MEDICAL POLICY	Inflammatory Bowel Disease: Serologic Testing and Therapeutic Monitoring (Medicare Only)
Effective Date: 1/1/2023  1/1/2023 Medical Officer Date	Medical Policy Number: 344 Medical Policy Committee Approved Date: 8/2022; 11/2022

See Policy CPT/HCPCS 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.

Service	Medicare Guidelines
Prometheus IBD sgi Diagnostic (California)	Local Coverage Determination (LCD): MolDX: Prometheus IBD sgi Diagnostic® Policy (L37299)
Thiopurine Methyltransferase (TPMT) and NUDT15 Genetic Testing	• **For testing performed in AK, ID, OR, WA, UT, AZ, MT, ND, SD, or WY:** Local Coverage Article (LCA): Billing and Coding: MolDX: Pharmacogenomics Testing (A57385) and LCD L38337 • **For testing performed in CA or NV:** LCA: Billing and Coding: MolDX: Pharmacogenomics Testing (A57384) and LCD L38335 **NOTES:** 1. **TPMT and NUDT15** testing may be medically necessary when treatment planning / medical management include consideration of the medication(s) associated with each gene specified in the above LCAs. Other uses of these

	gene tests would be considered not medically necessary otherwise. 2. The ***Prometheus® TPMT Genetics test*** (Prometheus Laboratories; California) **has** completed the technical assessment requirement to evaluate analytical validity, clinical validity, and clinical utility and may be medically necessary when the other requirements of the LCD/LCA are otherwise met. • **For testing performed in IL, MN, WI, CT, NY, ME, MA, NH, RI, or VT:** LCA: Billing and Coding: Molecular Pathology Procedures A56199 and LCD L35000. **NOTES:** 1. Apply the limited diagnosis code coverage detailed in the LCA A56199 for CPT **81335** (TPMT). 2. According to LCA A56199, CPT **81306** (NUDT15) testing is subject to individual review. Since the LCA doesn't provide specific guidance for this gene testing, apply the Company medical policy criteria below. 3. Apply the same TPMT and NUDT15 criteria to the tests represented by PLA codes **0034U and 0169U**, since these "panels" are targeted to just two gene tests. According to LCD L35000, panels require medical necessity for each component, so the criteria for **both** genes must be met in order for these panels to be considered medically necessary. 4. For **0203U and 0286U**, according to LCD L35000, analytical validity and clinical utility must be documented, but with no guidance in the LCD, apply the Company medical policy criteria below.
NOD2/CARD15 Genetic Testing	The ***Prometheus® NOD2/CARD15 test*** (Prometheus Laboratories; California) is **not medically necessary** according to the DEX™ Diagnostics Exchange Registry, which holds MolDX coverage decisions for individual tests. Other NOD2/CARD15 tests not listed will require individual review.
Prometheus® Crohn's Prognostic test (Prometheus Laboratories; California)	The ***Prometheus® Crohn's Prognostic test*** (Prometheus Laboratories; California) is **not medically necessary** according to the DEX™ Diagnostics Exchange Registry, which holds MolDX coverage decisions for individual tests.

Fecal Calprotectin Testing *Quantitative Polymerase Chain Reaction (PCR) Testing for the Diagnosis and/or Management of IBD* *Thiopurine Therapeutic Drug Monitoring (Measurement of 6-thioguanine nucleotide [6-TGN] and 6-methylmercaptopurine nucleotide [6-MMPN] [e.g.,* ***Prometheus Thiopurine Metabolites]****)* *Testing for Serological Markers for Diagnosis and/or Management of IBD** *Combination panel testing of serologic, genetic, and inflammatory markers for Diagnosis and/or Management of IBD* ***Examples:*** • ***IBS-Smart test kit,*** • ***PredictSURE IBD™ Test [KSL Diagnostics; 0203U; New York]*** • ***CNT [CEP72, TPMT and NUDT15] Genotyping Panel [RPRD Diagnostics; 0286U; Wisconsin])***	Company medical policy for Inflammatory Bowel Disease: Serologic Testing and Therapeutic Monitoring (All Lines of Business Except Medicare) I. These services may be considered **medically necessary** for Medicare when the Company medical policy criteria are met. II. These services are considered **not medically necessary** for Medicare Plan members either when the Company medical policy criteria are **not** met ***or*** when a service is deemed "investigational" by the Company policy. *Services deemed "investigational" are considered not medically necessary for Medicare Plan members.* See *Policy Guidelines below.*

POLICY GUIDELINES

*Serological Marker Testing for Diagnosis and/or Management of Inflammatory Bowel Disease

Examples of these tests/panels include, but are not limited to, the following:

- Anti-Saccharomyces cerevisiae antibodies (ASCA)
- Anti-glycan-associated Saccharomyces cerevisiae antibodies (gASCA)

- Anti-neutrophilic cytoplasmic antibody (ANCA)
- Perinuclear antineutrophil cytoplasmic autoantibodies (pANCA)
- Anti-outer membrane porin protein C of Escherichia coli antibodies (anti-OmpC)
- Anti-chitobioside carbohydrate antibodies (ACCA)
- Anti-laminaribioside carbohydrate antibodies (ALCA)
- Anti-mannobioside carbohydrate antibodies (AMCA)

Medicare and Medical Necessity

Medicare requires diagnostic laboratory tests be ordered by a provider who is treating the member for a specific medical problem **and** who will use the test results in the direct management of that specific medical problem.[1,2] Thus, diagnostic testing must have established clinical utility and analytic validity.

The Company policy for *PHA Medicare Medical Policy Development and Application* (MP50) provides details regarding Medicare's definition of medical necessity and the hierarchy of Medicare references and resources during the development of medical policies, as well as the Plan's use of evidence-based processes for policy development. In the absence of Medicare coverage policies (e.g., manual, national coverage determination [NCD], local coverage determination [LCD], article [LCA], etc.), Medicare regulatory guidelines do allow Medicare Advantage Organizations (MAOs) to make their own coverage determinations, as long as the MAO applies an objective, evidence-based process, based on authoritative evidence. *(Medicare Managed Care Manual, Ch. 4, §90.5)*

Following an evidence-based assessment of current peer-reviewed medical literature, the Company may consider certain medical services or technologies to be "investigational." The term "investigational" is not limited to devices or technologies which have not received the appropriate governmental regulatory approval (e.g., U.S. Food and Drug Administration [FDA]), but rather may also mean the procedure, device, or technology does not meet all of the Company's technology assessment criteria, as detailed within the Company policy for *Definition: Experimental/Investigational* (MP5).

Only medically reasonable and necessary services or items which treat illness or injury are eligible for Medicare coverage, as outlined in *Title XVIII of the Social Security Act, §1862(a)(1)(A)*. Thus, services which lack scientific evidence regarding safety and efficacy because they are investigational are "not medically reasonable or necessary" for Medicare Plan members. *(Medicare Claims Processing Manual, Ch. 23, §30 A)*

BILLING GUIDELINES

General

See the associated local coverage article (LCA) for related billing and coding guidance:

- LCA: Billing and Coding: MolDX: Prometheus IBD sgi Diagnostic Policy (A57516)

Only one genotypic (CPT code: 81401 or 84433) or phenotypic (CPT codes: 82542 and 82657) assay of TPMT is considered medically necessary, per individual, per lifetime.

Coding Policy 30.0 Laboratory Panel Billing

Testing panels must be billed using a single code. When no specific CPT or HCPCS code exists for the panel, the provider is required to bill the panel using an unlisted code. CPT guidelines state, "Do not select a CPT code that merely approximates the service provided. If no such specific code exists, then report the service using the appropriate unlisted procedure or service code."

Unbundling occurs when a laboratory bills separately for some or all tests analyzed as part of a panel. 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.

Both the Prometheus IBD sgi Diagnostic and Prometheus Crohn's Prognostic tests are not medically necessary, regardless of what single code or code combination they are billed with.

CPT/HCPCS CODES

Medicare Only	
Prior Authorization Required	
0034U	TPMT (thiopurine S-methyltransferase), NUDT15 (nudix hydroxylase 15) (eg, thiopurine metabolism) gene analysis, common variants (ie, TPMT *2, *3A, *3B, *3C, *4, *5, *6, *8, *12; NUDT15 *3, *4, *5) *(Used to report Thiopurine Methyltransferase [TPMT] and Nudix Hydrolase [NUDT15] Genotyping test, by Mayo Clinic; Minnesota)*
0169U	NUDT15 (nudix hydrolase 15) and TPMT (thiopurine S-methyltransferase) (eg, drug metabolism) gene analysis, common variants *(Used to report NT [NUDT15 and TPMT] Genotyping Panel test, by RPRD Diagnostics; Wisconsin)*
0203U	Autoimmune (inflammatory bowel disease), mRNA, gene expression profiling by quantitative RT-PCR, 17 genes (15 target and 2 reference genes), whole blood, reported as a continuous risk score and classification of inflammatory bowel disease aggressiveness *(Used to report the PredictSURE IBD™ Test, by KSL Diagnostics; New York)*
81306	NUDT15 (nudix hydrolase 15) (eg, drug metabolism) gene analysis, common variant(s) (eg, *2, *3, *4, *5, *6)
81335	TPMT (thiopurine S-methyltransferase) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3)
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)
84433	Thiopurine S-methyltransferase (TPMT)

No Prior Authorization Required Note: Inclusion of a code in this section does not guarantee reimbursement or coverage. The following codes do not require routine review for medical necessity, but they may be subject to audit or benefit denial.	
82542	Column chromatography, includes mass spectrometry, if performed (eg, HPLC, LC, LC/MS, LC/MS-MS, GC, GC/MS-MS, GC/MS, HPLC/MS), non-drug analyte(s) not elsewhere specified, qualitative or quantitative, each specimen
82657	Enzyme activity in blood cells, cultured cells, or tissue, not elsewhere specified; nonradioactive substrate, each specimen
83993	Calprotectin, fecal
Not Covered	
0286U	CEP72 (centrosomal protein, 72-KDa), NUDT15 (nudix hydrolase 15) and TPMT (thiopurine S-methyltransferase) (eg, drug metabolism) gene analysis, common variants *(Used to report CNT [CEP72, TPMT and NUDT15] genotyping panel, by RPRD Diagnostics; Wisconsin)*
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
84999	Unlisted chemistry 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.

MEDICAL POLICY CROSS REFERENCES

- Inflammatory Bowel Disease: Measurement of Antibodies to Immunosuppressive Therapies (Medicare Only), MP345

REFERENCES

1. 42 CFR §410.32(a); Available at: https://www.govinfo.gov/content/pkg/CFR-2011-title42-vol2/pdf/CFR-2011-title42-vol2-sec410-32.pdf
2. Medicare Benefit Policy Manual, Ch. 15 – Covered Medical and Other Health Services, §80.1 - Clinical Laboratory Services; Available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf