

# Medical Coverage Policy



## Measurement of Serum Antibodies to Infliximab

Device/Equipment  Drug  Medical  Surgery  Test  Other

Effective Date:	10/2/2012	Policy Last Updated:	10/2/2012
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Prospective review is recommended/required. Please check the member agreement for preauthorization guidelines.

Prospective review is not required.

### Description:

Infliximab (Remicade® Centocor) is a tumor necrosis factor alpha blocking agent approved by the U.S. Food and Drug Administration for the treatment of rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis, and ulcerative colitis. Secondary loss of response to infliximab is seen in a certain percentage of patients; the development of anti-infliximab antibodies has been suggested as one reason for nonresponse.

#### Autoimmune disease

Infliximab is a chimeric (mouse/human) anti-tumor necrosis factor alpha monoclonal antibody. Therapy with monoclonal antibodies like infliximab has revolutionized therapy in patients with immune diseases such as inflammatory bowel disease (Crohn's disease and ulcerative colitis), rheumatoid arthritis and psoriasis. These agents are generally given to patients who fail conventional medical therapy, and are typically highly effective for induction and maintenance of clinical remission. However, not all patients respond, and a high proportion of patients lose response over time. An estimated one-third of patients do not respond to induction therapy (primary nonresponse), and among initial responders, response wanes over time in approximately 20% to 60% of patients (secondary nonresponse). The reason for therapeutic failures remains a matter of debate. One proposed factor associated with loss of response is the production of antidrug antibodies, which accelerate clearance of the drug.<sup>1</sup> Antibodies to infliximab have also been associated with acute infusion reactions and delayed hypersensitivity to infliximab.

#### Detection of antidrug antibodies

The detection and quantitative measurement of anti-infliximab antibodies, also referred to as human antichimeric antibodies or antibodies to infliximab, has been fraught with difficulty. First-generation assays, (i.e., enzyme-linked immunoabsorbant assays [ELISA]) can only measure antidrug antibodies in the absence of detectable drug levels due to interference of the drug with the assay, limiting clinical utility. Other techniques available for measuring antibodies include the radioimmunoassay method, and more recently, the homogenous mobility shift assay using high-performance liquid chromatography.

Disadvantages of the radioimmunoassay method are associated with the complexity of the test and prolonged incubation time, and safety concerns related to the handling of radioactive material. The homogenous mobility shift assay has the advantage of being able to measure antidrug antibodies when infliximab is present in the serum. Studies evaluating the validation of the results between different assays are lacking, making interstudy comparisons difficult.

Treatment options for patients with secondary loss of response to infliximab

A diminished or suboptimal response to infliximab can be managed in several ways: shortening the interval between doses, increasing the dose, switching to a different anti-TNF agent (in patients who continue to have loss of response after receiving the increased dose), or switching to a non-anti-TNF agent.

Prometheus® Laboratories Inc. offers an ELISA-based test for the measurement of serum infliximab and human antichimeric antibodies. This test was discontinued in August 2012 and replaced with an homogenous mobility shift assay called the Anser™IFX test. The Anser IFX test is not ELISA-based and can measure antibodies to infliximab in the presence of serum infliximab, improving upon a major limitation of the ELISA method. Anser IFX is offered as a combined test measuring serum concentrations of infliximab and antibodies to infliximab. This test was developed and its performance characteristics determined by Prometheus Laboratories Inc. It has not been approved by the U.S. Food and Drug Administration and is not medically necessary as there is insufficient peer-reviewed scientific literature to demonstrate its efficacy..

**Medical Criteria:**

Not applicable

**Policy:**

Measurement of serum antibodies to infliximab has not received clearance by the FDA, and is **not medically necessary** as there is insufficient peer-reviewed scientific literature that demonstrates that the procedure is effective.

**Coverage:**

Benefits may vary between groups/contracts. Please refer to the appropriate Evidence of Coverage, Subscriber Agreement, or Benefit Booklet for applicable not medically necessary benefits/coverage.

**Coding:**

At this time there a code has not been assigned to the measurement of serum antibodies to infliximab, therefore unlisted code 84999 should be used.

84999

**Also known as:**

Not applicable

**Related to:**

Not applicable

Published:

*Provider Update*, December 2012

**References:**

<sup>1</sup> Ordas I, Mould DR, Feagan BG et al. *Anti-TNF monoclonal antibodies in inflammatory bowel disease: pharmacokinetics-based dosing paradigms*. Clin Pharmacol Ther 2012; 91(4):635-46.

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Steenholdt C, Bendtzen K, Brynskov J et al. *Measurement of Infliximab and Anti-Infliximab Antibody Levels Can Help Distinguish Maintenance Versus Loss of Response.* Gastroenterology & Hepatology; 8(2);February 2012.

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 2012; 382(1-2):177-88.

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