Medical Policy

Measurement of Serum Antibodies to Infliximab and Adalimumab

Table of Contents

- Policy: Commercial
- Coding Information
- Policy: Medicare
- Description
- Authorization Information
- Information Pertaining to All Policies
- Policy History
- References

Policy Number: 917
BCBSA Reference Number: 2.04.84

Related Policies
None

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity
Medicare HMO Blue®SM and Medicare PPO Blue®SM Members

Measurement of antibodies to infliximab in a patient receiving treatment with infliximab, either alone or as a combination test which includes the measurement of serum infliximab levels, is INVESTIGATIONAL.

Measurement of antibodies to adalimumab in a patient receiving treatment with adalimumab, either alone or as a combination test which includes the measurement of serum adalimumab levels, is INVESTIGATIONAL.

Prior Authorization Information

Pre-service approval is required for all inpatient services for all products. See below for situations where prior authorization may be required or may not be required for outpatient services.

Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.

<table>
<thead>
<tr>
<th>Outpatient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial Managed Care (HMO and POS)</td>
</tr>
<tr>
<td>Commercial PPO and Indemnity</td>
</tr>
<tr>
<td>Medicare HMO Blue®SM</td>
</tr>
<tr>
<td>Medicare PPO Blue®SM</td>
</tr>
</tbody>
</table>

CPT Codes / HCPCS Codes / ICD Codes

The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s
contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes
There is no specific CPT code for this service.

Diagnosis Codes
Investigational for the diagnoses described in the medical policy statement.

Description
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 antidrug- antibodies has been suggested as one reason for nonresponse.

Background
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 (infliximab). As a fully human antibody, adalimumab is considered less immunogenic than chimeric antibodies, such as infliximab.

Summary
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 antidrug 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 investigational.
**Policy History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/2016</td>
<td>New references added from BCBSA National medical policy.</td>
</tr>
<tr>
<td>1/2016</td>
<td>New references added from BCBSA National medical policy.</td>
</tr>
<tr>
<td>12/2014</td>
<td>New references added from BCBSA National medical policy.</td>
</tr>
</tbody>
</table>

**Information Pertaining to All Blue Cross Blue Shield Medical Policies**

Click on any of the following terms to access the relevant information:
- [Medical Policy Terms of Use](#)
- [Managed Care Guidelines](#)
- [Indemnity/PPO Guidelines](#)
- [Clinical Exception Process](#)
- [Medical Technology Assessment Guidelines](#)

**References**


