Medicare Medical Policy

Measurement of Antibodies to Immunosuppressive Therapies for Inflammatory Bowel Disease

MEDICARE MEDICAL POLICY NUMBER: 345

Effective Date: 3/1/2025

Last Review Date: 2/2025

Next Annual Review: 7/2025

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, and Providence Plan Partners 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

Medicare Coverage Criteria: "MA organizations may create publicly accessible internal coverage criteria… when coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs." *(§ 422.101(b)(6) – see Policy Guidelines below*)

- **Medicare Coverage Manuals:** Medicare does not have criteria for the measurement of antibody serum levels to infliximab, adalimumab, ustekinumab or vedolizumab, whether performed individually or as part of a panel, in a coverage manual. **However, broad coverage requirements are provided by Medicare for diagnostic laboratory testing in general.** Specifically, Medicare requires diagnostic laboratory tests be ordered by a provider who is treating the member for a specific medical problem and who will promptly use the test results in the direct management of that specific medical problem.[1,2] These coverage criteria are considered "not fully established" under CFR § 422.101(6)(i)(A) as additional criteria are needed to interpret or supplement these general coverage provisions in order to determine medical necessity consistently.
- **National Coverage Determination (NCD):** There is no NCD for testing measurement of antibody serum levels to infliximab, adalimumab, ustekinumab or vedolizumab.
- **Local Coverage Determination (LCD)/Local Coverage Article (LCA):** According to Medicare guidelines, "Jurisdiction of payment requests for laboratory services furnished by an independent laboratory… lies with the A/B MAC (B) serving the area in which the laboratory test is performed."[3] The diagnostic laboratory tests identified below do **not** have an available LCD or LCA for their respective service areas (Prometheus Laboratories and ProciseDx, Inc. are both located in California, under the MAC Noridian Jurisdiction **E**).
- Therefore, in the absence of established Medicare coverage criteria in a manual, NCD, LCD, or other regulatory guidance for the service area in which the testing is being performed, Company criteria below are applied for medical necessity decision-making. Medicare statutes and regulation provide general coverage criteria for diagnostic testing, but additional criteria to interpret or supplement the Medicare criteria are being used in order to determine medical necessity consistently. These additional criteria provide clinical benefits that are highly likely to outweigh any clinical harms, including from delayed or decreased access to items or services **because the use of this additional criteria based on peer-reviewed evidence evaluates how**

	testing is expected to improve diagnosis, improve patient management, change treatment decisions or improve health outcomes. Specifically, the literature review is used to evaluate whether or not each test has established clinical utility and/or analytic validity. Further studies of good methodological quality are required to determine if this testing aids in treatment decisions and improves patient outcomes, as well as evaluate the usefulness of these tests as a diagnostic tool. While antibody testing has become a more frequently performed test, despite low quality evidence that demonstrates it improves health outcomes, without a standardized reporting of antibody values, guiding treatment by these results may actually lead to *inaccurate* dosing adjustments. • ***NOTE:*** *The summary of evidence, as well as the list of citations/references used in the development of the Company's internal coverage criteria, are publicly available and can be found using the Company medical policy link below [CFR § 422.101(6)(ii)(A) and (B)].*
Measurement of Serum Levels and Antibodies to Infliximab, Adalimumab, Ustekinumab or Vedolizumab (e.g., PROMETHEUS® Anser® IFX, PROMETHEUS® Anser® ADA, PROMETHEUS® Anser®VDZ, PROMETHEUS® Anser®UST, PROMETHEUS® PredictrPK® tests, all by Prometheus Laboratories; California, as well as Procise ADL™ [0514U] and Procise IFX™ [0515U] tests, both by ProciseDx Inc.)	Company medical policy for Inflammatory Bowel Disease: Measurement of Antibodies to Immunosuppressive Therapies I. These services are considered **not medically necessary** for Medicare based on the Company medical policy. *See Policy Guidelines below.*

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: Serologic Testing and Therapeutic Monitoring, MP344

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

POLICY GUIDELINES

MEDICARE AND MEDICAL NECESSITY

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)*. MA organizations (MAOs) make medical necessity determinations based on coverage and benefit criteria, current

standards of care, the member's unique personal medical history (e.g., diagnoses, conditions, functional status, co-morbidities, etc.), physician recommendations, and clinical notes, as well as involvement of a plan medical director, where appropriate. *(§ 422.101(c)(1))*

In addition:

> "MA organizations may create publicly accessible internal coverage criteria that are based on current evidence in widely used treatment guidelines or clinical literature when coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs. Current, widely-used treatment guidelines are those developed by organizations representing clinical medical specialties, and refers to guidelines for the treatment of specific diseases or conditions. Acceptable clinical literature includes large, randomized controlled trials or prospective cohort studies with clear results, published in a peer-reviewed journal, and specifically designed to answer the relevant clinical question, or large systematic reviews or meta-analyses summarizing the literature of the specific clinical question." *(§ 422.101(b)(6) and Medicare Managed Care Manual, Ch. 4, §90.5)*

The peer-reviewed evidence must demonstrate how testing is expected to improve diagnosis, improve patient management, change treatment decisions or improve health outcomes. Specifically, the literature review must establish whether or not the test has documented clinical utility and/or 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.

There is a Noridian Jurisdiction E (J-E) non-coverage LCD policy for the Prometheus® IBD sgi Diagnostic® test (L37299); however, this is a **different** test than those addressed by this policy.

Since there are not fully established coverage criteria for these diagnostic tests available in applicable Medicare statutes, regulations, NCDs or LCDs (for the service area in which the testing is being performed), then Company medical policy criteria will be applied. See the Medicare Coverage Criteria table above for more information regarding the use of internal coverage criteria when Medicare coverage criteria are not fully established. **While antibody testing has become a more frequently performed test, despite low quality evidence that demonstrates it improves health outcomes, without a standardized reporting of antibody values, guiding treatment by these results may actually lead to inaccurate dosing adjustments.**

Table 1: Available Tests

Test Name	Associated Drug
Prometheus® Laboratories Inc.	
4nswer™IFX test	Infliximab
4nswer™ADA	Adalimumab
4nswer® UST	Ustekinumab
4nswer® VDZ	Vedolizumab

PredictrPK® IFX, - ADA	Infliximab, Adalimumab, etc.
LabCorp	
DoseASSURE™ ADL	Adalimumab
DoseASSURE™ UST	Ustekinumab
DoseASSURE™ IFX	Infliximab
DoseASSURE™ CTZ	Certolizumab
DoseASSURE™ ETN	Etanercept
DoseASSURE™ GOL	Golimumab
ProciseDx Inc.	
Procise ADL™	Adalimumab
Procise IFX™	Infliximab

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

CODES*		
CPT	0514U	Gastroenterology (irritable bowel disease [IBD]), immunoassay for quantitative determination of adalimumab (ADL) levels in venous serum in patients undergoing adalimumab therapy, results reported as a numerical value as micrograms per milliliter (µg/mL) *(Used to report the Procise ADL™ test, by ProciseDx Inc.)*
	0515U	Gastroenterology (irritable bowel disease [IBD]), immunoassay for quantitative determination of infliximab (IFX) levels in venous serum in patients undergoing infliximab therapy, results reported as a numerical value as micrograms per milliliter (µg/mL) *(Used to report the Procise IFX™ test, by ProciseDx Inc.)*
	80145	Adalimumab
	80230	Infliximab
	80280	Vedolizumab
	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
11/2022	New Medicare Advantage medical policy (converted to new format 2/2023)
6/2023	Interim update; Language revision due to Company policy change from "Investigational" to "not medically necessary"; removed CPT 80299
8/2023	Annual review; no changes to criteria
8/2024	Annual review; update to policy format, but no change to criteria
10/2024	Q4 2024 code updates
3/2025	Interim update; no change to criteria