of Tennessee

Policy

Reimbursement Policy

Biomarker Testing for Autoimmune Rheumatic Disease

I. Policy Description

Systemic autoimmune rheumatic diseases (SARDs) are a diverse group of conditions that primarily affect the joints, bones, muscle, and connective tissue.[1] SARDs are characterized by dysregulated immunity and inflammatory responses, resulting in damage and destruction to joints, connective tissues, skin, blood elements, and other target organs; however, considerable diversity in clinical presentation, disease course, and treatment response exists.[2] The diagnostic workup for SARDs may involve the antinuclear antibody (ANA) assay, which is used to detect autoantibodies (AAB) against intracellular antigens, originally known as antinuclear antibodies.[3] Commonly used as part of the initial diagnostic workup to screen for evidence of systemic autoimmunity,[4] detection and identification of AABs are important in the diagnosis of SARDs, such as systemic lupus erythematosus (SLE), Sjögren's syndrome (SjS), mixed connective tissue disease (MCTD), systemic sclerosis (SSc), and idiopathic inflammatory myopathies (IIMs).[5] Extractable nuclear antigens or ENAs (a historical term from when the antigens were extracted from the cell into saline solution prior to testing) include Sm, U1 ribonucleoprotein (RNP), Ro, and La antigens, and are also useful for evaluating individuals with suspected connective tissue disease.[6]

II. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. Specifications pertaining to Medicare and Medicaid can be found in the "Applicable State and Federal Regulations" section of this policy document.

1) For individuals with signs or symptoms of an autoimmune disease, screening for disease using antinuclear antibodies (ANA) **MEETS COVERAGE CRITERIA:**
2) Once during initial workup.
3) Up to two additional tests per lifetime if new or more severe signs or symptoms of an autoimmune disease develop.
4) For individuals with an abnormal, raised ANA titer and a clinical correlation with the appropriate autoimmune disorder, extractable nuclear antigens (ENA) panel testing of specific autoantibodies **MEETS COVERAGE CRITERIA.**

5) For individuals with painful and swollen joints suggestive of rheumatoid arthritis (RA), testing for rheumatoid factor (RF) and/or anti-cyclic citrullinated peptide (anti-CCP) antibodies **MEETS COVERAGE CRITERIA:**
   a) Once during initial workup.
   If initial testing did not result in a diagnosis of RA, up to two additional tests per lifetime if symptoms persist or additional symptoms of RA develop.
6) For individuals with an initial positive ANA test and a diagnosis of systemic autoimmune rheumatic disease, testing of dsDNA up to four (4) times per year **MEETS COVERAGE CRITERIA.**
7) For individuals with a negative or low positive ANA test, the following condition specific antibody testing **MEETS COVERAGE CRITERIA:**
   a) Testing for anti-Jo-1 in a unique clinical subset of myositis.
   b) Testing for anti-SSA in the setting of lupus or Sjögren's syndrome.
8) Monitoring of disease with ANA testing or ANA titers **DOES NOT MEET COVERAGE CRITERIA.**
9) For individuals without symptoms suggestive of an autoimmune disorder, ANA and/or ENA testing **DOES NOT MEET COVERAGE CRITERIA.**
10) For all other situations not described above, testing of specific antibodies in the absence of a positive ANA test **DOES NOT MEET COVERAGE CRITERIA.**
11) For asymptomatic individuals, testing of ANA and/or ENA during a wellness visit or a general exam without abnormal findings **DOES NOT MEET COVERAGE CRITERIA.** *The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual's illness.*
12) For the diagnosis of RA, testing for serum biomarkers not discussed above, alone or in a panel (e.g., Seronegative Rheumatoid Arthritis Profile), **DOES NOT MEET COVERAGE CRITERIA.**
13) For the management of RA, serum biomarker panel testing (e.g., Vectra DA score, PrismRA) **DOES NOT MEET COVERAGE CRITERIA**.
14) For the diagnosis of systemic lupus erythematosus (SLE), the use of cell-bound complement activation products (e.g., AVISE Lupus) **DOES NOT MEET COVERAGE CRITERIA.**
15) For the diagnosis, prognosis, or monitoring of SLE or connective tissue diseases, serum biomarker panel testing with proprietary algorithms and/or index scores (e.g., AVISE CTD, AVISE SLE Monitor, AVISE SLE Prognostic, aisle® DX Disease Activity Index, Early Sjögren's Syndrome Profile) **DOES NOT MEET COVERAGE CRITERIA.**

III. Applicable State and Federal Regulations

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DISCLAIMER: If there is a conflict between this Policy and any relevant, applicable government policy for a particular member [e.g., Local Coverage Determinations (LCDs) or National Coverage Determinations (NCDs) for Medicare and/or state coverage for Medicaid], then the government policy will be used to make the determination. For the most up-to-date Medicare policies and coverage, please visit the Medicare search website: https://www.cms.gov/medicare-coverage-database/search.aspx. For the most up-to-date Medicaid policies and coverage, visit the applicable state Medicaid website.

Food and Drug Administration (FDA)
Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

IV. Applicable CPT/HCPCS Procedure Codes

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CPT	Code Description
*81490	Autoimmune (rheumatoid arthritis), analysis of 12 biomarkers using immunoassays, utilizing serum, prognostic algorithm reported as a disease activity score Proprietary test: Vectra®DA Lab/Manufacturer: Crescendo Bioscience, Inc. ***This is considered experimental and investigative**
81599	Unlisted multianalyte assay with algorithmic analysis
86038	Antinuclear antibodies (ANA)
86039	Antinuclear antibodies (ANA); titer
86200	Cyclic citrullinated peptide (CCP), antibody
86225	Deoxyribonucleic acid (DNA) antibody; native or double stranded
86235	Extractable nuclear antigen, antibody to, any method (eg, nRNP, SS-A, SS-B, Sm, RNP, Sc170, J01), each antibody
86430	Rheumatoid factor; qualitative
86431	Rheumatoid factor; quantitative
0039U	Deoxyribonucleic acid (DNA) antibody, double stranded, high avidity Proprietary test: Anti-dsDNA, High Salt/Avidity Lab/Manufacturer: University of Washington, Department of Laboratory Medicine/Bio-Rad
0062U	"Autoimmune (systemic lupus erythematosus), IgG and IgM analysis of 80 biomarkers, utilizing serum, algorithm reported with a risk score Proprietary test: SLE-key® Rule Out Lab/Manufacturer: Veracis Inc"

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CPT	Code Description
0312U	"Autoimmune diseases (eg, systemic lupus erythematosus [SLE]), analysis of 8 IgG autoantibodies and 2 cell-bound complement activation products using enzyme-linked immunosorbent immunoassay (ELISA), flow cytometry and indirect immunofluorescence, serum, or plasma and whole blood, individual components reported along with an algorithmic SLE-likelihood assessment Proprietary test: Avise® Lupus Lab/Manufacturer: Exagen Inc"
0446U	Autoimmune diseases (systemic lupus erythematosus [SLE]), analysis of 10 cytokine soluble mediator biomarkers by immunoassay, plasma, individual components reported with an algorithmic risk score for current disease activity Proprietary test: aisle® DX Disease Activity Index Lab/Manufacturer: Progenotes Diagnostics, Inc
0447U	Autoimmune diseases (systemic lupus erythematosus [sle]), analysis of 11 cytokine soluble mediator biomarkers by immunoassay, plasma, individual components reported with an algorithmic prognostic risk score for developing a clinical flare Proprietary test: aisle® DX Disease Activity Index Lab/Manufacturer: Progenotes Diagnostics, Inc
0521U	Rheumatoid factor IgA and IgM, cyclic citrullinated peptide (CCP) antibodies, and scavenger receptor A (SR-A) by immunoassay, blood Proprietary test: Seronegative Rheumatoid Arthritis Panel Lab Manufacturer: KSL Diagnostics-Beutner Laboratories, Inc, KSL Biomedical, Inc

Procedure codes appearing in Medical Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.

V. Evidence-based Scientific References

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