MEDICAL POLICY	Genetic Testing: Inherited Susceptibility to Colorectal Cancer (Medicare Only)
Effective Date: 4/1/2022  4/1/2022 Medical Officer Date	Medical Policy Number: 117 Medical Policy Committee Approved Date: 1/17; 4/18; 1/19; 11/19; 03/2020; 12/2020; 05/2021; 10/2021; 3/2022

See Policy CPT CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:

Medicare only

MEDICARE POLICY CRITERIA

The following Centers for Medicare & Medicaid Service (CMS) guidelines should be utilized for medical necessity coverage determinations. Click the link provided in the table below to access applicable medical necessity criteria. All listed guidelines apply.

See "Policy Guidelines" for specific panel test information.

Service	Medicare Guidelines
Familial Adenomatous Polyposis (FAP), Attenuated FAP (AFAP) or MYH-associated polyposis (MAP) (APC *and* MUTYH *genes)*	For testing performed in the states of AK, ID, OR, WA, UT, AZ, MT, ND, SD, or WY: Local Coverage Determination (LCD): MolDX: APC and MUTYH Gene Testing (L36884)
Lynch syndrome	• For testing performed in the states of AK, ID, OR, WA, UT, AZ, MT, ND, SD, or WY: LCD: MolDX: Genetic Testing for Lynch Syndrome (L36374) • For testing performed in CA or NV: LCD: MolDX: Genetic Testing for Lynch Syndrome (L36370) • For testing performed in GA, TN, AL, NC, SC, VA, WV: LCD: MolDX: Genetic Testing for Lynch Syndrome (L35024)

	These tests are considered **medically necessary** when the above LCD criteria are met. • CancerNext, by Ambry Genetics (California) • ColoNext, by Ambry Genetics (California) • myRisk® Hereditary Cancer, by Myriad (Utah) • VistaSeq Hereditary Cancer Panel, by LabCorp / Integrated Genetics / Integrated Oncology (Any state; LabCorp is headquartered in North Carolina, so LCD used would be selected based on this location) • VistaSeq Hereditary Cancer without BRCA, by LabCorp / Integrated Genetics / Integrated Oncology (Any state; LabCorp is headquartered in North Carolina, so LCD used would be selected based on this location)
	These tests are considered **not medically necessary**, based on Medicare guidelines. • CancerNext-Expanded, by Ambry Genetics (California) • CancerNext-Expanded +RNAinsight™, by Ambry Genetics (California) • ColoNext +RNAinsight™, by Ambry Genetics (California) • myRisk® Hereditary Cancer ***Update***, by Myriad (Utah) • VistaSeq Colorectal Cancer Profile, by LabCorp / Integrated Genetics / Integrated Oncology (Any state; LabCorp is headquartered in North Carolina, so LCD used would be selected based on this location) *See "Policy Guidelines" below.*

POLICY GUIDELINES

Medicare and Medical Necessity

Laboratories performing tests in service areas which have adopted guidelines or coverage determinations made by the Medicare Molecular Diagnostics (MolDX) Program contractor are required to submit a technology assessment (TA) to establish analytical and clinical validity (AV/CV) and clinical utility (CU). Supporting LCDs regarding TA reviews include, but are not limited to, the following:

- Laboratories in CA & NV: LCD for MolDX: Molecular Diagnostic Tests (MDT) (L35160)
- Laboratories in NC, SC, GA, TN, AL, VA, & WV: LCD for MolDX: Molecular Diagnostic Tests (MDT) (L35025)

- Laboratories in AK, ID, OR, WA, UT, AZ, MT, ND, SD, & WY: LCD for MolDX: Molecular Diagnostic Tests (MDT) (L36256)

Coverage or non-coverage determinations made by MolDX are maintained in the DEX™ Diagnostics Exchange registry catalog and are available for public viewing. If a test does not have a coverage determination by the MolDX Program, then AV/CV and CU have **not** been established and the test is considered not medically reasonable and necessary under *SSA §1862(a)(1)(A)* until a MolDX review is complete and coverage is indicated by MolDX or Noridian. Therefore, tests identified in this policy as not meeting this requirement are not medically reasonable or necessary for Medicare under *SSA §1862(a)(1)(A).*

Related panel tests include:

Note: This list was accurate at the time of publication, but it is subject to change at any time by the Medicare MolDX Program contractor.

Proprietary Test Name *(When performed for colorectal cancer-related conditions)*	**Laboratory**	**MolDX TA Review Outcome (as found in the DEX™ Diagnostics Exchange registry)**
CancerNext	Ambry Genetics (California)	Covered
CancerNext-Expanded	Ambry Genetics (California)	Not Covered
CancerNext-Expanded +RNAinsight™	Ambry Genetics (California)	Not Covered
ColoNext	Ambry Genetics (California)	Covered
ColoNext +RNAinsight™	Ambry Genetics (California)	Not Covered
myRisk® Hereditary Cancer	Myriad (Utah)	Covered
myRisk® Hereditary Cancer *Update*	Myriad (Utah)	Not Covered
VistaSeq Colorectal Cancer Profile	LabCorp / Integrated Genetics / Integrated Oncology (Any state; LabCorp is headquartered in North Carolina, so LCD used would be selected based on this location)	Not Covered
VistaSeq Hereditary Cancer Panel	LabCorp / Integrated Genetics / Integrated Oncology (Any state; LabCorp is headquartered in North Carolina, so LCD used would be selected based on this location)	Covered
VistaSeq Hereditary Cancer without BRCA	LabCorp / Integrated Genetics / Integrated Oncology (Any state; LabCorp is headquartered in North Carolina, so LCD used would be selected based on this location)	Covered

BILLING GUIDELINES

Please refer to the following local coverage articles (LCAs) for coding and billing assistance:

- LCA: A57353, Billing and Coding: MolDX: APC and MUTYH Gene Testing
- LCA: A54996, Billing and Coding: MolDX: Genetic Testing for Lynch Syndrome
- LCA: A56104, Billing and Coding: MolDX: Microsatellite Instability-High (MSI-H) and Mismatch Repair Deficient (dMMR) Biomarker Billing and Coding Guidelines for Patients with Unresectable or Metastatic Solid Tumors

When no specific CPT or HCPCS code exists for the panel, the provider is required to bill using an unlisted code. It is not appropriate for the provider to bill any of the tests in a panel separately as if they were performed individually. This is a misrepresentation of services performed and is not appropriate based on either CPT or CMS guidelines. In a "Healthcare Fraud Prevention Partnership" white paper published in May, 2018, CMS identified unbundling of lab panels as an example of fraudulent billing.

CPT CODES

Medicare Only	
Prior Authorization Required	
0101U	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis), genomic sequence analysis panel utilizing a combination of NGS, Sanger, MLPA, and array CGH, with MRNA analytics to resolve variants of unknown significance when indicated (15 genes [sequencing and deletion/duplication], EPCAM and GREM1 [deletion/duplication only]) *(ColoNext®)*
0238U	Oncology (Lynch syndrome), genomic DNA sequence analysis of MLH1, MSH2, MSH6, PMS2, and EPCAM, including small sequence changes in exonic and intronic regions, deletions, duplications, mobile element insertions, and variants in non-uniquely mappable regions
81201	APC (adenomatous polyposis coli)(e.g. familial adenomatosis polyposis[FAP] gene analysis, full gene sequence
81202	APC (adenomatous polyposis coli)(e.g. familial adenomatosis polyposis [FAP] gene analysis, known familial variants
81203	APC (adenomatous polyposis coli)(e.g. familial adenomatosis polyposis [FAP] gene analysis; duplication/deletion variants
81288	MLH1 (mutl. Homolog1, colon cancer, non-polyposis type 2 (e.g. hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; promoter methylation analysis
81292	MLH1 (mutl. Homolog1, colon cancer, non-polyposis type 2 (e.g. hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81293	MLH1 (homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non- polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants

81294	MLH1 (mutL homolog 1, colon cancer, nonpolyposis type 2) (e.g., hereditary non- Polyposis colorectal cancer, Lynch Syndrome) gene analysis; duplication/deletion variants
81295	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81296	MSH2 (mutS homolog 2, colon cancer, nonpolyposis type 1) (e.g., hereditary non- polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81297	MSH2 (mutS homolog 2, colon cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81298	MSH6 (mutS homolog 6 [E.coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81299	MSH6 (mutS homolog 6 [E.coli])(e.g. hereditary nonpolyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81300	MSH6 (mutS homolog 6 [E.coli]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81317	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non- polyposis colorectal cancer, Lynch syndrome) gene analysis; full sequence analysis
81318	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non-polyposis colorectal cancer, Lynch syndrome) gene analysis; known familial variants
81319	PMS2 (postmeiotic segregation increased 2 [S. cerevisiae]) (e.g., hereditary non- polyposis colorectal cancer, Lynch syndrome) gene analysis; duplication/deletion variants
81401	Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat) – when used for MUTYH (mutY homolog [E. coli]) (eg, MYH-associated polyposis), common variants (eg, Y165C, G382D)
81403	Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons) – when used for EPCAM (epithelial cell adhesion molecule) (eg, Lynch syndrome), duplication/deletion analysis
81406	Molecular pathology procedure, Level 7 (eg, analysis of 11-25 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 26-50 exons, cytogenomic array analysis for neoplasia) – when used for MUTYH (mutY homolog [E. coli]) (eg, MYH-associated polyposis), full gene sequence
81435	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); genomic sequence analysis panel, must include sequencing of at least 10 genes, including APC, BMPR1A, CDH1, MLH1, MSH2, MSH6, MUTYH, PTEN, SMAD4, and STK11
81436	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis); duplication/deletion analysis panel, must include analysis of at least 5 genes, including MLH1, MSH2, EPCAM, SMAD4, and STK11
81445	Targeted genomic sequence analysis panel, solid organ neoplasm, DNA analysis, and RNA analysis when performed, 5-50 genes (eg, ALK, BRAF, CDKN2A, EGFR, ERBB2, KIT, KRAS, NRAS, MET, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed

81455	Targeted genomic sequence analysis panel, solid organ or hematolymphoid neoplasm, DNA analysis, and RNA analysis when performed, 51 or greater genes (eg, ALK, BRAF, CDKN2A, CEBPA, DNMT3A, EGFR, ERBB2, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MLL, NPM1, NRAS, MET, NOTCH1, PDGFRA, PDGFRB, PGR, PIK3CA, PTEN, RET), interrogation for sequence variants and copy number variants or rearrangements, if performed
Not Covered Based on an LCD or LCA, all codes in this section are **non-covered** by Medicare.	
0130U	Hereditary colon cancer disorders (eg, Lynch syndrome, PTEN hamartoma syndrome, Cowden syndrome, familial adenomatosis polyposis), targeted mRNA sequence analysis panel (APC, CDH1, CHEK2, MLH1, MSH2, MSH6, MUTYH, PMS2, PTEN, and TP53) (List separately in addition to code for primary procedure) *(RNAinsight™ for ColoNext®)*
0134U	Hereditary pan cancer (eg, hereditary breast and ovarian cancer, hereditary endometrial cancer, hereditary colorectal cancer), targeted mRNA sequence analysis panel (18 genes) (List separately in addition to code for primary procedure) *(RNAinsight™ for CancerNext®)*
0157U	APC (APC regulator of WNT signaling pathway) (eg, familial adenomatosis polyposis [FAP]) mRNA sequence analysis (List separately in addition to code for primary procedure) *(CustomNext + RNA: APC)*
0158U	MLH1 (mutL homolog 1) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) *(CustomNext + RNA: MLH1)*
0159U	MSH2 (mutS homolog 2) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) *(CustomNext + RNA: MSH2)*
0160U	MSH6 (mutS homolog 6) (eg, hereditary colon cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) *(CustomNext + RNA: MSH6)*
0161U	PMS2 (PMS1 homolog 2, mismatch repair system component) (eg, hereditary non-polyposis colorectal cancer, Lynch syndrome) mRNA sequence analysis (List separately in addition to code for primary procedure) *(CustomNext + RNA: PMS2)*
0162U	Hereditary colon cancer (Lynch syndrome), targeted mRNA sequence analysis panel (MLH1, MSH2, MSH6, PMS2) (List separately in addition to code for primary procedure) *(CustomNext + RNA: Lynch (MLH1, MSH2, MSH6, PMS2))*
No Prior Authorization Required	
81210	BRAF (v-raf murine sarcoma viral oncogene homolog B1) (e.g. Colon Cancer) gene analysis, V600E variant
Unlisted Codes All unlisted codes will be reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is billed related to services addressed in this policy then **prior-authorization is required.**	
81479	Unlisted molecular pathology procedure

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

REGULATORY STATUS

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.