MEDICAL POLICY

POLICY TITLE	MISCELLANEOUS GENETIC AND MOLECULAR DIAGNOSTIC TESTS
POLICY NUMBER	MP-2.277

Original Issue Date (Created):	**6/1/2015**
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Effective Date:	**3/1/2019**

I. POLICY

All of the tests listed in this policy are considered **investigational**, and are grouped according to the categories of genetic testing as outlined in MP-2.326, General Approach to Genetic Testing:

- Testing of an affected (symptomatic) individual's germline to benefit the individual (excluding reproductive testing)
- Diagnostic testing
- Prognostic testing
- Therapeutic testing
- Testing an asymptomatic individual to determine future risk of disease.

There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with these tests.

POLICY GUIDELINES

Genetic testing is considered **investigational** when criteria are not met, including when there is insufficient evidence to determine whether the technology improves health outcomes.

Genetic Counseling

Genetic counseling is primarily aimed at patients who are at risk for inherited disorders, and experts recommend formal genetic counseling in most cases when genetic testing for an inherited condition is considered. The interpretation of the results of genetic tests and the understanding of risk factors can be very difficult and complex. Therefore, genetic counseling will assist individuals in understanding the possible benefits and harms of genetic testing, including the possible impact of the information on the individual's family. Genetic counseling may alter the utilization of genetic testing substantially and may reduce inappropriate testing. Genetic counseling should be performed by an individual with experience and expertise in genetic medicine and genetic testing methods.

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Cross-reference:

MP-2.326 General Approach to Genetic Testing
MP 2.360 Gene Expression Profiling for Melanoma

II. PRODUCT VARIATIONS

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This policy is applicable to all programs and products administered by Capital BlueCross unless otherwise indicated below.

III. DESCRIPTION/BACKGROUND

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TESTS ADDRESSED IN THIS MEDICAL POLICY

Tests assessed in this medical policy are listed in Table 1. Three types of tests are related to testing of an affected (symptomatic) individual's germline to benefit the individual (excluding reproductive testing): diagnostic testing, prognostic testing, and therapeutic testing. The fourth type of test reviewed is testing of an asymptomatic individual to determine future risk of disease.

Table 1. Genetic and Molecular Diagnostic Tests in This Medical Policy

Test Name	Manufacturer	Date Added	Diagnostic	Prognostic	Therapeutic	Future Risk
Celiac PLUS	Prometheus	Oct 2014	•			•
ColonSentry®	GeneNews[a]	Aug 2015				•
Crohn's Prognostic	Prometheus	Oct 2014		•		
DecisionDx-Thymoma	Castle	Jan 2015		•		
DNA Methylation Pathway Profile	Great Plains Laboratory	Jan 2015	•			
PreciseType™ HEA	Immucor	Mar 2017	•			
GI Effects® (Stool)	Genova Dxcs	Jan 2015	•			
IBD sgi Diagnostic™	Prometheus	Oct 2014	•			
ImmunoGenomic® Profile	Genova Dxcs	Aug 2015				•
Know Error™	Strand Dxcs	July 2016	•			
ResponseDX®: Colon	Response Gxcs	Jan 2015			•	
SEPT9 methylated DNA[b]	Several[c]	Oct 2014	•			
TransPredict Fc gamma 3A	Transgenomic	Oct 2014			•	

Castle: Castle Biosciences; Dxcs: Diagnostics; Gxcs: Genetics.
[a] In a joint venture with Innovative Diagnostic Laboratory.
[b] For example, ColoVantage®, Epi proColon®.
[c] ARUP, Quest, Clinical Genomics, Epigenomics.

DIAGNOSTIC TESTS

Multiple Conditions

Single-nucleotide variants (SNVs) are the most common type of genetic variation, and each SNV represents a difference in a single nucleotide in the DNA sequence. Most commonly, SNVs are found in the DNA between genes and can act as biologic markers of genes and disease association. When SNVs occur within a gene or a gene regulatory region, they can play a more direct role in disease by affecting the gene's function. SNVs may predict an individual's

response to certain drugs, susceptibility to environmental factors, and the risk of developing certain diseases.

DNA specimen provenance assays can be used to confirm that tissue specimens are correctly matched to the patient of origin. Specimen provenance errors may occur in up to 1% to 2% of pathology tissue specimens[1] and have serious negative implications for patient care if the error is not corrected.[2] Analysis of DNA microsatellites from tissue specimens can be performed by analyzing long tandem repeats (LTR) and comparing the LTRs of the tissue specimen with LTRs from a patient sample.

Test Description: DNA Methylation Pathway Profile
The DNA Methylation Pathway Profile (Great Plains Laboratory) analyzes SNVs associated with certain biochemical processes, including methionine metabolism, detoxification, hormone imbalances, and vitamin D function. Intended uses for the test include clarification of a diagnosis suggested by other testing and as an indication for supplements and diet modifications.

Test Description: Know Error DNA Specimen Provenance Assay
The Know Error test (Strand Diagnostics) compares the LTRs of tissue samples with LTRs from a buccal swab of the patient. The intended use of the test is to confirm tissue of origin and avoid specimen provenance errors due to switching of patient samples, mislabeling, or sample contamination.

Celiac Disease
Previously called sprue, celiac sprue, gluten-sensitive enteropathy, gluten intolerance, nontropical sprue, or idiopathic steatorrhea, celiac disease is an immune-based reaction to gluten (water insoluble proteins in wheat, barley, rye) that primarily affects the small intestine. Celiac disease occurs almost exclusively in patients who carry at least 1 human leukocyte antigen DQ2 or DQ8 allele; the negative predictive value of having neither allele exceeds 98%.[3] Serum antibodies to tissue transglutaminase, endomysium, and deamidated gliadin peptide (DGP) support a diagnosis of celiac disease, but diagnostic confirmation requires duodenal biopsy taken when patients are on a gluten-containing diet.[4]

Test Description: Celiac PLUS
Celiac PLUS (Prometheus Therapeutics & Diagnostics) is a panel of 2 genetic and 5 serologic markers associated with celiac disease. Per the manufacturer, Celiac PLUS is a diagnostic test that also stratifies future risk of celiac disease.[5] Genetic markers (human leukocyte antigen DQ2 and DQ8) are considered predictive of the risk of developing celiac disease[6]; serologic markers (immunoglobulin A [IgA] anti-tissue transglutaminase antibody, IgA anti-endomysial antibodies, IgA anti-DGP antibodies, IgG anti-DGP, and total IgA) are considered diagnostic for celiac disease. Celiac PLUS is intended for patients at risk for disease (e.g., with an affected first-degree relative) or with symptoms suggestive of disease.

Irritable Bowel Syndrome
Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) disorder that affects 10% to 20% of the general population in the United States and worldwide.[7,8] Symptoms include

abdominal pain and/or bloating associated with disordered bowel habit (constipation, diarrhea, or both).[9] Pathophysiology is poorly understood but may be related to chronic low-grade mucosal inflammation and disturbances in GI flora.[10] Recommended treatments include dietary restriction and pharmacologic symptom control.[7,11,12] As living microorganisms that promote health when administered to a host in therapeutic doses,[13] probiotics are being investigated as a treatment for IBS. Several systematic reviews of randomized controlled trials (RCTs) have found evidence to support efficacy,[8,10,14-16] but results from recent RCTs have been mixed.[17-22] This discrepancy may be due in part to the differential effects of different probiotic strains and doses.

Test Description: GI Effects Comprehensive Stool Profile

The GI Effects Comprehensive Stool Profile (Genova Diagnostics) is a multianalyte stool assay.[23] The test uses polymerase chain reaction (PCR) to quantify 26 commensal gut bacteria and standard biochemical and culture methods to measure levels of other stool components (e.g., lipids, fecal occult blood) and potential pathogens (ova and parasites, opportunistic bacteria, yeast). The test is purported to optimize management of gut health and to differentiate IBS from inflammatory bowel disease (IBD).

Inflammatory Bowel Disease

IBD is an autoimmune condition characterized by inflammation of the bowel wall and has clinical symptoms of abdominal pain, diarrhea, and associated symptoms. Crohn disease (CD) and ulcerative colitis are the 2 main entities under the category of IBD. The diagnosis is typically made by endoscopy or colonoscopy with biopsy and histologic analysis. This requires a semi-invasive procedure; as a result, a blood test to diagnose IBD could avoid the need for the procedures.

Test Description: IBD sgi Diagnostic

IBD sgi Diagnostic (Prometheus Therapeutics & Diagnostics) is a panel of 17 serologic (n=8), genetic (n=4), and inflammatory biomarkers (n=5). A proprietary algorithm produces an IBD score; results are reported as consistent with IBD (consistent with ulcerative colitis, consistent with CD, or inconclusive for UC vs CD) or not consistent with IBD. The test is intended for use in patients with clinical suspicion of IBD.

Colon Cancer

Early detection of colorectal cancer (CRC) reduces disease-related mortality, yet many individuals do not undergo recommended screening with fecal occult blood test or colonoscopy. A simpler screening blood test may have the potential to encourage screening and decrease mortality if associated with increased screening compliance. Serum biomarkers that are shed from colorectal tumors have been identified and include Septin 9 hypermethylated DNA (*SEPT9*). The Septin 9 protein is involved in cell division, migration, and apoptosis and acts as a tumor suppressor; when hypermethylated, expression of *SEPT9* is reduced.

A cofounder of the biotechnology firm GeneNews developed a patented platform technology based on the sentinel principle.[24] The sentinel principle posits that because blood interacts with all bodily tissues, “subtle changes occurring in association with injury or disease, within the cells and tissues of the body, may trigger specific changes in gene expression in blood cells reflective

of the initiating stimulus."[24] In this way, blood cells (specifically, leukocytes) may act as sentinels of disease. In studies that led to the formulation of this principle, investigators compared gene expression (total RNA levels) in blood samples with cataloged genes from 9 different organs (brain, colon, heart, kidney, liver, lung, prostate, spleen, stomach) and estimated that 66% to 82% of genes encoded in the human genome are expressed in human leukocytes.[24]

***Test Descriptions: SEPT9* Methylated DNA**

ColoVantage (various manufacturers) blood tests for serum *SEPT9* methylated DNA are offered by several laboratories (ARUP Laboratories, Quest Diagnostics, Clinical Genomics). Epi proColon (Epigenomics) received U.S. Food and Drug Administration (FDA) approval in April 2016. Epigenomics has licensed its Septin 9 DNA biomarker technology to ARUP and Quest. ColoVantage and Epi proColon are both PCR assays; however, performance characteristics vary across tests, presumably due to differences in methodology (e.g., DNA preparation, PCR primers, probes). Sensitivity as high as 90%, with 88% specificity and 99.9% negative predictive value (4% positive predictive value) have been reported for ColoVantage.[25,26] By comparison, reported sensitivity and specificity for Epi proColon were 68% and 80%, respectively.[27] Serum *SEPT9* methylated DNA testing is intended for individuals 50 years of age or older who have an average risk of CRC.[26]

Test Description: ColonSentry

ColonSentry (GeneNews; Innovative Diagnostic Laboratory) is a PCR assay that uses a blood sample to detect expression of 7 genes found to be differentially expressed in CRC patients compared with controls[28]: *ANXA3*, *CLEC4D*, *TNFAIP6*, *LMNB1*, *PRRG4*, *VNN1*, and *IL2RB*. Per the company website, these genes are early-warning signs of colon cancer, and test results can indicate the odds of having CRC compared with an average-risk person.[29] An average-risk person is defined as one who is "at least 50 years old, is asymptomatic for CRC, has no personal history of benign colorectal polyps, colorectal adenomas, CRC, or inflammatory bowel disease, and does not have a first-degree relative with CRC."[29] The test is intended for use in adults who are averse to colonoscopy and/or fecal occult blood testing. "Because of its narrow focus, the test is not expected to alter clinical practice for patients who comply with recommended screening schedules."[30]

Prognostic Tests

Crohn Disease

Recent studies have identified serologic[27,] and genetic[28,29,] correlates of aggressive CD that is characterized by fistula formation, fibrostenosis, and the need for surgical intervention. Prometheus has developed a blood test that aims to identify patients with CD who are likely to experience an aggressive disease course.

Test Description: Crohn's Prognostic

Crohn's Prognostic (Prometheus Therapeutics & Diagnostics) is a panel of 6 serologic (n=3) and genetic (n=3) biomarkers. Limited information about the test is available on the manufacturer's website.

Thymomas and Thymic Carcinomas

Thymomas and thymic carcinomas are rare epithelial tumors of the thymus. Most are diagnosed in individuals between 40 and 60 years of age. Thymic epithelial tumors range from histologically benign tumors to microscopically or macroscopically invasive low- or high-grade malignant tumors. However, even tumors that are histologically benign can behave aggressively.

Test Description: DecisionDx-Thymoma

DecisionDx-Thymoma (Castle Biosciences) is a gene expression profile test that measures the activity of 23 genes within the thymic tumor. Its intended use is to distinguish between thymic carcinoma and thymoma and to predict tumor aggressiveness by the likelihood that the tumor will metastasize.

Therapeutic Tests

Test Description: ResponseDX: Colon

Response Genetics currently markets 2 colon cancer genetic panels to guide treatment selection, as well as separate tests for 11 genes associated with colon cancer prognosis and/or treatment response. The Driver Profile panel comprises PCR variant testing in *KRAS*, *BRAF*, and mismatch repair genes (microsatellite instability), plus *NRAS* exon 2 and 3 sequencing. These gene tests are reviewed elsewhere (see evidence reviews 2.04.08 and 2.04.53), and this panel is not considered here. The ResponseDX: Colon test comprises the 4 tests in the Driver Profile plus: EGFR expression; PI3K exon 1, 9, and 20 sequencing; TS expression; ERCC1 expression; UGT1A1 SNV testing (rs8175347, rs4148323); VEGFR2 expression; and MET amplification by fluorescence in situ hybridization.

Non-Hodgkin

Rituximab is a humanized IgG monoclonal antibody against the CD20 antigen, which is commonly expressed on B lymphocytes. It is Food and Drug Administration-approved for the treatment of non-Hodgkin lymphoma, chronic lymphocytic leukemia, and nononcologic uses (e.g., rheumatoid arthritis).[30] Rituximab has demonstrated better response and survival rates in combination chemotherapy regimens in patients with follicular lymphoma, chronic lymphocytic leukemia, and diffuse large B-cell lymphoma than chemotherapy alone, though not all patients responded. Altered binding to lymphocyte-bound rituximab by cytotoxic effector cells (e.g., natural killer cells, macrophages) has been identified as a mechanism of reduced rituximab

efficacy. Effector cells with a Val158Phe substitution variant in their surface receptors for IgG molecules (e.g., rituximab) have impaired binding affinity, and cellular cytotoxicity is reduced. A genetic test for the Val158Phe variant of the gene that encodes the IgG receptor on effector cells (*FCGR3A*) has been developed and investigated as a means of predicting response to rituximab.

Tests for Future Risk of Disease

Immunologic Disorders

Test Description: ImmunoGenomic Profile

The ImmunoGenomic Profile (Genova Diagnostics) is a buccal swab test that evaluates SNVs in 6 genes associated with immune function and inflammation: interleukin (IL)-10, IL-13, IL-1β, IL-4, IL-6, and tumor necrosis factor α.[31,] According to the company website, variations in these genes "can affect balance between cell (Th-1) and humoral (Th-2) immunity, trigger potential defects in immune system defense, and stimulate mechanisms underlying chronic, overactive inflammatory responses." "The test uncovers potential genetic susceptibility to: Asthma, Autoimmune Disorders, Certain Cancers, Allergy, Infectious Diseases, Bone Inflammation, Arthritis, Inflammatory Bowel Disease, Heart Disease, Osteopenia, and *Helicobacter pylori* infection (cause of ulcers)."

Regulatory Status

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments. Genetic tests evaluated in this evidence review are available under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer laboratory-developed tests must be licensed under the Clinical Laboratory Improvement Amendments for high-complexity testing. To date, the Food and Drug Administration has chosen not to require any regulatory review of these tests.

Other

Test Description: PreciseType™ HEA

PreciseType™ HEA test is a multiplexed molecular assay that generates detailed molecular information from patient and donor samples, rapidly detecting genotypes for accurate prediction of phenotypes which can assist in determining donor-patient compatibility. This test screens blood donors and recipients to prevent a mismatch via molecular typing of red blood cell antigens.

IV. RATIONALE

TOP

SUMMARY OF EVIDENCE

Diagnostic Testing

For individuals with symptoms of various conditions thought to be hereditary or with a known genetic component who receive diagnostic testing with a miscellaneous genetic or molecular test (e.g., DNA Methylation Pathway Profile, Know Error, Celiac PLUS, GI Effects [Stool], IBD sgi Diagnostic), the evidence includes case series, cross-sectional studies, diagnostic accuracy studies, and cohort studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, change in disease status, and morbid events. The lack of demonstrated clinical utility of these tests is based on the following factors: (1) there is no or extremely limited published data addressing the test; and/or (2) there is insufficient evidence demonstrating the clinical validity of the test. For each test addressed, a literature review was conducted. The literature review was not comprehensive, but sufficient to establish lack of clinical utility. A test will be removed from this evidence review and addressed separately if it is determined that enough evidence has accumulated to reevaluate its potential clinical utility. The evidence is insufficient to determine the effects of the technologies on health outcomes.

For individuals who are being screened for colorectal cancer who receive *SEPT9*methylated DNA testing (e.g., ColoVantage, Epi proColon, ColonSentry), the evidence includes case-control, cross-sectional, and prospective diagnostic accuracy studies along with systematic reviews of those studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, change in disease status, and morbid events. The PRESEPT prospective study estimated the sensitivity and specificity of Epi proColon detection of invasive adenocarcinoma at 48% and 92%, respectively. Other studies were generally low to fair quality. Based on results from these studies, the clinical validity of *SEPT9*methylated DNA screening is limited by the low sensitivity of the test given that the sensitivity of the test is lower than imaging screening strategies. Optimal intervals for retesting are not known. The evidence is insufficient to determine the effects of the technologies on health outcomes.

Prognostic Testing

For individuals who are diagnosed with various conditions (e.g., Crohn disease, thymomas and thymic carcinomas, rheumatoid arthritis) who receive therapeutic testing with a miscellaneous genetic or molecular test (e.g., Crohn's Prognostic, DecisionDx-Thymoma), there are no published studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, change in disease status, and morbid events. The evidence is insufficient to determine the effects of the technologies on health outcomes.

Therapeutic Testing

For individuals who are diagnosed with various conditions (e.g., colon cancer, non-Hodgkin lymphoma) who receive therapeutic testing with a miscellaneous genetic or molecular test (e.g., ResponseDX: Colon, TransPredict Fc gamma 3A), the evidence includes case series, cross-sectional studies, diagnostic accuracy studies, and cohort studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, change in disease status, and morbid events. The lack of demonstrated clinical utility of these tests is based on the following factors: (1) there is no or extremely limited published data addressing the test; and/or (2) there is insufficient evidence demonstrating the clinical validity of the test. For each test addressed, a literature review was conducted. The literature review was not comprehensive, but sufficient to establish lack of clinical utility. A test will be removed from this evidence review and addressed separately if it is determined that enough evidence has accumulated to reevaluate its potential clinical utility. The evidence is insufficient to determine the effects of the technologies on health outcomes.

Testing for Future Risk of Disease

For individuals with a family history of various conditions thought to be hereditary or with a known genetic component who receive testing for future risk of disease with a miscellaneous genetic or molecular test (e.g., ImmunoGenomic Profile), the evidence includes diagnostic accuracy studies. Relevant outcomes are overall survival, disease-specific survival, test accuracy and validity, change in disease status, and morbid events. The lack of demonstrated clinical utility of these tests is based on the following factors: (1) there is no or extremely limited published data addressing the test; and/or (2) there is insufficient evidence demonstrating the clinical validity of the test. For each test addressed, a literature review is conducted. The literature review was not comprehensive, but sufficient to establish lack of clinical utility. A test will be removed from this evidence review and addressed separately if it is determined that enough evidence has accumulated to reevaluate its potential clinical utility. The evidence is insufficient to determine the effects of the technologies on health outcomes.

V. DEFINITIONS TOP

N/A

VI. BENEFIT VARIATIONS TOP

The existence of this medical policy does not mean that this service is a covered benefit under the member's contract. Benefit determinations should be based in all cases on the applicable contract language. Medical policies do not constitute a description of benefits. A member's individual or group customer benefits govern which services are covered, which are excluded, and which are subject to benefit limits and which require preauthorization. Members and providers should consult the member's benefit information or contact Capital BlueCross for benefit information.

VII. DISCLAIMER TOP

Capital BlueCross's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. Capital BlueCross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION TOP

Note: The genetic tests identified below do not have specific codes; therefore, identification of a code in this section does not denote coverage. When several or all of the codes listed below are used to identify these tests they are considered investigational. The list of codes may not be all-inclusive, and are subject to change at any time. Eligibility is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Investigational; therefore, not covered, Prometheus Celiac PLUS:

CPT Codes®								
81382	82784	83520	86255	88346	88350			

Investigational; therefore, not covered, GeneNews ColonSentry®:

CPT Codes®								
81479								

Investigational; therefore, not covered, Prometheus Crohn's Prognostic:

CPT Codes®								
81479	83520	86021	86255	88346	88350			

Investigational; therefore, not covered, Castle Decision Dx-Thymoma:

CPT Codes®								
81479								

Investigational; therefore, not covered, Great Plains Laboratory DNA Methylation Pathway Profile:

CPT Codes®								
81479								

Investigational; therefore, not covered, Genova Dxcs GI Effects ® (Stool):

CPT Codes®								
87045	87046	87075	87102	87177	87209	87328	87329	87336
87798								

Investigational; therefore, not covered, Prometheus IBD sgi Diagnostic™:

CPT Codes®								
81479	82397	83520	86021	86140	86671	88346	88350	

Investigational; therefore, not covered, Genova Dxcs ImmunoGenomic® Profile:

CPT Codes®								
81479								

Investigational; therefore, not covered, Strand Dxcs Know Error™:

CPT Codes®								
84999								

Investigational; therefore, not covered, Response Gxcs ResponseDX®: Colon:

CPT Codes®								
81479								

Investigational; therefore, not covered, SEPT9 methylated DNA:

CPT Codes®								
81327								

Investigational; therefore, not covered, Transgenomic TransPredict Fc gamma 3a:

CPT Codes®								
81479								

Investigational; therefore, not covered, The PreciseType HEA:

CPT Codes®								
0001U								

Investigational; therefore, not covered, tests for Genetic Variants That Alter Response to Treatment or to an Environmental Factor (e.g. G6PD):

CPT Codes®								
81247	81248	81249						

IX. REFERENCES

TOP

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X. POLICY HISTORY

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MP 2.277	**CAC 1/27/15** New policy. BCBSA adopted. All tests listed in this policy are considered investigational, and are grouped according to the categories of genetic testing as outlined in MP- 2.236 General Approach to Genetic Testing. Coding Reviewed.
	CAC 1/26/16 Consensus review. No changes to the policy statements, References and rationale updated. Genetic tests added to Table 1 which is now in the rationale section**.** Appendix added, coding reviewed.

POLICY TITLE	MISCELLANEOUS GENETIC AND MOLECULAR DIAGNOSTIC TESTS
POLICY NUMBER	MP-2.277

	Administrative 2/4/16: 2016 coding update, removed end dated code 88347 and added replacement codes.
	Administrative Update 11/10/16 Variation reformatting
	Administrative Update 1/1/17: New code 81327, for SEPT9, added and 81401 removed; effective 1/1/17.
	CAC 3/28/17 Consensus review. Added info regarding Precise Type HEA. No changes to the policy statements. Background, references, and rationale updated. Coding reviewed. Added new code 0001U for PreciseType HEA; effective 2/1/17. Coding revised 4/25/17
	Medicare update 6/1/17 – added variation to reference LCD 35396 Biomarkers for Oncology for SEPT9 methylated DNA and LCD L35062 Biomarkers Overview for the PreciseType HEA
	Admin Update 1/1/18: Added new codes 81247-81249; effective 1/1/18 Medicare variations removed from Commercial Policies.
	1/19/18 Minor revision. Policy statements updated to organize types of tests with language that corresponds to MP-2.326; all tests remain investigational. 'Adoption Type' changed to 'BCBSA Partial Adoption' as the *PreciseType™ HEA* test was added in 2017 which is not specifically addressed by BCBSA. Policy Guidelines section added. Description/Background, Rationale and Reference sections updated. Coding reviewed.
	10/9/18 Admin update. Cross-references updated. Appendix removed.
	12/1/18 Admin update. Removed cutaneous melanoma information. See MP 2.360.
	1/25/19 Consensus. No change to policy statements. Background and references updated.

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