ADMINISTRATIVE POLICY STATEMENT
Arkansas PASSE

Policy Name & Number	Date Effective
Serum Biomarker Panel Testing-AR PASSE-AD-1014	10/01/2022-10/31/2023
Policy Type	
ADMINISTRATIVE	

Administrative Policy Statement prepared by CareSource and its affiliates are derived from literature based on and supported by clinical guidelines, nationally recognized utilization and technology assessment guidelines, other medical management industry standards, and published MCO clinical policy guidelines. Medically necessary services include, but are not limited to, those health care services or supplies that are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part, or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative, and are not provided mainly for the convenience of the member or provider. Medically necessary services also include those services defined in any Evidence of Coverage documents, Medical Policy Statements, Provider Manuals, Member Handbooks, and/or other policies and procedures.

Administrative Policy Statements prepared by CareSource and its affiliates do not ensure an authorization or payment of services. Please refer to the plan contract (often referred to as the Evidence of Coverage) for the service(s) referenced in the Administrative Policy Statement. If there is a conflict between the Administrative Policy Statement and the plan contract (i.e., Evidence of Coverage), then the plan contract (i.e., Evidence of Coverage) will be the controlling document used to make the determination.

According to the rules of Mental Health Parity Addiction Equity Act (MHPAEA), coverage for the diagnosis and treatment of a behavioral health disorder will not be subject to any limitations that are less favorable than the limitations that apply to medical conditions as covered under this policy.

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A. Subject

Serum Biomarker Panel Testing in Systemic Lupus Erythematosus and Rheumatoid Arthritis

B. Background

Rheumatoid arthritis (RA) is an autoimmune and inflammatory disease which mainly attacks the joints, most commonly the hands, wrists, and knees. In a joint affected by RA, the lining of the joint becomes inflamed, causing joint damage, which can lead to chronic pain, unsteadiness, and deformity. RA can also affect other tissues throughout the body, including the lungs, heart, and eyes. Systemic lupus erythematosus (SLE) is the most common type of lupus, an autoimmune disease that causes widespread inflammation and tissue damage to affected organs, which can include the joints, skin, brain, lungs, kidneys, and blood vessels. Individuals with either disease may experience fatigue, fevers, and pain or swelling in the joints. While there is no cure for either disease, medical intervention can improve overall health and delay disease progression.

Both RA and SLE have a widely variable clinical expression, which makes diagnosis difficult. The diagnosis of SLE or RA is often based upon clinical judgement, careful integration of the patient's history, physical findings, and selected laboratory and radiographic tests, often with serial assessments over time. Several sets of classification criteria have been developed for epidemiological and research purposes for SLE. The 1982 American College of Rheumatology (ACR) criteria, revised in 1997, have been widely used to diagnose SLE over the past three decades. More recently, the evidence-based 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria were developed for diagnosing SLE. The estimated sensitivity and specificity of these two methods are 83% and 96% for the ACR, and 97% and 84% for the SLICC criteria, respectively. The 2018 European League Against Rheumatism (EULAR) criteria were developed for research use only, with sensitivity and specificity of 89% and 90%, respectively. Similar diagnostic methods have been developed for RA, including the ACR/EURAL 2010 criteria, which was designed to diagnose RA earlier in patients who may not meet the 1987 ACR classification criteria.

Clinical workups for these diseases may include erythrocyte sedimentation rate, C-reactive protein, complement levels (C3, C4, and CH50), antiphospholipid antibodies, antinuclear antibodies, rheumatoid factor, and anti-citrullinated peptide/protein antibodies. The sensitivity and specificity of these serum immune biomarkers varies considerably among patients, limiting their value. As a result, investigative laboratories have sought to establish proprietary algorithms and index scoring methodologies to assist in establishing a diagnosis, estimating prognosis, and monitoring disease activity. These include, but are not limited to, the following:

The Vectra DA™ test (Crescendo Bioscience Inc.) is a multi-biomarker panel blood test developed by analysis of clinical disease activity and the levels of serum immune markers. Utilizing a weighted algorithm, a single number (ranging from zero to 100) reflecting the multi-biomarker disease activity is calculated. This value is proposed to correlate with disease activity (i.e., low = 1 to 29, moderate = 30 to 44, and high > 44). While Vectra DA™ is not a diagnostic test and does not guide selection of specific pharmacologic agents or therapies, it has been suggested that results may inform

treatment decisions of rheumatologists in the outpatient setting when used in combination with more standard clinical assessments. Peer-reviewed published literature demonstrates the overall quality of the industry-sponsored evidence is low with conflicting data. There are no long-term outcome studies.

The Avise tests (Exagen Diagnostics) are commercially available panels meant to diagnose, prognose, and monitor SLE, containing a variety of different biomarkers. Peer-reviewed published literature also demonstrates an overall low quality of evidence for these industry-sponsored studies, with no independent validation to assess the safety or impact on health outcomes or patient management.

While clinical laboratories may develop, validate, and market tests under the regulatory standards of the Centers for Medicare & Medicaid Services (CMS) Clinical Laboratory Improvement Act (CLIA) of 1988, these regulatory standards do not establish the validity or utility of Vectra DA, Avise, and other clinically available tests.

C. Definitions

- **Rheumatoid Arthritis** (RA) - A symmetric, inflammatory, peripheral polyarthritis of unknown etiology. It typically leads to deformity through the stretching of tendons and ligaments and destruction of joints through the erosion of cartilage and bone. If it is untreated or unresponsive to therapy, inflammation and joint destruction lead to loss of physical function, inability to carry out daily tasks of living, and difficulties in maintaining employment.
- **Systemic Lupus Erythematosus** (SLE) - A chronic inflammatory disease of unknown cause that most commonly affects the skin, heart, joints, lungs, blood vessels, liver, kidneys, and/or nervous system. Immunologic abnormalities, especially the production of a number of antinuclear antibodies (ANA), are a prominent feature of the disease. Symptoms may include severe joint and muscle pain that impacts quality of life and ability to function, cognitive impairment, lupus nephritis, fibromyalgia, and alopecia. SLE also increases risks of infection, cancer, avascular necrosis, and complications in pregnancy such as preeclampsia and preterm birth.
- **Biomarkers** - biologic characteristic that can be objectively measured to serve as an indicator of normal or pathologic processes or as measures of the response to therapy.

D. Policy

I. CareSource considers the following laboratory-developed biomarker panel tests (not an all-inclusive list) experimental, investigational, and not medically necessary for the diagnosis, prognosis, and/or management of RA, SLE, and all other indications based on a lack of evidence in current peer-reviewed medical literature and insufficient evidence of clinical validity:

- Anti-dsDNA, high salt/avidity lab test (University of Washington).
- Avise CTD.
- Avise Lupus.
- Avise Vasculitis-AAV.
- Avise SLE Prognostic.

The ADMINISTRATIVE Policy Statement detailed above has received due consideration as defined in the ADMINISTRATIVE Policy Statement Policy and is approved.

- Avise Anti-CarP.
- Avise SLE Monitor.
- Avise MTX.
- Avise HCQ.
- SLE-key Rule Out test (Veracis Inc.).
- Vectra DA™ panel.

There is insufficient documentation in the medical literature to determine whether these tests are as good as or better than other measures of disease activity, and their clinical utility for improving patient clinical outcomes has not been proven.

E. Conditions of Coverage

NA

F. Related Policies/Rules

Experimental or Investigational Item or Service

G. Review/Revision History

	DATES	ACTION
Date Issued	01/06/2021	
Date Revised	07/06/2022	Annual review: updated references, background, definitions, re-organized coverage information, added test names
Date Effective	10/01/2022	
Date Archived	10/31/2023	This Policy is no longer active and has been archived. Please note that there could be other Policies that may have some of the same rules incorporated and CareSource reserves the right to follow CMS/State/NCCI guidelines without a formal documented Policy.

H. References

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