

TEST ID: ADALX

ADALIMUMAB QUANTITATIVE WITH REFLEX TO ANTIBODY, SERUM

USEFUL FOR

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

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 tumor necrosis factor-alpha (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, which protects the body from infection, treatment with adalimumab may increase the risk of infections. Treatment with adalimumab is effective in reducing disease activity, and 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. Anti-drug antibody formation may increase drug clearance in treated patients and/or neutralize the drug effect, thereby potentially contributing to the loss of response. Anti-drug 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.

REFERENCE VALUES

Adalimumab Quantitative With Reflex to Antibody

Limit of quantitation is 0.8 mcg/mL. Optimal therapeutic ranges are disease specific.

Adalimumab Antibody

<14.0 AU/mL

ANALYTIC TIME

1 day

SPECIMEN REQUIRED

Type

Serum

Container/Tube

Preferred: Serum gel

Acceptable: Red top

Volume

0.5 mL

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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 TB or hepatitis B, infusion or injection site reactions, cutaneous reactions, and reports of hepatotoxicity, 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.

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 in inflammatory bowel disease (IBD) patients on adalimumab therapy 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 (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, 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 5 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 5 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 less than or equal to 5.0 mcg/mL, testing for antibodies to ATA is suggested.

For adalimumab trough concentrations above 5.0 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.