

Medical Coverage Policy | Measurement of Serum Antibodies to Infliximab and Adalimumab



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OVERVIEW

This policy documents secondary loss of response to infliximab and adalimumab as seen in a certain percentage of patients; the development of anti-drug antibodies has been suggested as one reason for nonresponse.

PRIOR AUTHORIZATION

Not Applicable

POLICY STATEMENT

BlueCHiP for Medicare and Commercial:

Measurement of antibodies to infliximab in a patient receiving treatment with infliximab, either alone or as combination test which includes the measurement of serum infliximab levels is considered not medically necessary as there is insufficient peer-reviewed scientific literature that demonstrates that the procedure/service is effective

MEDICAL CRITERIA

None.

BACKGROUND

Infliximab (Remicade® Janssen Biotech) is an intravenous tumor necrosis factor (TNF) alpha blocking agent approved by the U.S. Food and Drug Administration (FDA) for the treatment of rheumatoid arthritis, Crohn's disease, ankylosing spondylitis, psoriatic arthritis, plaque psoriasis, and ulcerative colitis. Adalimumab (Humira® AbbVie) is a subcutaneous TNF alpha inhibitor that is FDA-approved for treatment of the above indications (Crohn's disease and ulcerative colitis in adults only) plus juvenile idiopathic arthritis. Secondary loss of response to infliximab and adalimumab is seen in a certain percentage of patients; the development of anti-drug antibodies has been suggested as one reason for nonresponse.

Infliximab and adalimumab in autoimmune disease

Infliximab is a chimeric (mouse/human) anti-tumor necrosis factor (TNF)-alpha monoclonal antibody. Adalimumab is a fully human monoclonal antibody to TNF-alpha. Therapy with monoclonal antibodies has revolutionized therapy in patients with immune diseases such as inflammatory bowel disease (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. 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. (1) Antidrug antibodies also have been associated with acute infusion reactions (both drugs) and with delayed hypersensitivity reactions. As a fully human antibody, adalimumab is considered less immunogenic than chimeric antibodies, such as infliximab.

Detection of antidrug antibodies:

The detection and quantitative measurement of antidrug antibodies, has been fraught with difficulty. First-generation assays, (i.e., enzyme-linked immunosorbent 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 (RIA) method, and more recently, the homogenous mobility shift assay (HMSA) using high-performance liquid chromatography.

Disadvantages of the RIA method are associated with the complexity of the test and prolonged incubation time, and safety concerns related to the handling of radioactive material. The HMSA 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. One retrospective study in 63 patients demonstrated comparable diagnostic accuracy between 2 different ELISA methods, i.e., double antigen ELISA and antihuman lambda chain ELISA. (2) This study did not include an objective, clinical and endoscopic scoring system for validation of results.

Treatment options for patients with secondary loss of response to anti-TNF therapy:

A diminished or suboptimal response to infliximab or adalimumab 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 nonradiolabeled, fluid-phase HMSA tests called Anser™IFX for infliximab and Anser™ADA for adalimumab. Neither test is ELISA-based, and each can measure antidrug antibodies in the presence of detectable drug levels, improving upon a major limitation of the ELISA method. Both tests measure serum drug concentrations and antidrug antibodies to infliximab. These tests were developed and their performance characteristics determined by Prometheus Laboratories Inc. Neither has been cleared or approved by the U.S. Food and Drug Administration.

Antibodies to infliximab (ATI) or to adalimumab (ATA) are present in a substantial number of patients treated with infliximab or adalimumab, respectively, and there may be a correlation between the level of these antibodies and clinical response. However, the clinical utility of measuring drug antibody concentrations has not been established, as it is not known how patient management would change based on test results. Limited evidence describes changes in management after measurement of ATI, but does not compare these management changes to those made in the absence of ATI measurement. In addition, there are technical factors relating to the use of different assay methods across studies, it has not yet been established whether the use of threshold levels aids in the discrimination of treatment response, nor has the optimal timing of when to measure antibody levels been established.

Therefore, the measurement of antibodies to infliximab in a patient receiving treatment with infliximab is considered investigational, and the measurement of antibodies to adalimumab in a patient receiving treatment with adalimumab is considered not medically necessary as there is no proven efficacy.

COVERAGE

BlueCHiP for Medicare and Commercial:

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

CODING

BlueCHiP for Medicare and Commercial:

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

RELATED POLICIES

None

PUBLISHED

Provider Update Jan 2014

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