**Medicare Advantage Policy Manual** **Policy ID:** M-LAB65

# *Measurement of Serum Antibodies to Infliximab, Adalimumab, Ustekinumab, and Vedolizumab*

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***IMPORTANT REMINDER***

*The Medicare Advantage Medical Policy manual is not intended to override the member Evidence of Coverage (EOC), which defines the insured's benefits, nor is it intended to dictate how providers are to practice medicine. Physicians and other health care providers are expected to exercise their medical judgment in providing the most appropriate care for the individual member.*

*The Medicare Advantage Medical Policies are designed to provide guidance regarding the decision-making process for the coverage or non-coverage of services or procedures in accordance with the member EOC and the Centers of Medicare and Medicaid Services (CMS) policies, when available. In the event of a conflict, applicable CMS policy or EOC language will take precedence over the Medicare Advantage Medical Policy. In the absence of CMS guidance for a requested service or procedure, the health plan may apply their Medical Policy Manual or MCG™ criteria, both of which are developed with an objective, evidence-based process using scientific evidence, current generally accepted standards of medical practice, and authoritative clinical practice guidelines.*

*Medicare and EOCs exclude from coverage, among other things, services or procedures considered to be investigational, cosmetic, or not medically necessary, and in some cases, providers may bill members for these non-covered services or procedures. Providers are encouraged to inform members in advance when they may be financially responsible for the cost of non-covered or excluded services.*

## DESCRIPTION

Therapy with monoclonal antibodies has revolutionized treatment of patients with inflammatory diseases such as inflammatory bowel disease (IBD; Crohn's disease [CD] and ulcerative colitis [UC]), rheumatoid arthritis and psoriasis. These agents are generally given to patients who fail conventional medical therapy, and they are typically highly effective for induction and maintenance of clinical remission.

- Infliximab (Remicade®, Janssen Biotech) is an intravenous tumor necrosis factor alpha (TNFα) blocking agent approved by the U.S. Food and Drug Administration (FDA) for the treatment of rheumatoid arthritis, CD, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis, and UC. Infliximab is a chimeric (mouse/human) anti-TNFα monoclonal antibody.

- Adalimumab (Humira® AbbVie) is a subcutaneous TNFα inhibitor that is FDA-approved for treatment of the above indications (CD and UC in adults only) plus juvenile idiopathic arthritis (JIA). Adalimumab is a fully human monoclonal antibody to TNFα.
- Vedolizumab (Entyvio®, Millennium Pharmaceuticals) is an intravenous blocking agent for integrin α4β7 and is FDA-approved for adults with CD or UC.
- Ustekinumab (Stelara®, Janssen Biotech) is an antibody that blocks interleukin IL-12 and IL-23 and is FDA-approved to treat psoriasis and certain patients with CD.

Following primary response to infliximab and adalimumab, some patients become nonresponders (secondary nonresponse), and the development of antidrug antibodies (ADA) is considered to be a cause of secondary nonresponse.

## MEDICARE ADVANTAGE POLICY CRITERIA

| | |
|---|---|
| **CMS Coverage Manuals*** | None |
| **National Coverage Determinations (NCDs)*** | None |
| **Noridian Healthcare Solutions (Noridian) Local Coverage Determinations (LCDs) and Articles (LCAs)*** | None |
| **Medical Policy Manual** | *Medicare coverage guidance is not available for the measurement of serum antibodies to infliximab, adalimumab, ustekinumab, or vedolizumab. Therefore, the health plan's medical policy is applicable.*<br><br>Measurement of Serum Antibodies to Infliximab, Adalimumab, Ustekinumab, and Vedolizumab, Laboratory, Policy No. 65 *(see "NOTE" below)* |

**NOTE:** If a procedure or device lacks scientific evidence regarding safety and efficacy because it is investigational or experimental, the service is noncovered as not reasonable and necessary to treat illness or injury. (*Medicare IOM Pub. No. 100-04, Ch. 23, §30 A*). According to Title XVIII of the Social Security Act, §1862(a)(1)(A), only medically reasonable and necessary services are covered by Medicare. In the absence of a NCD, LCD, or other coverage guideline, CMS guidelines allow a Medicare Advantage Organization (MAO) to make coverage determinations, applying an ***objective, evidence-based process, based on authoritative evidence***. (*Medicare IOM Pub. No. 100-16, Ch. 4, §90.5*). The Medicare Advantage Medical Policy - Medicine Policy No. M-149 - provides further details regarding the plan's evidence-assessment process (see Cross References).

## POLICY GUIDELINES

### MEDICARE AND MEDICAL NECESSITY

To be eligible for Medicare coverage, Medicare requires diagnostic laboratory tests be ordered by the physician who is treating the beneficiary for a specific medical problem and who will use

the test results in the management of that specific medical problem.[1,2] The clinical usefulness of measuring ADA is based on whether the test results will inform management changes that lead to improved outcomes, as compared with management of symptoms, clinical assessment, and standard laboratory evaluation.

**REGULATORY STATUS**

Prometheus® Laboratories Inc., a College of American Pathologists–accredited lab under CLIA, offers non-radiolabeled fluid-phase HMSA tests called the Anser™IFX test (infliximab), Anser™ADA (adalimumab), Anser® UST (ustekinumab), and Anser® VDZ (vedolizumab). None of these tests are ELISA-based and they can measure antidrug antibodies in the presence of detectable drug levels, improving upon a major limitation of the ELISA method. All tests measure serum concentrations and antidrug antibodies. These tests are laboratory developed tests (LDTs) by Prometheus Laboratories Inc., and none have been cleared or approved by the U.S. Food and Drug Administration (FDA).

## CROSS REFERENCES

Investigational (Experimental) Services and New and Emerging Medical Technologies and Procedures, Medicine, Policy No. M-149

## REFERENCES


1. 42 CFR §410.32(a)
2. Medicare Benefit Policy Manual, Ch. 15 – Covered Medical and Other Health Services, §80.1 - Clinical Laboratory Services


## CODING

| Codes | Number | Description |
|---|---|---|
| **CPT** | 84999 | Unlisted chemistry procedure |
| **HCPCS** | None | |

***IMPORTANT NOTE:** Medicare Advantage medical policies use the most current Medicare references available at the time the policy was developed. Links to Medicare references will take viewers to external websites outside of the health plan's web control as these sites are not maintained by the health plan.*