Test Definition: INTAD

Adalimumab Panel, Interpretation

Overview

Useful For

Interpretation of therapeutic drug monitoring of adalimumab concentration and antibody levels

Method Name

Only orderable as part of a profile. For more information see ADALP / Adalimumab Quantitative with Antibody, Serum.

Technical Interpretation

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Serum	Refrigerated (preferred)	28 days	
	Frozen	28 days	

Clinical & Interpretive

Clinical Information

Adalimumab, sold under the brand names Amjevita and Humira, is a medication used to treat rheumatoid arthritis, psoriatic arthritis, Crohn disease, ulcerative colitis, and chronic psoriasis, among others. Adalimumab is a tumor necrosis factor (TNF)-inhibiting, antiinflammatory, biologic medication. TNF-alpha binds to TNF-alpha receptors, leading to the inflammatory response of autoimmune diseases. By binding to TNF-alpha, adalimumab can reduce the inflammatory response. Because TNF-alpha is also a part of the immune system that protects the body from infection, treatment with adalimumab may increase the risk of infections. Treatment with adalimumab is effective in reducing disease activity, offers significant benefits in quality of life, and may have the potential to slow or halt the progression of the disease when given early. However, over 30% of patients fail to respond to anti-TNF-alpha therapy and approximately 60% of patients who responded initially lose the response over time and require either drug dose-escalation or a switch to an alternative therapy in order to maintain response.(1)

This assay has been verified to measure the reference product adalimumab (Humira, AbbVie) and the biosimilar adalimumab-atto (Amjevita, Amgen) with no analytical differences in the quantitation of the medications. Humira and

Amjevita have the same primary amino acid sequence. Therefore, adalimumab will be used to refer to both the reference product and the biosimilar product interchangeably. This test cannot distinguish between Humira and the adalimumab biosimilar product.

Reasons for primary loss of response may include disease processes mediated by proinflammatory molecules other than TNF. Secondary loss of response, on the other hand, is associated with low serum albumin, high body-mass index, the degree of systemic inflammation and development of an immune response to therapy, or immunogenicity.(2,3) Antidrug antibody formation may increase drug clearance in treated patients or neutralize the drug effect, thereby potentially contributing to the loss of response. Antidrug antibodies could also cause adverse events such as serum sickness and hypersensitivity reactions.(4) Currently, adalimumab quantitation is commonly performed in conjunction with immunogenicity assessment for antibodies to adalimumab (ATA). Most often, this testing is ordered in patients on therapy who are experiencing partial or complete loss of response but can also be performed in any stage during therapy, when patients are responding well to the therapy or not.

Currently, adalimumab quantitation is commonly performed in conjunction with immunogenicity assessment for antibodies to adalimumab. Most often, this testing is ordered in patients on therapy who are experiencing partial or complete loss of response. Proactive monitoring in the maintenance stage of therapy has gained space after therapeutic drug monitoring was associated with favorable outcomes without disease worsening a year after measurements.(5)

TNF inhibitor therapies are expensive and adverse events include greater risk for infections, such as reactivation of latent tuberculosis or hepatitis B, infusion or injection site reactions, cutaneous reactions, and reports of hepatoxicity, demyelinating disease, and higher incidence of mortality and hospitalization in heart failure patients have been documented.

Reference Values

Only orderable as part of a profile. For more information see ADALP / Adalimumab Quantitative with Antibody, Serum.

Interpretation

Adalimumab quantitation is generally performed in conjunction with immunogenicity assessment for antibodies to adalimumab (ATA). Most often, this testing is ordered for patients with inflammatory bowel disease (IBD) who are on adalimumab therapy and who are experiencing loss of response (reactive monitoring),(5) but the testing may be ordered for anyone on adalimumab-even when treatment is going well (proactive monitoring).(6-8)

Results from adalimumab and ATA testing play an important role in patient management. In the setting of loss of response to adalimumab therapy for adults with active IBD, a clinical decision tool from the American Gastroenterology Association(9,10) suggests the following scenarios for a blood draw that occurred at trough, immediately before the next injection dose:

-For patients who have undetectable or low concentrations of adalimumab (<8 mcg/mL) but no detectable ATA, the patient care team may choose to increase the dose of adalimumab in an attempt to increase the amount of the drug in circulation.

-If the patient has subtherapeutic adalimumab concentrations (<8 mcg/mL) in the presence of an ATA, the patient care team may switch the patient to another TNF inhibitor.

-For patients with increased trough concentrations of adalimumab (therapeutic or greater), whether an ATA is present or not, it may be necessary to switch the patient to a therapy with a different mechanism of action such as the anti-alpha 4-beta-7-integrin antibody vedolizumab or the IL12/IL23 antibody ustekinumab.

-Low trough concentrations may be correlated with loss of response to adalimumab.

Adalimumab concentration results above 35 mcg/mL are suggestive of a blood draw at a time-point in treatment other than trough.

Test interpretation relies on clinical presentation and may differ from the statements above, which were designed for adults with IBD experiencing loss of response. For individuals on adalimumab therapy for other conditions such as rheumatoid arthritis, or pediatric patient populations or proactive monitoring, drug concentration therapeutic targets and patient management decision may be individualized. When both the drug quantitation and anti-drug-antibodies are ordered, an interpretive guide is offered below.

Adalimumab quantitation, mcg/mL	ATA, AU/mL	Comment
<8	Negative	Absence of detectable antibody-to-adalimumab (ATA). Low concentration of adalimumab (ADL) may be attributable to other parameters related to adalimumab clearance.
<8	Positive	Presence of antibody-to-adalimumab (ATA) detected, which correlates with low concentration of adalimumab (ADL). ATAs may be associated with increased clearance and lower circulating concentrations of ADL.
8.1-15	Negative	Absence of detectable antibody-to-adalimumab (ATA). At this concentration of adalimumab (ADL), a low-titer (50-150 AU/mL) or moderate titer (150-500 AU/mL) ATA cannot be excluded. However, the presence of a high-titer ATA (> or =500 U/mL) is unlikely. If there is clinical suspicion for a low-titer ATA, suggest submission of a new sample obtained at trough. This test has demonstrated drug tolerance up to 40 mcg/mL for ATAs > or =500 AU/mL, up to 15 mcg/mL for ATAs between 150-500 and up to 8 mcg/mL ADL for ATAs between 50-150 AU/mL.
	Low or moderate positive (14-499)	Presence of antibody-to-adalimumab (ATA) detected. At this concentration of adalimumab (ADL), the detected titer of the ATA may be modestly underestimated. This test has demonstrated drug tolerance up to 40 mcg/mL for ATAs > or =500 AU/mL, up to 15 mcg/mL for ATAs between 150-500 and up to 8 mcg/mL ADL for ATAs between 50-150 AU/mL.
	High positive (> or =500)	Presence of antibody-to-adalimumab (ATA) detected. This test has demonstrated drug tolerance up to 40 mcg/mL for ATAs

		> or =500 AU/mL, up to 15 mcg/mL for ATAs between 150-500 and up to 8 mcg/mL ADL for ATAs between 50-150 AU/mL.
>15	Negative	At this concentration of adalimumab (ADL), a low (50-150 AU/mL) or moderate titer (150-500 AU/mL) ATA cannot be excluded. The presence of a high-titer ATA (> or =500 U/mL) is unlikely but also cannot be completely excluded. If there is clinical suspicion for an ATA, suggest submission of a new sample obtained at trough, preferably during the maintenance phase of therapy. This test has demonstrated drug tolerance up to 40 mcg/mL for ATAs > or =500 AU/mL, up to 15 mcg/mL for ATAs between 150-500 and up to 8 mcg/mL ADL for ATAs between 50-150 AU/mL.
	Low positive (14-149)	Presence of antibody-to-adalimumab (ATA) detected. At this concentration of adalimumab (ADL), the detected titer of the ATA is likely underestimated. Suggest submission of a new sample obtained at trough, preferably during the maintenance phase of therapy. This test has demonstrated drug tolerance up to 40 mcg/mL for ATAs > or =500 AU/mL, up to 15 mcg/mL for ATAs between 150-500 and up to 8 mcg/mL ADL for ATAs between 50-150 AU/mL.
	Moderate positive (150-499 U/mL)	Presence of antibody-to-adalimumab (ATA) detected. At this concentration of adalimumab (ADL), the detected titer of the ATA may be underestimated. Suggest submission of a new sample obtained at trough, preferably during the maintenance phase of therapy. This test has demonstrated drug tolerance up to 40 mcg/mL for ATAs > or =500 AU/mL, up to 15 mcg/mL for ATAs between 150-500 and up to 8 mcg/mL ADL for ATAs between 50-150 AU/mL.
	High positive (> or =500)	Presence of antibody-to-adalimumab (ATA) detected. This test has demonstrated drug tolerance up to 40 mcg/mL for ATAs > or =500 AU/mL, up to 15 mcg/mL for ATAs between 150-500 and up to 8 mcg/mL ADL for ATAs between 50-150 AU/mL.

Cautions

Tumor necrosis factor (TNF) measurement is not the analyte of choice for monitoring therapy with TNF inhibitors (such as adalimumab or infliximab), since TNF testing would not distinguish between free TNF and TNF bound to the monoclonal antibody, either in the extracellular or membrane-bound form of the cytokine.

Toxicity effects other than acute hypersensitivity infusion reactions have not been described nor correlated with high

adalimumab concentrations.

Optimal therapeutic concentrations of adalimumab may vary according to the disease.(12-14) For adults with active inflammatory bowel disease, a concentration of 7.5 mcg/mL or greater is considered therapeutic.(6)

For patients taking biotin supplements, it is recommended to wait at least 12 hours after the last ingestion of biotin to collect a blood sample for this test.

Clinical Reference

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Performance

Method Description
This interpretation is generated by the laboratory information system based on adalimumab quantitation and antibody to adalimumab test results.

PDF Report
No

Day(s) Performed
Monday, Wednesday, Friday

Report Available
2 to 4 days

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
Not Applicable

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
INTAD	Adalimumab Interpretation	No LOINC Needed

Result ID	Test Result Name	Result LOINC® Value
INTAD	Adalimumab Interpretation	77202-0