BSC_CON_2.21	Genetic Testing: Immune, Autoimmune, and Rheumatoid Disorders		
Original Policy Date:	December 1, 2023	**Effective Date:**	December 1, 2023
Section:	2.0 Medicine	**Page:**	Page 1 of 12

Example Test Table

The tests and associated laboratories and CPT codes contained within this document serve only as examples to help users navigate claims and corresponding coverage criteria; as such, they are not comprehensive and are not a guarantee of coverage or non-coverage. Please see the Concert Genetics Platform for a comprehensive list of registered tests.

Policy Statement Sections	Example Tests (Labs)	Common CPT Codes
Known Familial Variant Analysis for Immune, Autoimmune, and Rheumatoid Disorders		
Known Familial Variant Analysis for Immune, Autoimmune, and Rheumatoid Disorders	Targeted Mutation Analysis for a Known Familial Variant	81403
Periodic Fever Syndromes		
Periodic Fever Syndromes Multigene Panel	Periodic Fever Syndromes Panel (Invitae)	81404, 81479
	Periodic Fever Syndromes Panel (PreventionGenetics, part of Exact Sciences)	
	Periodic Fever Syndromes Panel (7 genes) (GeneDx)	
Rheumatoid Arthritis Biomarker Activity Panels		
Rheumatoid Arthritis Biomarker Activity Panels	Vectra (Labcorp)	81490
	Vectra with CV Risk (Labcorp)	
Genetic Algorithmic Rheumatoid Arthritis Tests		
Genetic Rheumatoid Arthritis for Tumor Necrosis Factor inhibitor (TNFi) Treatment	PrismRA (Scipher Medicine)	81599, 81479
HLA Typing for Ankylosing Spondylitis, Rheumatoid Arthritis, and Autoimmune Disorders		
HLA Typing for Ankylosing Spondylitis, Rheumatoid Arthritis, and Autoimmune Disorders	HLA-B27 DNA Typing (Quest Diagnostics)	81374
	HLA-B51 Behcet's Disease Association Test (Quest Diagnostics)	
	HLA DRB1 Typing, High Resolution (Quest Diagnostics)	81382

Policy Statement Sections	Example Tests (Labs)	Common CPT Codes
Other Covered Immune, Autoimmune, and Rheumatoid Disorders		
Other Covered Immune Disorders	See below	81400, 81401, 81402, 81403, 81404, 81405, 81406, 81407, 81408

Policy Statement

KNOWN FAMILIAL VARIANT ANALYSIS FOR IMMUNE, AUTOIMMUNE, AND RHEUMATOID DISORDERS

I. Targeted mutation analysis for a known familial variant (81403) for an immune, autoimmune, and rheumatoid disorder may be considered **medically necessary** when:
   A. The member has a close relative with a known pathogenic or likely pathogenic variant causing the condition.

II. Targeted mutation analysis for a known familial variant (81403) for an immune, autoimmune, and rheumatoid disorder is considered **investigational** for all other indications.

PERIODIC FEVER SYNDROME

Periodic Fever Syndromes Multigene Panel

III. Genetic testing for periodic fever syndromes, also called hereditary recurrent fever syndromes, (e.g., Familial Mediterranean Fever, tumor necrosis factor receptor-associated periodic fever [TRAPS]) via multigene panel (81404, 81479) may be considered **medically necessary** when **BOTH** of the following criteria are met:
   A. The member has three or more episodes of unexplained fever in a six-month period, occurring at least seven days apart
   B. Common causes of fever have been ruled out, including viral or bacterial infection.

IV. Genetic testing for periodic fever syndromes, also called hereditary recurrent fever syndromes, (e.g., Familial Mediterranean Fever, tumor necrosis factor receptor-associated periodic fever [TRAPS]) via multigene panel (81404, 81479) is considered **investigational** for all other indications.

RHEUMATOID ARTHRITIS BIOMARKER ACTIVITY PANELS

Rheumatoid Arthritis Biomarker Activity Panels

V. The use of multibiomarker disease activity scores for rheumatoid arthritis (81490) is considered **investigational**.

GENETIC ALGORITHMIC RHEUMATOID ARTHRITIS TESTS

Tumor Necrosis Factor Inhibitor (TNFi) Treatment

VI. The use of genetic algorithmic rheumatoid arthritis tests to determine appropriateness of TNFi treatment (i.e., PrismRA) (81599, 81479) is considered **investigational**.

HLA TYPING FOR ANKYLOSING SPONDYLITIS, RHEUMATOID ARTHRITIS, AND AUTOIMMUNE DISORDERS

VII. The use of HLA-B27 typing (81374, 81382) to confirm or establish the diagnosis of ankylosing spondylitis, or another spondyloarthropathies, may be considered **medically necessary** when **BOTH** of the following criteria are met:
   A. The member has clinical or radiographic features of ankylosing spondylitis, or another spondyloarthropathy

B. HLA-B27 results are needed to establish a diagnosis of ankylosing spondylitis, or another spondyloarthropathy.

VIII. The use of HLA typing (81374, 81382) for ankylosing spondylitis, rheumatoid arthritis, and autoimmune disorders is considered **investigational** for all other indications.

OTHER COVERED IMMUNE, AUTOIMMUNE, AND RHEUMATOID DISORDERS

The following is a list of conditions that have a known genetic association. Due to their relative rareness, it may be appropriate to cover these genetic tests to establish or confirm a diagnosis.

IX. Genetic testing to establish or confirm one of the following immune, autoimmune, or rheumatoid disorders to guide management may be considered **medically necessary** when the member demonstrates clinical features* consistent with the disorder (the list is not meant to be comprehensive, see X below):

A. Agammaglobulinemia: X-Linked and Autosomal Recessive
B. Autoimmune Lymphoproliferative Syndrome (ALPS)
C. Chronic Granulomatous Disease (CGD)
D. Common Variable Immune Deficiency (CVID)
E. Complement Deficiencies
F. Congenital Neutropenia Syndromes (e.g., *ELANE*-Related Neutropenia)
G. Familial Hemophagocytic Lymphohistiocytosis (HLH)
H. Hyper IgE Syndrome (HIES)
I. Hyper IgM Syndromes
J. Leukocyte Adhesion Deficiency (LAD)
K. NEMO Deficiency Syndrome
L. Severe Combined Immune Deficiency (SCID) and Combined Immune Deficiency
M. WHIM Syndrome (Warts, Hypogammaglobulinemia, Infections, and Myelokathexis)
N. Wiskott-Aldrich Syndrome

X. Genetic testing to establish or confirm the diagnosis of all other immune, autoimmune, or rheumatoid disorders not specifically discussed within this or another medical policy will be evaluated by the criteria outlined in *General Approach to Genetic and Molecular Testing* (see policy for coverage criteria).

*Clinical features for a specific disorder may be outlined in resources such as GeneReviews, OMIM, National Library of Medicine, Genetics Home Reference, or other scholarly source.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

NOTES AND DEFINITIONS

1. **Close relatives** include first, second, and third degree blood relatives on the same side of the family:
   a. **First-degree relatives** are parents, siblings, and children
   b. **Second-degree relatives** are grandparents, aunts, uncles, nieces, nephews, grandchildren, and half siblings
   c. **Third-degree relatives** are great grandparents, great aunts, great uncles, great grandchildren, and first cousins

2. **Multibiomarker disease activity (MBDA)** tests for rheumatoid arthritis are an approach that uses serum biomarkers to measure rheumatoid arthritis disease activity.

3. **Unexplained fever** (or fever of unknown origin [FUO]) is defined as a temperature higher than 38.3 C (100.9 F) that lasts for more than three weeks with no obvious source despite appropriate investigation. The four categories of potential etiology of FUO are classic, nosocomial, immune deficient, and human immunodeficiency virus–related. The four subgroups of the differential diagnosis of FUO are infections, malignancies, autoimmune conditions, and miscellaneous.

Description

Immunodeficiency disorders typically result from the use of a drug or from a long-lasting significant disorder (e.g., cancer), however a subset of immunodeficiency disorders are inherited. Immunodeficiency disorders impair the immune system's ability to defend the body against foreign substances, such as bacteria, viruses, and cancer cells. As a result, infections or cancers can develop. Individuals with immunodeficiency can also have an autoimmune disorder, such as rheumatoid arthritis.

There are two types of immunodeficiency disorders: primary and secondary. Primary disorders are relatively rare and usually present at birth, genetic in origin, and hereditary; however, some primary immunodeficiency disorders are not recognized until adulthood. Secondary disorders are more common and generally develop later in life as a result of the use of certain drugs or from conditions such as diabetes or HIV infection.

Related Policies

This policy document provides coverage criteria for Genetic Testing for Immune, Autoimmune, and Rheumatoid Disorders. Please refer to:

- ***Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability, and Developmental Delay*** for coverage criteria related to genetic disorders that affect multiple organ systems *(to be published)*
- ***Genetic Testing: General Approach to Genetic and Molecular Testing*** for coverage criteria related to immune disorders not specifically addressed in the policy reference table.

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Rationale

BACKGROUND AND RATIONALE

Known Familial Variant Analysis for Immune, Autoimmune, and Rheumatoid Disorders

Genetic Support Foundation

The Genetic Support Foundation's Genetics 101 information on genetic testing says the following about testing for familial pathogenic variants:

Genetic testing for someone who may be at risk for an inherited disease is always easier if we know the specific genetic cause. Oftentimes, the best way to find the genetic cause is to start by testing someone in the family who is known or strongly suspected to have the disease. If their testing is positive, then we can say that we have found the familial pathogenic (harmful) variant. We can use this as a marker to test other members of the family to see who is also at risk.

Periodic Fever Syndromes Multigene Panel

Soon and Laxer (2017)

A 2017 clinical review by Soon and Laxer addressing recurrent fever in childhood stated the following: "Recurrent or periodic fever syndromes are defined by 3 or more episodes of unexplained fever in a 6-month period, occurring at least 7 days apart." The authors recommend that: "Once infections, immunodeficiency, malignancy, inflammatory bowel disease, and adverse drug reactions have been ruled out, autoinflammatory diseases–including periodic fever syndromes–should be considered."

Rheumatoid Arthritis Biomarker Activity Panels

American College of Rheumatology

In 2019, The American College of Rheumatology updated guidelines on the treatment of rheumatoid arthritis (2019). In this update, the following 11 measures of disease activity were identified as fulfilling a minimum standard for regular use in most clinical settings:

Disease Activity Score (DAS)
Routine Assessment of Patient Index Data 3 (RAPID3)
Routine Assessment of Patient Index Data 5 (RAPID5)
Clinical Disease Activity Index (CDAI)
Disease Activity Score with 28 joints (DAS28-ESR/CRP)
Patient Derived DAS28, Hospital Universitario La Princesa Index (HUPI)
Multibiomarker Disease Activity Score (MBDA score, Vectra DA)
Rheumatoid Arthritis Disease Activity Index (RADAI)
Rheumatoid Arthritis Disease Activity Index 5 (RADAI-5)
Simplified Disease Activity Index (SDAI)

Although the original Vectra DA test is included in this list, the current commercially available version of the test that is now called Vectra, includes the leptin-adjusted MBDA score (now called the "adjusted MBDA score") that was not addressed in the 2019 ACR guideline. This is because evidence on Vectra with the adjusted MBDA score was published subsequent to the ACR review end date.

ter Haar, et. al 2015

An expert committee of pediatric and adult rheumatologists convened and created a set of recommendations for the management of autoinflammatory disease, using the European League Against Rheumatism standard operating procedure, that included the following regarding genetic evaluation:

- Management of patients with AID should ideally be guided by a multidisciplinary team in a tertiary centre with expertise in AID, with access to genetic counseling (Expert opinion, based on level 4 evidence).

Genetic Algorithmic Rheumatoid Arthritis Tests - Genetic Rheumatoid Arthritis for Tumor Necrosis Factor Inhibitor (TNFi) Treatment

Concert Genetics

The 2021 statement for the treatment of rheumatoid arthritis by the American College of Rheumatology includes recommendations for genetic testing to determine the effectiveness of TNFi therapy. The peer-reviewed published clinical utility studies show there is the possibility of management changes and improved outcomes based on results of PrismRA. However, these studies have flaws, such as concern for investigator group bias and lack of randomization, as well as limited study population. Additional real-world evidence on larger and more diverse populations is needed.

At the present time, Genetic Algorithmic Rheumatoid Arthritis Tests for Anti-Tumor Necrosis Factor Inhibitor (TNFi) Treatment tests such as PrismRA have insufficient evidence in peer-reviewed publications to effectively result in improved health outcomes compared to the current standard of care.

HLA Typing for Ankylosing Spondylitis, Rheumatoid Arthritis, and Autoimmune Disorders
Rudwaleit et al 2009
"Refinement of the candidate criteria resulted in new ASAS [Assessment of SpondyloArthritis International Society] classification criteria that are defined as: the presence of sacroiliitis by radiography or by magnetic resonance imaging (MRI) plus at least one SpA feature ("imaging arm") or the presence of HLA-B27 plus at least two SpA features ("clinical arm")."

Akgul and Ozgocmen, 2011
"HLA B-27 positivity is extremely relevant to the early diagnosis of SpA [spondyloarthropathies]. Five to 10% of the population are HLA B-27 positive and in patients with AS [ankylosing spondylitis] and SpA the positivity of HLA B-27 changes to 70% to 95% and nearly 70%, respectively."

Yu and van Tubergen, UpToDate, 2020
"HLA-B27 can be useful to increase the confidence of a diagnosis of axSpA [axial spondyloarthritis] in patients in whom plain radiographs or magnetic resonance imaging (MRI) also exhibit abnormalities consistent with axSpA. HLA-B27 can also be used as a screening tool in primary care in patients presenting with chronic back pain or IBP [inflammatory back pain] suspected by the primary clinician as having a significant probability for axSpA, depending upon the availability and the costs of local HLA-B27 testing. Several diagnostic criteria sets include HLA-B27, including the Amor criteria, and ASAS [Assessment of SpondyloArthritis International Society] axial and peripheral spondyloarthritis criteria."

References

1. England BR, Tiong BK, Bergman MJ, et al. 2019 Update of the American College of Rheumatology Recommended Rheumatoid Arthritis Disease Activity Measures. Arthritis Care Res (Hoboken). 2019;71(12):1540-1555. doi:10.1002/acr.24042
2. ter Haar NM, Oswald M, Jeyaratnam J, et al. Recommendations for the management of autoinflammatory diseases. Ann Rheum Dis. 2015;74(9):1636-1644. doi:10.1136/annrheumdis-2015-207546
3. Immune Deficiency Foundation. "Specific PI Diagnoses". 2020. https://primaryimmune.org/specific-pi-diagnoses. Accessed February 22, 2021.
4. Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1116/
5. Online Mendelian Inheritance in Man, OMIM. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD). World Wide Web URL: https://omim.org/
6. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US). Available from: https://medlineplus.gov/genetics/.
7. Rudwaleit M, van der Heijde D, Landewe R, et al. The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis. Jun 2009;68(6):777-83. doi:10.1136/ard.2009.108233
8. Akgul O, Ozgocmen S. Classification criteria for spondyloarthropathies. World J Orthop. 2011;2(12):107-115. doi:10.5312/wjo.v2.i12.07

9. Yu D, van Tubergen A. Diagnosis and differential diagnosis of axial spondyloarthritis (ankylosing spondylitis and nonradiographic axial spondyloarthritis) in adults. In: Romain PL, ed. UpToDate. UpToDate; 2021. Accessed December 15, 2021. https://uptodate.com/contents/diagnosis-and-differential-diagnosis-of-axial-spondyloarthritis-ankylosing-spondylitis-and-nonradiographic-axial-spondyloarthritis-in-adults
10. Concert Genetics. Evidence Review for Coverage Determination for Genetic Algorithmic Rheumatoid Arthritis Tests for TNFi treatment. V2023.1
11. Soon GS, Laxer RM. Approach to recurrent fever in childhood. Can Fam Physician. 2017;63(10):756-762.
12. Genetic Support Foundation. Genetics 101 Genetic Testing: Familial Pathogenic Variant. Accessed 10/4/2022. https://geneticsupportfoundation.org/genetics-101/#

Documentation for Clinical Review

Please provide the following documentation:

- Name of the test being requested or the Concert Genetics GTU identifier.
  The Concert Genetics GTU can be found at https://app.concertgenetics.com
- CPT codes to be billed for the particular genetic test (GTU required for unlisted codes)
- History and physical and/or consultation notes including:
  - Clinical findings:
    - Signs/symptoms leading to a suspicion of genetic condition
    - Family history if applicable
  - Prior evaluation/treatment:
    - Previous test results (i.e., imagining, lab work, etc.) related to reason for genetic testing
    - Family member's genetic test result, if applicable
  - Rationale
    - Reason for performing test
    - How test result will impact clinical decision making

Post Service (in addition to the above, please include the following):

- Results/reports of tests performed

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	81374	HLA Class I typing, low resolution (e.g., antigen equivalents); one antigen equivalent (e.g., B*27), each
	81382	HLA Class II typing, high resolution (i.e., alleles or allele groups); one locus (e.g., HLA-DRB1, -DRB3/4/5, -DQB1, -DQA1, -DPB1, or -DPA1), each
	81400	MOLECULAR PATHOLOGY PROCEDURE LEVEL 1

Type	Code	Description
	81401	MOLECULAR PATHOLOGY PROCEDURE LEVEL 2
	81402	MOLECULAR PATHOLOGY PROCEDURE LEVEL 3
	81403	MOLECULAR PATHOLOGY PROCEDURE LEVEL 4
	81404	MOLECULAR PATHOLOGY PROCEDURE LEVEL 5
	81405	MOLECULAR PATHOLOGY PROCEDURE LEVEL 6
	81406	MOLECULAR PATHOLOGY PROCEDURE LEVEL 7
	81407	MOLECULAR PATHOLOGY PROCEDURE LEVEL 8
	81408	MOLECULAR PATHOLOGY PROCEDURE LEVEL 9
	81479	Unlisted molecular pathology procedure
	81490	Autoimmune (rheumatoid arthritis), analysis of 12 biomarkers using immunoassays, utilizing serum, prognostic algorithm reported as a disease activity score
	81599	Unlisted multianalyte assay with algorithmic analysis
HCPCS	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
12/01/2023	New policy.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an

authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT	
BEFORE Red font: Verbiage removed	AFTER Blue font: Verbiage Changes/Additions
Multibiomarker Disease Activity Blood Test for Rheumatoid Arthritis 2.04.119 Policy Statement:	Genetic Testing: Immune, Autoimmune, and Rheumatoid Disorders BSC_CON_2.21 Policy Statement: KNOWN FAMILIAL VARIANT ANALYSIS FOR IMMUNE, AUTOIMMUNE, AND RHEUMATOID DISORDERS I. Targeted mutation analysis for a known familial variant (81403) for an immune, autoimmune, and rheumatoid disorder may be considered **medically necessary** when: A. The member has a close relative with a known pathogenic or likely pathogenic variant causing the condition. II. Targeted mutation analysis for a known familial variant (81403) for an immune, autoimmune, and rheumatoid disorder is considered **investigational** for all other indications. PERIODIC FEVER SYNDROME Periodic Fever Syndromes Multigene Panel III. Genetic testing for periodic fever syndromes, also called hereditary recurrent fever syndromes, (e.g., Familial Mediterranean Fever, tumor necrosis factor receptor-associated periodic fever [TRAPS]) via multigene panel (81404, 81479) may be considered **medically necessary** when **BOTH** of the following criteria are met: A. The member has three or more episodes of unexplained fever in a six-month period, occurring at least seven days apart B. Common causes of fever have been ruled out, including viral or bacterial infection. IV. Genetic testing for periodic fever syndromes, also called hereditary recurrent fever syndromes, (e.g., Familial Mediterranean Fever, tumor necrosis factor receptor-associated periodic fever [TRAPS]) via multigene panel (81404, 81479) is considered **investigational** for all other indications.

POLICY STATEMENT	
BEFORE Red font: Verbiage removed	**AFTER** Blue font: Verbiage Changes/Additions
I. The use of a multibiomarker disease activity score for rheumatoid arthritis (RA) (e.g., Vectra® score) is considered **investigational** in **all** situations.	**RHEUMATOID ARTHRITIS BIOMARKER ACTIVITY PANELS** **Rheumatoid Arthritis Biomarker Activity Panels** V. The use of multibiomarker disease activity scores for rheumatoid arthritis (81490) is considered **investigational**. **GENETIC ALGORITHMIC RHEUMATOID ARTHRITIS TESTS** **Tumor Necrosis Factor Inhibitor (TNFi) Treatment** VI. The use of genetic algorithmic rheumatoid arthritis tests to determine appropriateness of TNFi treatment (i.e., PrismRA) (81599, 81479) is considered **investigational**. **HLA TYPING FOR ANKYLOSING SPONDYLITIS, RHEUMATOID ARTHRITIS, AND AUTOIMMUNE DISORDERS** VII. The use of HLA-B27 typing (81374, 81382) to confirm or establish the diagnosis of ankylosing spondylitis, or another spondyloarthropathies, may be considered **medically necessary** when **BOTH** of the following criteria are met: A. The member has clinical or radiographic features of ankylosing spondylitis, or another spondyloarthropathy B. HLA-B27 results are needed to establish a diagnosis of ankylosing spondylitis, or another spondyloarthropathy. VIII. The use of HLA typing (81374, 81382) for ankylosing spondylitis, rheumatoid arthritis, and autoimmune disorders is considered **investigational** for all other indications. **OTHER COVERED IMMUNE, AUTOIMMUNE, AND RHEUMATOID DISORDERS** The following is a list of conditions that have a known genetic association. Due to their relative rareness, it may be appropriate to cover these genetic tests to establish or confirm a diagnosis. IX. Genetic testing to establish or confirm one of the following immune, autoimmune, or rheumatoid disorders to guide management may be considered **medically necessary** when the member

POLICY STATEMENT	
BEFORE Red font: Verbiage removed	**AFTER** **Blue font: Verbiage Changes/Additions**
	demonstrates clinical features* consistent with the disorder (the list is not meant to be comprehensive, see X below): A. Agammaglobulinemia: X-Linked and Autosomal Recessive B. Autoimmune Lymphoproliferative Syndrome (ALPS) C. Chronic Granulomatous Disease (CGD) D. Common Variable Immune Deficiency (CVID) E. Complement Deficiencies F. Congenital Neutropenia Syndromes (e.g., *ELANE*-Related Neutropenia) G. Familial Hemophagocytic Lymphohistiocytosis (HLH) H. Hyper IgE Syndrome (HIES) I. Hyper IgM Syndromes J. Leukocyte Adhesion Deficiency (LAD) K. NEMO Deficiency Syndrome L. Severe Combined Immune Deficiency (SCID) and Combined Immune Deficiency M. WHIM Syndrome (Warts, Hypogammaglobulinemia, Infections, and Myelokathexis) N. Wiskott-Aldrich Syndrome X. Genetic testing to establish or confirm the diagnosis of all other immune, autoimmune, or rheumatoid disorders not specifically discussed within this or another medical policy will be evaluated by the criteria outlined in *General Approach to Genetic and Molecular Testing* (see policy for coverage criteria). *Clinical features for a specific disorder may be outlined in resources such as GeneReviews, OMIM, National Library of Medicine, Genetics Home Reference, or other scholarly source.