Medicare Medical Policy

Inflammatory Bowel Disease: Serologic Testing and Therapeutic Monitoring

MEDICARE MEDICAL POLICY NUMBER: 344

Effective Date: 3/1/2023

Last Review Date: 1/2023

Next Annual Review: 8/2023

INSTRUCTIONS FOR USE: Company Medicare Medical Policies serve as guidance for the administration of plan benefits and do not constitute medical advice nor a guarantee of coverage. Company Medicare Medical Policies are reviewed annually to guide the coverage or non-coverage decision-making process for services or procedures in accordance with member benefit contracts (otherwise known as Evidence of Coverage or EOCs) and Centers of Medicare and Medicaid Services (CMS) policies, manuals, and other CMS rules and regulations. In the absence of a CMS coverage determination or specific regulation for a requested service, item or procedure, Company policy criteria or applicable utilization management vendor criteria may be applied. These are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. 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.

The Company reserves the right to determine the application of Medicare Medical Policies and make revisions to these policies at any time. Any conflict or variance between the EOC and Company Medical Policy will be resolved in favor of the EOC.

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”).

PRODUCT AND BENEFIT APPLICATION

☒ Medicare Only

MEDICARE COVERAGE CRITERIA

IMPORTANT NOTE: More than one Centers for Medicare and Medicaid Services (CMS) reference may apply to the same health care service, such as when more than one coverage policy is available (e.g., both an NCD and LCD exist). All references listed should be considered for coverage decision-making. The Company uses the most current version of a Medicare reference available at the time of publication; however, these websites are not maintained by the Company, so Medicare references and their corresponding hyperlinks may change at any time. If there is a conflict between the Company Medicare Medical Policy and CMS guidance, the CMS guidance will govern.

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. I. 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*	Company medical policy for Inflammatory Bowel Disease: Serologic Testing and Therapeutic Monitoring 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.*

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])***	

IMPORTANT NOTICE: While some services or items may appear medically indicated for an individual, they may also be a direct exclusion of Medicare or the member's benefit plan. Such excluded services or items by Medicare and member EOCs include, but are not limited to, services or procedures considered to be cosmetic, not medical in nature, or those considered not medically reasonable or necessary under *Title XVIII of the Social Security Act, §1862(a)(1)(A).* If there is uncertainty regarding coverage of a service or item, please review the member EOC or submit a pre-service organization determination request. Note that the Medicare Advance Beneficiary Notice of Noncoverage (ABN) form **cannot** be used for Medicare Advantage members. *(Medicare Advance Written Notices of Non-coverage. MLN006266 May 2021)*

POLICY CROSS REFERENCES

- Inflammatory Bowel Disease: Measurement of Antibodies to Immunosuppressive Therapies, MP345

The full Company portfolio of Medicare Medical Policies is available online and can be accessed here.

POLICY GUIDELINES

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)*

REGULATORY STATUS

U.S. FOOD & DRUG ADMINISTRATION (FDA)

While clearance by the Food and Drug Administration (FDA) is a prerequisite for Medicare coverage, the 510(k) premarket clearance process does not in itself establish medical necessity. Medicare payment policy is determined by the interaction of numerous requirements, including but not limited to, the availability of a Medicare benefit category and other statutory requirements, coding and pricing guidelines, as well as national and local coverage determinations and clinical evidence.

BILLING GUIDELINES AND CODING

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.

CODES*		
CPT	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)*
	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)*
	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)
	81479	Unlisted molecular pathology procedure
	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
	84433	Thiopurine S-methyltransferase (TPMT)
	84999	Unlisted chemistry procedure
HCPCS	None	

***Coding Notes:**

- The code list above is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit. According to Medicare, "presence of a payment amount in the MPFS and the Medicare physician fee schedule database (MPFSDB) does not imply that CMS has determined that the service may be covered by Medicare." The issuance of a CPT or HCPCS code or the provision of a payment or fee amount by Medicare does **not** make a procedure medically reasonable or necessary or a covered benefit by Medicare. *(Medicare Claims Processing Manual, Chapter 23 - Fee Schedule Administration and Coding Requirements, §30 - Services Paid Under the Medicare Physician's Fee Schedule, A. Physician's Services)*
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is

submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.

- **See the non-covered and prior authorization lists on the Company Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website for additional information.**
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as "medically unlikely edits" (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

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

POLICY REVISION HISTORY

DATE	REVISION SUMMARY
1/2023	Q1 2023 code updates (converted to new format 2/2023)
3/2023	Interim update (code configuration change only). Converted to new policy template.