MAYO CLINIC LABORATORIES

Test Definition: ADALX

Adalimumab QN with Reflex to Ab, S

Overview

Useful For

Detection and quantification of antibodies directed against adalimumab in serum
Trough level quantitation for evaluation of patients with loss of response to adalimumab

Testing Algorithm

If the result is 8.0 mcg/mL or less, then adalimumab antibody test will be performed at an additional charge.

Highlights

Adalimumab (tradename Humira, manufactured by AbbVie) is a fully human therapeutic monoclonal antibody targeting tumor necrosis factor alpha, a proinflammatory cytokine that is upregulated in several autoimmune inflammatory states.
Adalimumab is FDA-approved for treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis; ankylosing spondylitis, pediatric and adult Crohn disease, ulcerative colitis, plaque psoriasis, hidradenitis suppurativa and uveitis. Adalimumab is a subcutaneous injection, usually self-administered every other week at a fixed dose of 40 mg in adults, although dosing can vary.
Testing for adalimumab concentration and presence of anti-adalimumab antibodies is helpful to adjust therapeutic strategies for patients starting therapy (proactive monitoring), and to adjust dosing when partial response or loss of response to therapy is observed, manifested as recurrence of symptoms.

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
ADLAB	Adalimumab Ab, S	No	No

Method Name

Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available

Yes

Specimen

Specimen Type

Serum

Specimen Required

Container/Tube:
Preferred: Serum gel
Acceptable: Red top
Specimen Volume: 0.5 mL

Forms

If not ordering electronically, complete, print, and send Gastroenterology and Hepatology Client Test Request (T728)

with the specimen

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject

Specimen Minimum Volume

0.35 mL

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 trade name Humira, is a medication used to treat rheumatoid arthritis, psoriatic arthritis, Crohn disease, ulcerative colitis, chronic psoriasis, amongst others. Adalimumab is a tumor necrosis factor (TNF)-inhibiting, anti-inflammatory, biologic medication. It binds to TNF-alpha, which normally binds to TNF-alpha receptors, leading to the inflammatory response of autoimmune diseases. By binding to TNF-alpha, adalimumab reduces inflammatory response. Because TNF-alpha is also 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 change 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 switch to an alternative agent in order to maintain response. Antidrug antibody formation may increase drug clearance in treated patients and/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. 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 loss of response.
Results from drug concentration measurement combined to ATA testing play an important role in patient management. When measured at trough, for patients who have undetectable or low concentrations of drug but no detectable ATA, the physician may choose to increase the dose of adalimumab in an attempt to increase the amount of the drug in circulation. If the patient has low adalimumab in the presence of an ATA, in many cases, the physician may switch the patient to another TNF inhibitor. In contrast, for patients with increased trough concentrations of adalimumab, whether or not an ATA is present, it may be necessary to switch the patient to a therapy with a different mechanism of action.
For patients on biologics, assessing response to therapy is critical, since 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. Despite their therapeutic efficacy, more than one-third of patients on TNF inhibitors show no response to induction therapy (primary nonresponders) and in up to 50% of the responders, therapy becomes ineffective over time (secondary nonresponders). Reasons for primary loss of response are not well understood but may include disease processes mediated by proinflammatory molecules other

than TNF. Secondary loss of response, on the other hand, is associated with low albumin, high body-mass index, the degree of systemic inflammation and immune response to therapy, or immunogenicity. Laboratory testing of patients for quantitation of adalimumab and assessment of immunogenicity (development of autoantibodies against adalimumab) can help optimize therapy when partial response or loss of response to therapy are observed.

Reference Values

ADALIMUMAB QUANTITIATIVE
Limit of quantitation is 0.8 mcg/mL. Optimal therapeutic ranges are disease specific.
ADALIMUMAB ANTIBODY
<14.0 AU/mL

Interpretation

Currently, adalimumab quantitation is one of the most commonly tested monoclonal antibodies in routine practice; this testing 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, but the testing may be ordered for anyone on adalimumab. Results from adalimumab and ATA testing play an important role in patient management. When measured at trough, for patients who have undetectable or low concentrations of adalimumab, but no detectable ATA, the physician may choose to increase the dose of adalimumab in an attempt to increase the amount of the drug in circulation. If the patient has low adalimumab in the presence of an ATA, in many cases the physician may switch the patient to another tumor necrosis factor inhibitor. In contrast, for patients with increased trough concentrations of adalimumab, whether or not an ATA is present, it may be necessary to switch the patient to a therapy with a different mechanism of action, such as the anti-alpha4-beta-7-integrin antibody vedolizumab or the IL12/IL23 antibody ustekinumab, in the setting of IBD.
Adalimumab quantitation will be interpreted in 2 different ways. When measured at trough, individuals may be considered to have adequate trough levels when drug concentrations are above 8 mcg/mL, and faster clearance of the drug, which may warrant a dosing adjustment or additional action if adalimumab trough concentration is below or equal to 8 mcg/mL. Adalimumab quantitation may influence patient management decisions as to whether therapy should continue as is, dose escalation is necessary, or a switch to a new therapeutic regimen is needed.
Low trough concentrations may be correlated with loss of response to adalimumab. For adalimumab trough concentrations of 8.0 mcg/mL or less, testing for ATA is suggested.
For adalimumab trough concentrations above 8.0 mcg/mL, the presence of ATA is unlikely; patients experiencing loss of response to adalimumab may benefit from an increased dose or more frequent dosing.
Adalimumab concentration results above 35 mcg/mL are suggestive of a blood draw at a time-point in treatment other than trough.

Cautions

Laboratory testing of patients for quantitation of adalimumab and assessment of immunogenicity (development of autoantibodies against adalimumab) can help optimize therapy when partial response or loss of response to therapy is observed. As a side note, tumor necrosis factor (TNF) measurement is not the analyte of choice for monitoring therapy with TNF inhibitors (such as adalimumab or infliximab), since it 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 adalimumab concentrations.
Optimal therapeutic concentrations of adalimumab may vary according to the disease (eg, Crohn disease verses ulcerative colitis verses rheumatoid arthritis).

Clinical Reference

1. Silva-Ferreira F, Afonso J, Pinto-Lopes P, Magro F: A systematic review on infliximab and adalimumab drug monitoring: Levels, Clinical Outcomes and Assays. Inflamm Bowel Dis. 2016;22:2289-2301
2. Baert F, Kondragunta V, Lockton S, et al: Antibodies to adalimumab are associated with future inflammation in Crohn's patients receiving maintenance adalimumab therapy: a post hoc analysis of the Karmiris trial. Gut. 2016 Jul;65(7):1126-1131
3. Willrich MA, Murray DL, Snyder MR: Tumor necrosis factor inhibitors: clinical utility in autoimmune diseases. Transl Res. 2015 Feb;165(2):270-282. doi: 10.1016/j.trsl.2014.09.006

Performance

Method Description

Adalimumab Quantitation:
The adalimumab enzyme-linked immunosorbent assay (ELISA) is designed to determine the quantity of free adalimumab (therapeutic antibody against tumor necrosis factor-alpha: TNF-alpha) in EDTA plasma or serum samples. In a first incubation step, the free adalimumab from the sample is bound to the specific monoclonal anti-adalimumab antibody coated on the plate. To remove all unbound substances, a washing step is carried out. In a further incubation step, peroxidase-labeled antibody is added. Tetramethylbenzidine (TMB) is used as a substrate for peroxidase. Finally, an acidic stop solution is added to terminate the reaction. The color changes from blue to yellow. The intensity of the yellow color is directly proportional to the concentration of free adalimumab in the sample. A dose response curve of the absorbance unit (optical density:OD) verses concentration is generated, using the values obtained from standard. The concentrations of free adalimumab in the samples are determined directly from this curve.(Package insert: Adalimumab Drug Level ELISA reagent. Immun Diagnostik; KR9657, ver 07/2019)
Antibodies to Adalimumab:
This ELISA serves for the determination of antibodies against TNF-alpha blocker adalimumab (Humira). During sample preparation, the antibodies-to-adalimumab (ATA) are separated from the therapeutic antibody adalimumab using an acid dissociation in order to acquire free ATA. By adding the peroxidase conjugate (POD-therapeutic antibody adalimumab) and the tracer (biotinylated therapeutic antibody adalimumab), the unlabeled therapeutic antibodies are replaced, and the labeled antibodies can form a complex with the ATA. This complex binds via biotin to the streptavidin-coated microtiter plate. It is detected via the peroxidase conjugate with the peroxidase converting the substrate t TMB to a blue product. The enzymatic reaction is stopped by adding an acidic solution. The samples convert from blue to yellow. The color change should be measured in a photometer at 450 nm. The interpretation is made using the cut-off control.(Package insert: Adalimumab Total ADA ELISA reagent. Immun Diagnostik; KR9651, ver 02/2019)

PDF Report

No

Specimen Retention Time

14 days

Performing Laboratory Location

Rochester

Fees & Codes

Test Classification

This test was developed, and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

80145
83520 (if appropriate)