017.11.014

Wallace, D. J., Alexander, R. V., O'Malley, T., Khosroshahi, A., Hojjati, M., Loupasakis, K., . . . Dervieux, T. (2019). Randomised prospective trial to assess the clinical utility of multianalyte assay panel with complement activation products for the diagnosis of SLE. *Lupus Science & Medicine*, 6(1), e000349. doi:10.1136/lupus-2019-000349. (Accession No. 31592328)

Wallace, D. J., & Gladman, D. (2019, 12/10/2019). Clinical manifestations and diagnosis of systemic lupus erythematosus in adults. Retrieved from [https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-systemic-lupus-erythematosus-in-adults?search=Clinical%20manifestations%20and%20diagnosis%20of%20systemic%20lupus%20erythematosus%20in%20adults&source=search\\_result&selectedTitle=1~150&usage\\_type=default&display\\_rank=1](https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-systemic-lupus-erythematosus-in-adults?search=Clinical%20manifestations%20and%20diagnosis%20of%20systemic%20lupus%20erythematosus%20in%20adults&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1)

Yazdany, J., Schmajuk, G., Robbins, M., Daikh, D., Beall, A., Yelin, E., . . . The American College of Rheumatology Core Membership, G. (2013). Choosing wisely: The American College of Rheumatology's top 5 list of things physicians and patients should question. *Arthritis Care Res (Hoboken)*, 65(3), 329-339. doi:10.1002/acr.21930

Yeo, A. L., Le, S., Ong, J., Connelly, K., Ojaimi, S., Nim, H., . . . Leech, M. (2020). Utility of repeated antinuclear antibody tests: a retrospective database study. *The Lancet Rheumatology*, 2(7), e412-e417. doi:https://doi.org/10.1016/S2665-9913(20)30084-9

Yoo, I. Y., Oh, J. W., Cha, H. S., Koh, E. M., & Kang, E. S. (2017). Performance of an Automated Fluorescence Antinuclear Antibody Image Analyzer. *Ann Lab Med*, 37(3), 240-247. doi:10.3343/alm.2017.37.3.240

Zucchi, D., Elefante, E., Calabresi, E., Signorini, V., Bortoluzzi, A., & Tani, C. (2019). One year in review 2019: systemic lupus erythematosus. *Clin Exp Rheumatol*, 37(5), 715-722. Retrieved from <https://pubmed.ncbi.nlm.nih.gov/31376267/>

### Policy Update History:

5/1/2022	New policy
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