

MEDICAL POLICY

POLICY TITLE	INVESTIGATIONAL MISCELLANEOUS GENETIC AND MOLECULAR TESTS
POLICY NUMBER	MP 2.277

CLINICAL BENEFIT	<input type="checkbox"/> MINIMIZE SAFETY RISK OR CONCERN. <input checked="" type="checkbox"/> MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. <input type="checkbox"/> ASSURE APPROPRIATE LEVEL OF CARE. <input type="checkbox"/> ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. <input type="checkbox"/> ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. <input type="checkbox"/> ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	1/1/2025

[POLICY RATIONALE](#)
[DISCLAIMER](#)
[POLICY HISTORY](#)

[PRODUCT VARIATIONS](#)
[DEFINITIONS](#)
[CODING INFORMATION](#)
[APPENDIX](#)

[DESCRIPTION/BACKGROUND](#)
[BENEFIT VARIATIONS](#)
[REFERENCES](#)

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 general 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.

MEDICAL POLICY

POLICY TITLE	INVESTIGATIONAL MISCELLANEOUS GENETIC AND MOLECULAR TESTS
POLICY NUMBER	MP 2.277

Cross-reference:

MP 2.326 General Approach to Genetic Testing

MP 4.002 Experimental and Investigational Procedures

II. PRODUCT VARIATIONS

[TOP](#)

This policy is only applicable to certain programs and products administered by Capital Blue Cross please see additional information below, and subject to benefit variations as discussed in Section VI below.

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

<https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies>

III. DESCRIPTION/BACKGROUND

[TOP](#)

There are numerous commercially available genetic and molecular diagnostic, prognostic, and therapeutic tests for individuals with certain diseases or asymptomatic individuals with future risk. This evidence review evaluates miscellaneous genetic and molecular tests not addressed in a separate review. If a separate evidence review exists, then conclusions reached there supersede conclusions here. The main criterion for inclusion in this review is the limited evidence on the clinical validity for the test. As a result, these tests do not have clinical utility, and the evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Tests Addressed in This Medical Policy

Tests assessed in this medical policy are listed in Table 1. All coding information is also found in this Table. 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 Tests in This Medical Policy

All tests listed in this table are considered **investigational** therefore not covered.

Test Name	Manufacturer	Coding Information
Augusta Hematology Optical Genome Mapping	Georgia Esoteric and Molecular Labs	0331U
Avantect Pancreatic Cancer Test	ClearNote Health	0410U
Aventa FusionPlus	Aventa Genomics	0444U
BeScreened-CRC	Beacon Biomedical	0163U

MEDICAL POLICY

POLICY TITLE	INVESTIGATIONAL MISCELLANEOUS GENETIC AND MOLECULAR TESTS
POLICY NUMBER	MP 2.277

Test Name	Manufacturer	Coding Information
BluePrint	Agendia	81479
BTG Early Detection of Pancreatic Cancer	Breakthrough Genomics	0405U
Catechol-O-Methyltransferase (COMT) Genotype	Mayo Clinic	0032U
ColonSentry®	Stage Zero Life Sciences	81479
Cxbladder Detect+	Pacific Edge Diagnostics	0420U
Decipher Bladder TURBT	Veracyte	0016M
DecisionDx® - SCC	Castle Biosciences	0315U
DetermaRx™	Oncocyte Corporation	0288U
DH Optical Genome Mapping Assay	Dartmouth Health/Bionano Genomics	0413U
DNA Methylation Pathway Profile	Great Plains Laboratory (now Mosaic Dxcs)	81479
Envisia® Genomic Classifier	Veracyte, Inc	81554
EpiSwitch® CiRT	Next Bio-Research Services	0332U
GI Effects® (Stool)	Genova Diagnostics	82274, 82542, 82653, 82715, 82725, 82784, 83520, 83993, 84311, 87045, 87046, 87075, 87102, 87177, 87209, 87328, 87329, 87336, 87505, 87798
Guardant360 Response	Guardant Health	0422U
HelioLiver™ Test	Fulgent Genetics LLC	0333U
HeproDX™	GoPath Laboratories LLC	0006M
HPV-SEQ Test	Sysmex Inostics Inc	0470U
IBSchek®	Commonwealth Diagnostics International	0176U
ibs-smart®	Gemelli Biotech	0164U
Kelch-Like Protein 11 Antibody	Mayo Clinic	0432U
Know Error™	Strand Diagnostics	84999
LC-MS/MS Targeted Proteomic Assay	OncoOmicDx Laboratory	0174U
Lifetime Genomics Risk Assessment, VTE	GenomicMD	0529U
LungLB®, LungLife®	LungLife AI	0317U

MEDICAL POLICY

POLICY TITLE	INVESTIGATIONAL MISCELLANEOUS GENETIC AND MOLECULAR TESTS
POLICY NUMBER	MP 2.277

Test Name	Manufacturer	Coding Information
LungOI	Image AI	0414U
Lymph 2 Cx and Lymph3Cx Lymphoma Molecular Subtyping Assay	Mayo Clinic	0017M, 0120U
Merkel smT Oncoprotein Antibody Titer and Merkel Virus VP1 Capsid Antibody	University of Washington, Department of Laboratory Medicine	0058U, 0059U
MindX Blood Test™- Longevity	MindX Sciences™ Laboratory	0294U
Molecular Microscope® MMDx-Heart	Kashi Clinical Laboratories	0087U
NavDx®	Naveris, Inc	0356U
NETest	Wren Laboratories LLC	0007M
Northstar Response™	BillionToOne Laboratory	0486U
OncoSignal 7 Pathway Signal	Protean Bio-diagnostics	0262U
Oncotype DX® Breast DCIS Score™	Genomic Health, Inc	0045U
Optical Genome Mapping	NA	81195
OptiSeq Dual Cancer Panel Kit	DiaCarta	0499U
OptiSeq Colorectal Cancer NGS Panel	DiaCarta	0498U
PolypDX™	Atlantic Diagnostic Laboratories	0002U
Praxis Somatic Whole Genome Sequencing/Transcriptome/Optical Genome Mapping/Combined Whole Genome Sequencing and Optical Genome Mapping	Praxis Genomics LLC	0297U, 0298U, 0299U, 0300U
PredictSURE IBD™ Test	KSL Diagnostics	0203U
Prometheus® Celiac	Prometheus Laboratories	81382, 82784, 83520, 86231, 86258, 86364, 88346
PuriST	Tempus AI	0510U
ResponseDX®: Colon	Cancer Genetics	81479
RightMed® Gene Report	OneOme® LLC	0350U
SEPT9 methylated DNA (example ColoVantage and Epi proColon)	Several*	81327
SyncView®Rx	Phenomix Health™ Inc.	0520U

MEDICAL POLICY

POLICY TITLE	INVESTIGATIONAL MISCELLANEOUS GENETIC AND MOLECULAR TESTS
POLICY NUMBER	MP 2.277

Test Name	Manufacturer	Coding Information
UNITY Fetal Risk Screen™	BillionToOne Laboratory	0489U
UroAmp MRD	Convergent Genomics	0467U

* ARUP, Quest, Clinical Genomics and Epigenomics.

Note: Some genetic tests identified above do not have specific codes (i.e., GI Effects, Prometheus® Celiac, etc.); therefore, identification of a code in this section does not denote coverage. When several or all of the codes listed 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.

IV. RATIONALE

[TOP](#)

SUMMARY OF EVIDENCE

The literature review was not comprehensive, but sufficient to establish lack of clinical utility. If it is determined that enough evidence has accumulated to reevaluate its potential clinical utility, the test will be removed from this evidence review and addressed separately. 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.

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 health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits, and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

VII. DISCLAIMER

[TOP](#)

Capital Blue Cross' 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

MEDICAL POLICY

POLICY TITLE	INVESTIGATIONAL MISCELLANEOUS GENETIC AND MOLECULAR TESTS
POLICY NUMBER	MP 2.277

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. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. REFERENCES

[TOP](#)

1. Pfeifer JD, Zehnbaauer B, Payton J. The changing spectrum of DNA-based specimen provenance testing in surgical pathology. *Am J Clin Pathol*. Jan 2011; 135(1): 132-8. PMID 21173135
2. Beauvais W, Fournié G, Jones BA, et al. Modelling the expected rate of laboratory biosafety breakdowns involving rinderpest virus in the post-eradication era. *Prev Vet Med*. Nov 01 2013; 112(3-4): 248-56. PMID 24029703
3. Pallav K, Kabbani T, Tariq S, et al. Clinical utility of celiac disease-associated HLA testing. *Dig Dis Sci*. Sep 2014; 59(9): 2199-206. PMID 24705698
4. Ludvigsson JF, Leffler DA, Bai JC, et al. The Oslo definitions for coeliac disease and related terms. *Gut*. Jan 2013; 62(1): 43-52. PMID 22345659
5. Prometheus Laboratories. Celiac PLUS. Accessed May 20, 2024.
6. Pietzak MM, Schofield TC, McGinniss MJ, et al. Stratifying risk for celiac disease in a large at-risk United States population by using HLA alleles. *Clin Gastroenterol Hepatol*. Sep 2009; 7(9): 966-71. PMID 19500688
7. Ford AC, Quigley EM, Lacy BE, et al. Efficacy of prebiotics, probiotics, and synbiotics in irritable bowel syndrome and chronic idiopathic constipation: systematic review and meta-analysis. *Am J Gastroenterol*. Oct 2014; 109(10): 1547-61; quiz 1546, 1562. PMID 25070051
8. National Institute for Health and Care Excellence (NICE). Irritable bowel syndrome in adults: diagnosis and management [CG61]. 2017; Accessed June 2, 2024.
9. McKenzie YA, Alder A, Anderson W, et al. British Dietetic Association evidence-based guidelines for the dietary management of irritable bowel syndrome in adults. *J Hum Nutr Diet*. Jun 2012; 25(3): 260-74. PMID 22489905
10. Weinberg DS, Smalley W, Heidelbaugh JJ, et al. American Gastroenterological Association Institute Guideline on the pharmacological management of irritable bowel syndrome. *Gastroenterology*. Nov 2014; 147(5): 1146-8. PMID 25224526
11. Hill C, Guarner F, Reid G, et al. Expert consensus document. The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nat Rev Gastroenterol Hepatol*. Aug 2014; 11(8): 506-14. PMID 24912386
12. Trinkley KE, Nahata MC. Treatment of irritable bowel syndrome. *J Clin Pharm Ther*. Jun 2011; 36(3): 275-82. PMID 21545610
13. Hungin AP, Mulligan C, Pot B, et al. Systematic review: probiotics in the management of lower gastrointestinal symptoms in clinical practice -- an evidence-based international guide. *Aliment Pharmacol Ther*. Oct 2013; 38(8): 864-86. PMID 23981066

MEDICAL POLICY

POLICY TITLE	INVESTIGATIONAL MISCELLANEOUS GENETIC AND MOLECULAR TESTS
POLICY NUMBER	MP 2.277

14. Ortiz-Lucas M, Tobías A, Saz P, et al. Effect of probiotic species on irritable bowel syndrome symptoms: A bring up to date meta-analysis. *Rev Esp Enferm Dig.* Jan 2013; 105(1): 19-36. PMID 23548007
15. Whelan K. Probiotics and prebiotics in the management of irritable bowel syndrome: a review of recent clinical trials and systematic reviews. *Curr Opin Clin Nutr Metab Care.* Nov 2011; 14(6): 581-7. PMID 21892075
16. Stevenson C, Blaauw R, Fredericks E, et al. Randomized clinical trial: effect of *Lactobacillus plantarum* 299 v on symptoms of irritable bowel syndrome. *Nutrition.* Oct 2014; 30(10): 1151-7. PMID 25194614
17. Shavakhi A, Minakari M, Farzamnia S, et al. The effects of multi-strain probiotic compound on symptoms and quality-of-life in patients with irritable bowel syndrome: A randomized placebo-controlled trial. *Adv Biomed Res.* 2014; 3: 140. PMID 25161987
18. Ludidi S, Jonkers DM, Koning CJ, et al. Randomized clinical trial on the effect of a multispecies probiotic on visceroperception in hypersensitive IBS patients. *Neurogastroenterol Motil.* May 2014; 26(5): 705-14. PMID 24588932
19. Rogha M, Esfahani MZ, Zargarzadeh AH. The efficacy of a synbiotic containing *Bacillus Coagulans* in treatment of irritable bowel syndrome: a randomized placebo-controlled trial. *Gastroenterol Hepatol Bed Bench.* 2014; 7(3): 156-63. PMID 25120896
20. Urgesi R, Casale C, Pistelli R, et al. A randomized double-blind placebo-controlled clinical trial on efficacy and safety of association of simethicone and *Bacillus coagulans* (Colinox®) in patients with irritable bowel syndrome. *Eur Rev Med Pharmacol Sci.* 2014; 18(9): 1344-53. PMID 24867512
21. Sissou G, Ayis S, Sherwood RA, et al. Randomised clinical trial: A liquid multi-strain probiotic vs. placebo in the irritable bowel syndrome--a 12 week double-blind study. *Aliment Pharmacol Ther.* Jul 2014; 40(1): 51-62. PMID 24815298
22. Genova Diagnostics. GI Effects Comprehensive Profile - Stool. n.d.; Accessed May 20, 2024.
23. Targan SR, Landers CJ, Yang H, et al. Antibodies to CBir1 flagellin define a unique response that is associated independently with complicated Crohn's disease. *Gastroenterology.* Jun 2005; 128(7): 2020-8. PMID 15940634
24. Ippoliti A, Devlin S, Mei L, et al. Combination of innate and adaptive immune alterations increased the likelihood of fibrostenosis in Crohn's disease. *Inflamm Bowel Dis.* Aug 2010; 16(8): 1279-85. PMID 20027650
25. Abreu MT, Taylor KD, Lin YC, et al. Mutations in NOD2 are associated with fibrostenosing disease in patients with Crohn's disease. *Gastroenterology.* Sep 2002; 123(3): 679-88. PMID 12198692
26. Genova Diagnostics. Immunogenomic Profile. n.d.; Accessed May 19, 2024.
27. Pfeifer JD, Singleton MN, Gregory MH, et al. Development of a decision-analytic model for the application of STR-based provenance testing of transrectal prostate biopsy specimens. *Value Health.* 2012; 15(6): 860-7. PMID 22999136
28. Rubio-Tapia A, Hill ID, Kelly CP, et al. ACG clinical guidelines: diagnosis and management of celiac disease. *Am J Gastroenterol.* May 2013; 108(5): 656-76; quiz 677. PMID 23609613
29. Hanaway P. Ask the experts. *Explore (NY).* May 2006; 2(3): 284. PMID 16781657
30. Prometheus Laboratories. IBD sgi Diagnostic. Accessed May 10, 2024.

MEDICAL POLICY

POLICY TITLE	INVESTIGATIONAL MISCELLANEOUS GENETIC AND MOLECULAR TESTS
POLICY NUMBER	MP 2.277

31. Shirts B, von Roon AC, Tebo AE. The entire predictive value of the prometheus IBD sgi diagnostic product may be due to the three least expensive and most available components. *Am J Gastroenterol*. Nov 2012; 107(11): 1760-1. PMID 23160303
32. Conrad K, Roggenbuck D, Laass MW. Diagnosis and classification of ulcerative colitis. *Autoimmun Rev*. 2014; 13(4-5): 463-6. PMID 24424198
33. Laass MW, Roggenbuck D, Conrad K. Diagnosis and classification of Crohn's disease. *Autoimmun Rev*. 2014; 13(4-5): 467-71. PMID 24424189
34. Ordás I, Eckmann L, Talamini M, et al. Ulcerative colitis. *Lancet*. Nov 03 2012; 380(9853): 1606-19. PMID 22914296
35. Kornbluth A, Sachar DB. Ulcerative colitis practice guidelines in adults: American College Of Gastroenterology, Practice Parameters Committee. *Am J Gastroenterol*. Mar 2010; 105(3): 501-23; quiz 524. PMID 20068560
36. Baumgart DC, Sandborn WJ. Crohn's disease. *Lancet*. Nov 03 2012; 380(9853): 1590-605. PMID 22914295
37. Lichtenstein GR, Hanauer SB, Sandborn WJ, et al. Management of Crohn's disease in adults. *Am J Gastroenterol*. Feb 2009; 104(2): 465-83; quiz 464, 484. PMID 19174807
38. Reese GE, Constantinides VA, Simillis C, et al. Diagnostic precision of anti-Saccharomyces cerevisiae antibodies and perinuclear antineutrophil cytoplasmic antibodies in inflammatory bowel disease. *Am J Gastroenterol*. Oct 2006; 101(10): 2410-22. PMID 16952282
39. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice guidelines in oncology: colon cancer. Version 2.2024. Accessed May 20, 2024.
40. Singh S, Ananthakrishnan AN, Nguyen NH, et al. AGA Clinical Practice Guideline on the Role of Biomarkers for the Management of Ulcerative Colitis. *Gastroenterology*. Mar 2023; 164(3): 344-372. PMID 36822736
41. Lichtenstein GR, Loftus EV, Isaacs KL, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol*. Apr 2018; 113(4): 481-517. PMID 29610508
42. Blue Cross Blue Shield Association Medical Policy Reference Manual. 2.04.121 Miscellaneous Genetic and Molecular Diagnostic Tests. September 2024

IX. POLICY HISTORY

[Top](#)

MP 2.277	<p>12/30/2021 Major Review. Policy title updated (added "Investigational")</p> <p>Removed: DecisionDx-Thymoma and TransPredict FC gamma 3A (no longer marketed). Removed G6PD testing from coding section (see MP 2.326)</p> <p>Added: BeScreened, ibs-smart (moved from MP 4.002 policy) and insight TNBC. Added tests listed in coding section to table 1: Decipher Bladder, IBSChek, Oncosignal 7 and PreductSURE IBC. Added coding for Crohns Prognostic to align with company website. Removed 5 columns from table 1 (date added, diagnostic, therapeutic, prognostic, and future risk) and added one column (coding information). Coding information from the bottom of the policy was moved to coding information column in Table 1.</p> <p>Description/background updated. Updated references. Added NCCN statement.</p>
-----------------	--

MEDICAL POLICY

POLICY TITLE	INVESTIGATIONAL MISCELLANEOUS GENETIC AND MOLECULAR TESTS
POLICY NUMBER	MP 2.277

03/13/2022 Administrative Update. New code added 0317U; effective 4-1-22.
12/29/2022 Consensus Review. No change to policy statement, all tests on policy remain. Reformatted and updated background to include OncoSignal 7 and LungLB®. Updated references.
03/16/2023 Administrative Update. New codes added 0365U, 0366U & 0367U; effective 4-1-23.
09/07/2023 Administrative Update. New codes added 0405U, 0410U, 0413U, 0414U. Effective 10/1/2023.
10/16/2023 Consensus Review. No changes to policy statement. Added codes: 0006M, 0007M, 0017M, 0002U, 0032U, 0045U, 0058U, 0059U, 0087U, 0120U, 0174U, 0288U, 0294U, 0297U, 0298U, 0299U, 0300U, 0315U, 0331U, 0332U, 0333U, 0350U, 0356U, 81554, 82274, 82542, 82653, 82715, 82725, 83993, 84311, 86231, 86258, 86364, 87505. Removed codes 0001U, 0153U, 0365U-0367U, 81401, 86021, 86036, 86255, 88350. Updated references.
12/12/2023 Administrative Update. Added 0420U, 0422U, and 0432U. Effective 1/1/2024
03/15/2024 Administrative Update. Added 0444U. Effective 4/1/2024.
06/07/2024 Administrative Update. Added New Codes 0467U and 0470U. Effective date 7/1/2024.
09/18/2024 Administrative Update. Added codes 0486U, 0489U, 0498U, 0499U, 0510U, 0520U. Effective 10/1/2024.
09/25/2024 Consensus Review. No changes to policy statement. References updated.
12/11/2024 Administrative Update. Added 0529U, 81195. Effective 1/1/2025.
12/16/2024 Administrative Update. Removed NCCN Statement.

[Top](#)

Health care benefit programs issued or administered by Capital Blue Cross and/or its subsidiaries, Capital Advantage Insurance Company®, Capital Advantage Assurance Company® and Keystone Health Plan® Central. Independent licensees of the BlueCross BlueShield Association. Communications issued by Capital Blue Cross in its capacity as administrator of programs and provider relations for all companies.