

Reimbursement Policy

Immunopharmacologic Monitoring of Therapeutic Serum Antibodies

[POLICY DESCRIPTION](#) | [INDICATIONS AND/OR LIMITATIONS OF COVERAGE](#) | [APPLICABLE STATE AND FEDERAL REGULATIONS](#) | [APPLICABLE CPT/HCPCS PROCEDURE CODES](#) | [EVIDENCE-BASED SCIENTIFIC REFERENCES](#) | [REVISION HISTORY](#)

I. Policy Description

To manage loss of response due to the development of anti-drug antibodies, immunopharmacologic monitoring of circulating drug and anti-drug antibody levels has been proposed. The presence of anti-drug antibodies may promote adverse effects and diminish drug efficacy.^{1,2}

Targeted inhibitors of tumor necrosis factor-alpha (TNF) are widely used in the treatment of several inflammatory conditions, including rheumatoid arthritis (RA), spondyloarthritis, inflammatory bowel disease, and psoriasis. Some of these targeted inhibitors include, but are not limited to, infliximab, adalimumab, etanercept, and golimumab.¹

II. Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. Specifications pertaining to Medicare and Medicaid can be found in "Applicable State and Federal Regulations" section of this policy document.

- 1) For individuals with inflammatory bowel disease (IBD), drug and/or antibody concentration testing once every two weeks for anti-tumor necrosis factor (anti-TNF) therapies, vedolizumab therapy, or ustekinumab therapy **MEETS COVERAGE CRITERIA**.

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual's illness.

- 2) For individuals with conditions other than IBD (e.g., spondyloarthritis, rheumatoid arthritis, psoriatic arthritis, and psoriasis), drug and/or antibody concentration testing for anti-TNF therapies **DOES NOT MEET COVERAGE CRITERIA**.
- 3) For all other situations not addressed above, measurement of the serum drug levels **and/or** measurement of the antibodies to the drugs **DOES NOT MEET COVERAGE CRITERIA** for any of the following drugs (alone or as a combination test):

Reimbursement Policy

- a) adalimumab
- b) certolizumab
- c) etanercept
- d) golimumab
- e) infliximab
- f) infliximab-dyyb
- g) infliximab-abda
- h) rituximab
- i) ustekinumab
- j) vedolizumab

III. Applicable State and Federal Regulations

DISCLAIMER: If there is a conflict between this Policy and any relevant, applicable government policy for a particular member [e.g., Local Coverage Determinations (LCDs) or National Coverage Determinations (NCDs) for Medicare and/or state coverage for Medicaid], then the government policy will be used to make the determination. For the most up-to-date Medicare policies and coverage, please visit the Medicare search website: <https://www.cms.gov/medicare-coverage-database/search.aspx>. For the most up-to-date Medicaid policies and coverage, visit the applicable state Medicaid website.

Food and Drug Administration (FDA)

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

IV. Applicable CPT/HCPCS Procedure Codes

CPT	Code Description
80145	Adalimumab
80230	Infliximab
80280	Vedolizumab
80299	Quantitation of therapeutic drug, not elsewhere specified
82397	Chemiluminescent assay
84999	Unlisted chemistry procedure

Reimbursement Policy

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) Proprietary test: Procise ADL™ Lab/Manufacturer: 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) Proprietary test: Procise IFXT™ Lab/Manufacturer: ProciseDx Inc

Current Procedural Terminology© American Medical Association. All Rights reserved.

Procedure codes appearing in Medical Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.

V. Evidence-based Scientific References

1. Kirkham B. Tumor necrosis factor-alpha inhibitors: Induction of antibodies, autoantibodies, and autoimmune diseases. Updated March 17, 2025.
<https://www.uptodate.com/contents/tumor-necrosis-factor-alpha-inhibitors-induction-of-antibodies-autoantibodies-and-autoimmune-diseases>
2. Tighe D, McNamara D. Clinical impact of immunomonitoring in the treatment of inflammatory bowel disease. *World journal of gastroenterology*. Jan 21 2017;23(3):414-425. doi:10.3748/wjg.v23.i3.414
3. Lis K, Kuzawińska O, Bałkowiec-Iskra E. Tumor necrosis factor inhibitors – state of knowledge. *Arch Med Sci*. 2014;1175-85. vol. 6.
4. Wallace ZS, Sparks JA. Therapeutic Drug Monitoring for Immune-Mediated Inflammatory Diseases. *JAMA*. 2021;326(23):2370-2372. doi:10.1001/jama.2021.21315
5. Lichtenstein G. Treatment of Crohn disease in adults: Dosing and monitoring of tumor necrosis factor-alpha inhibitors. Updated December 04, 2023.
<https://www.uptodate.com/contents/treatment-of-crohn-disease-in-adults-dosing-and-monitoring-of-tumor-necrosis-factor-alpha-inhibitors>
6. UpToDate®. Ustekinumab (including biosimilars): Drug information.
<https://www.uptodate.com/contents/ustekinumab-including-biosimilars-drug-information>
7. UpToDate®. Vedolizumab: Drug information.
<https://www.uptodate.com/contents/vedolizumab-drug-information>
8. Theradiag. Miraca Life Sciences, Theradiag's partner in the USA, becomes Inform Diagnostics. Updated January 19, 2018. https://www.theradiag.com/wp-content/uploads/2017/12/PR_Theradiag_19012018_InformDX.pdf

Reimbursement Policy

9. Prometheus Laboratories. Therapeutic Drug Monitoring.
<https://prometheuslabs.com/anser/about-the-tests/>
10. LabCorp. Certolizumab and Anti-Certolizumab Antibody, DoseASSURE™ CTZ.
<https://www.labcorp.com/tests/504627/certolizumab-and-anti-certolizumab-antibody-i-dose-i-assure-ctz>
11. Wang SL, Ohrmund L, Hauenstein S, et al. Development and validation of a homogeneous mobility shift assay for the measurement of infliximab and antibodies-to-infliximab levels in patient serum. *Journal of immunological methods*. Aug 31 2012;382(1-2):177-88. doi:10.1016/j.jim.2012.06.002
12. Wang SL, Hauenstein S, Ohrmund L, et al. Monitoring of adalimumab and antibodies-to-adalimumab levels in patient serum by the homogeneous mobility shift assay. *Journal of pharmaceutical and biomedical analysis*. May 5 2013;78-79:39-44. doi:10.1016/j.jpba.2013.01.031
13. Van Stappen T, Bollen L, Vande Casteele N, et al. Rapid Test for Infliximab Drug Concentration Allows Immediate Dose Adaptation. *Clinical and translational gastroenterology*. Dec 08 2016;7(12):e206. doi:10.1038/ctg.2016.62
14. Steenholdt C, Brynskov J, Thomsen OO, et al. Individualised therapy is more cost-effective than dose intensification in patients with Crohn's disease who lose response to anti-TNF treatment: a randomised, controlled trial. *Gut*. Jun 2014;63(6):919-27. doi:10.1136/gutjnl-2013-305279
15. Roblin X, Rinaudo M, Del Tedesco E, et al. Development of an algorithm incorporating pharmacokinetics of adalimumab in inflammatory bowel diseases. *The American journal of gastroenterology*. Aug 2014;109(8):1250-6. doi:10.1038/ajg.2014.146. Epub 2014 Jun 10.
16. Mitchell RA, Shuster C, Shahidi N, et al. The Utility of Infliximab Therapeutic Drug Monitoring among Patients with Inflammatory Bowel Disease and Concerns for Loss of Response: A Retrospective Analysis of a Real-World Experience. *Canadian journal of gastroenterology & hepatology*. 2016;2016:5203898. doi:10.1155/2016/5203898
17. Barlow NL, Mohammed P, Berg JD. Serum trough infliximab and anti-infliximab antibodies in a cohort of gastroenterology and rheumatology patients' infliximab therapeutic drug monitoring. *Annals of clinical biochemistry*. Jul 2016;53(Pt 4):477-84. doi:10.1177/0004563215604866
18. Moore C, Corbett G, Moss AC. Systematic Review and Meta-Analysis: Serum Infliximab Levels During Maintenance Therapy and Outcomes in Inflammatory Bowel Disease. *Journal of Crohn's & colitis*. May 2016;10(5):619-25. doi:10.1093/ecco-jcc/jjw007
19. Fernandes SR, Bernardo S, Simoes C, et al. Proactive Infliximab Drug Monitoring Is Superior to Conventional Management in Inflammatory Bowel Disease. *Inflammatory bowel diseases*. Jun 27 2019;doi:10.1093/ibd/izz131
20. Negoescu DM, Enns EA, Swanhorst B, et al. Proactive Vs Reactive Therapeutic Drug Monitoring of Infliximab in Crohn's Disease: A Cost-Effectiveness Analysis in a Simulated Cohort. *Inflammatory bowel diseases*. Jun 10 2019;doi:10.1093/ibd/izz113

Reimbursement Policy

21. Papamichael K, Juncadella A, Wong D, et al. Proactive Therapeutic Drug Monitoring of Adalimumab Is Associated With Better Long-term Outcomes Compared With Standard of Care in Patients With Inflammatory Bowel Disease. *Journal of Crohn's & colitis*. Aug 14 2019;13(8):976-981. doi:10.1093/ecco-jcc/jjz018
22. Guido AJ, Crandall W, Homan E, et al. Improving Post-induction Antitumor Necrosis Factor Therapeutic Drug Monitoring in Pediatric Inflammatory Bowel Disease. *J Pediatr Gastroenterol Nutr*. Jan 2020;70(1):48-54. doi:10.1097/MPG.0000000000002486
23. Syversen SW, Jørgensen KK, Goll GL, et al. Effect of Therapeutic Drug Monitoring vs Standard Therapy During Maintenance Infliximab Therapy on Disease Control in Patients With Immune-Mediated Inflammatory Diseases: A Randomized Clinical Trial. *JAMA*. 2021;326(23):2375-2384. doi:10.1001/jama.2021.21316
24. Cox M, Smith R, Wild G, Dunkley L. P001 What is the role of antidrug antibody and drug level testing in patients treated with infliximab and adalimumab? *Rheumatology*. 2021;60(Supplement_1):keab247. doi:10.1093/rheumatology/keab247
25. Pan Y, Ahmed W, Mahtani P, et al. Utility of Therapeutic Drug Monitoring for Tumor Necrosis Factor Antagonists and Ustekinumab in Postoperative Crohn's Disease. *Inflammatory bowel diseases*. Dec 1 2022;28(12):1865-1871. doi:10.1093/ibd/izac030
26. NICE. Therapeutic monitoring of TNF-alpha inhibitors in Crohn's disease (LISA-TRACKER ELISA kits, IDKmonitor ELISA kits, and Promonitor ELISA kits) | Guidance and guidelines | NICE. NICE. <https://www.nice.org.uk/guidance/dg22/chapter/1-Recommendations>
27. NICE. Therapeutic monitoring of TNF-alpha inhibitors in Crohn's disease (LISA-TRACKER ELISA kits, IDKmonitor ELISA kits, and Promonitor ELISA kits) | Guidance and guidelines | NICE. NICE. <https://www.nice.org.uk/guidance/dg36/chapter/1-Recommendations>
28. Feuerstein JD, Nguyen GC, Kupfer SS, Falck-Ytter Y, Singh S. American Gastroenterological Association Institute Guideline on Therapeutic Drug Monitoring in Inflammatory Bowel Disease. *Gastroenterology*. Sep 2017;153(3):827-834. doi:10.1053/j.gastro.2017.07.032
29. Vande Casteele N, Herfarth H, Katz J, Falck-Ytter Y, Singh S. American Gastroenterological Association Institute Technical Review on the Role of Therapeutic Drug Monitoring in the Management of Inflammatory Bowel Diseases. *Gastroenterology*. 2017;153(3):835-857.e6. doi:10.1053/j.gastro.2017.07.031
30. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. *Arthritis Care & Research*. 2019/01/01 2019;71(1):2-29. doi:10.1002/acr.23789
31. Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG Clinical Guideline: Management of Crohn's Disease in Adults. 2018;113(4):481-517. doi:10.1038/ajg.2018.27

Reimbursement Policy

32. Lichtenstein GR, Loftus EV, Afzali A, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Official journal of the American College of Gastroenterology | ACG*. 2025;120(6):1225-1264. doi:10.14309/ajg.0000000000003465
33. Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG Clinical Guideline: Ulcerative Colitis in Adults. *The American journal of gastroenterology*. Mar 2019;114(3):384-413. doi:10.14309/ajg.0000000000000152
34. Papamichael K, Cheifetz AS, Melmed GY, et al. Appropriate Therapeutic Drug Monitoring of Biologic Agents for Patients With Inflammatory Bowel Diseases. *Clin Gastroenterol Hepatol*. Aug 2019;17(9):1655-1668.e3. doi:10.1016/j.cgh.2019.03.037
35. Cheifetz AS, Abreu M, Afif W, et al. A comprehensive literature review and expert consensus statement on therapeutic drug monitoring of biologics in inflammatory bowel disease. *Am J Gastroenterol*. 2021;doi:10.14309/ajg.0000000000001396

VI. Revision History

Review Date	Summary of Changes
09/04/2025	Reviewed and Updated: Updated the background, guidelines and recommendations, and evidence-based scientific references. Literature review did not necessitate any modifications to coverage criteria.