MAYO CLINIC LABORATORIES

Test Definition: INFXR

Infliximab Quantitation with Reflex to Antibodies to Infliximab, Serum

Overview

Useful For

Evaluating patients for loss of response, partial response on initiation of therapy, autoimmune or hypersensitivity reactions, primary nonresponse, reintroduction after drug holiday, endoscopic/computed tomography enterography recurrence (in inflammatory bowel disease), acute infusion reactions and proactive monitoring

This test **does not** differentiate between the originator and biosimilar products.

Profile Information

Test Id	Reporting Name	Available Separately	Always Performed
INFX	Infliximab, S	No	Yes

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
INXAB	Infliximab Ab, S	No	No

Testing Algorithm

Infliximab quantitation will be performed by liquid chromatography tandem mass spectrometry on all specimens. When infliximab results are below 5.1 mcg/mL, testing for antibodies to infliximab will be performed at an additional charge.

For more information see Ulcerative Colitis and Crohn Disease Therapeutic Drug Monitoring Algorithm

Special Instructions

- Ulcerative Colitis and Crohn Disease Therapeutic Drug Monitoring Algorithm

Method Name

INFXR, INFX: Selective Reaction Monitoring Liquid Chromatography Tandem Mass Spectrometry (LC-MS/MS)
INXAB: Electrochemiluminescent Bridging Immunoassay with Acid Dissociation

NY State Available

Yes

Specimen

Specimen Type

Serum Red

Specimen Required

Patient Preparation:

1. Draw blood immediately before next scheduled dose (trough specimen).
2. For 12 hours before specimen collection, patient **should not** take multivitamins or dietary supplements (eg, hair, skin, and nail supplements) containing biotin (vitamin B7).

Collection Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Submission Container/Tube: Plastic vial

Specimen Volume: 1 mL Serum

Collection Instructions: Within 2 hours of collection, centrifuge and aliquot serum into plastic vial.

Forms

If not ordering electronically, complete, print, and send 1 of the following with specimen:

-Gastroenterology and Hepatology Test Request (T728)

-Therapeutics Test Request (T831)

-General Request (T239)

Specimen Minimum Volume

Serum: 0.5 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	OK
Gross icterus	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Drug and target:

Infliximab (IFX) is a chimeric monoclonal antibody (IgG1 kappa) which targets tumor necrosis factor (TNF)-alpha. IFX works by preventing TNF-alpha from binding its cellular receptors through competitive inhibition. IFX recognizes both soluble TNF-alpha trimers circulating in plasma and transmembrane TNF-alpha on cell surfaces.(1) IFX also exhibits anti-inflammatory properties by downregulating several cytokines while enhancing interleukin 10 production.(2,3) The reference product for IFX is Remicade (Janssen Pharmaceuticals).(4) Several biosimilars are US Food and Drug

Administration (FDA)-approved, including but not limited to: Renflexis (infliximab-abda, Organon), Inflectra (infliximab-dyyb, Pfizer Inc), Ixifi (infliximab-qbtx, Pfizer Inc), and Avsola (infliximab-axxq, Amgen). Biosimilars have the same primary amino acid sequence as Remicade. Therefore, "infliximab" will be used to refer to the reference product and the biosimilar products interchangeably. This test cannot distinguish between the reference product Remicade and the infliximab biosimilar products.

Indications:
As of December 2025, infliximab is FDA-approved for Crohn disease (adult and pediatric), ulcerative colitis (adult and pediatric), rheumatoid arthritis (in combination with methotrexate), ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis.(5) Doses vary by indication, and follow a main framework of intravenous (IV) infusions of induction at weeks 0, 2 and 6, followed by scheduled maintenance IV infusions every 8 weeks thereafter. For Crohn disease and ulcerative colitis, the initial dosing regimen is 5 mg/kg IV over at least 2 hours. For rheumatoid arthritis, the dosing starts at 3 mg/kg IV. There is a newer subcutaneous formulation of IFX, not entirely interchangeable with IV IFX. Its availability depends on the geographic location and indication. In the United States, it is approved for maintenance stages of Crohn disease and ulcerative colitis.

Pharmacokinetic highlights:
Infliximab has a volume of distribution of 3-6 liters and clearance rates of 11-15 mL/hr with a half-life of 14 days. Steady-state concentrations in the body are achieved by week 14.(5,6) IFX clearance is affected by disease state, concomitant use of immunosuppressants, high concentrations of TNF-alpha and C-reactive protein, low albumin concentrations, high body mass index, and presence of anti-drug-antibodies.(7-9) Male patients seem to clear IFX faster than female patients.(9)

Immunogenicity:
Patients may develop anti-drug antibodies-to-infliximab (ATI).(5,10-12) Concomitant use of immunomodulators can reduce the formation of ATI in some patients.(5) ATI formation may increase drug clearance in treated patients or neutralize the drug effect, thereby potentially contributing to the loss of response. ATI could also cause adverse events such as serum sickness and hypersensitivity reactions. Infliximab drug level quantitation is commonly performed in conjunction with immunogenicity assessment for ATI.

Evidence for therapeutic drug monitoring:
Therapeutic drug monitoring (TDM) of IFX is supported by evidence for both reactive and proactive strategies, with stronger consensus for reactive use. Reactive TDM is performed in the setting of loss of response or infusion reactions. Reactive TDM is well validated to distinguish pharmacokinetic failure (low drug, absent antibodies) from immunogenicity (anti-drug antibodies), enabling rational dose escalation or switching and improving cost-effectiveness.(13-15) Proactive TDM studies, involving routine measurement during maintenance stages of therapy, suggests benefits in reducing immunogenicity, maintaining remission, and optimizing long-term exposure, particularly early in therapy and in high-risk patients.(16)

Measurement of IFX concentration is indicated at trough, immediately prior to the next scheduled infusion.(5,6) IFX concentrations tend to reach steady state and stabilize after 14 weeks (approximately 100 days).(17) Quantitation of peak IFX concentration is strongly discouraged.

Reference Values

INFLIXIMAB QUANTITATION:
Limit of quantitation is 1.0 mcg/mL. Therapeutic ranges are disease specific.

Pediatric reference ranges are not established.

INFLIXIMAB ANTIBODIES
Absence of antibodies to infliximab (ATI) is defined as <50 U/mL
Presence of ATI is reported as positive when concentrations are > or =50 U/mL

Interpretation

Low trough concentrations may be associated with loss of response to infliximab (IFX) due to possible development of an immune response to IFX. Testing for antibodies-to-infliximab (ATI) is suggested in patients with trough concentrations less than or equal to 5.0 mcg/mL.

Infliximab trough concentrations greater than or equal to 5.0 mcg/mL in patients with loss of response to therapy may suggest a possible benefit of treatment with a different monoclonal antibody therapy.

Infliximab concentrations greater than or equal to 35 mcg/mL suggest possible testing at a time point other than trough if intravenous infusions are used and should be evaluated within the clinical context of the patient.

Interpretation and patient management will be different according to disease state, clinical presentation (symptomatic versus appropriate response to therapy), results of other laboratory tests, and a combination of the drug concentration and presence of ATI.

A low titer ATI is reported with a quantitative value of 50 to 499 U/mL. A high-titer ATI is reported with a quantitative value greater than or equal to 500 U/mL, using the Mayo Clinic assay.

Infliximab quantitation, mcg/mL	**Antibodies-to-infliximab, U/mL**	**Comment**
<5	Negative	Absence of detectable antibodies-to-infliximab (ATI). Low concentration of infliximab (IFX) may be attributable to other parameters related to IFX clearance.
<5	Positive	Presence of ATI detected, which correlates with low concentration of IFX. ATIs may be associated with increased clearance and lower circulating concentrations of IFX.
5-10	Negative	Absence of detectable ATI. At this concentration of IFX, a low-titer ATI (50-499 U/mL) cannot be completely excluded. However, the presence of a high-titer ATI (> or =500 U/mL) is unlikely.

		If there is clinical suspicion for a low-titer ATI, suggest submission of a new sample obtained at trough. This test has demonstrated drug tolerance of up to 100 mcg/mL IFX for ATI > or =500 U/mL and up to 10 mcg/mL IFX for ATI <500 U/mL.
5-10	Low positive (50-499 U/mL)	Presence of ATI detected. At this concentration of IFX, the detected titer of the ATI may be modestly underestimated. This test has demonstrated drug tolerance of up to 100 mcg/mL IFX for ATI > or =500 U/mL and up to 10 mcg/mL IFX for ATI <500 U/mL.
5-10	High positive (> or =500 U/mL)	Presence of ATI detected. This test has demonstrated drug tolerance of up to 100 mcg/mL IFX for ATI > or =500 U/mL and up to 10 mcg/mL IFX for ATI <500 U/mL.
>10	Negative	Absence of detectable ATI. At this concentration of IFX, a low-titer ATI (50-499 U/mL) cannot be completely excluded. The presence of a high-titer ATI (> or =500 U/mL) is unlikely but also cannot be completely excluded. If there is clinical suspicion for an ATI, suggest submission of a new sample at trough, preferably during maintenance phase. This test has demonstrated drug tolerance of up to 100 mcg/mL IFX for ATI > or =500 U/mL and up to 10 mcg/mL IFX for ATI <500 U/mL.
>10	Low positive (50-499 U/mL)	Presence of ATI detected. At this concentration of IFX, the detected titer of the ATI may be underestimated. Suggest submission of a new sample obtained at trough, preferably during maintenance phase. This test has demonstrated drug tolerance of up to 100 mcg/mL IFX for ATI > or =500 U/mL and up to 10 mcg/mL IFX for ATI <500 U/mL.
>10	High positive (> or =500 U/mL)	Presence of ATI detected. This test has demonstrated drug tolerance of up to 100 mcg/mL IFX for ATI > or =500 U/mL and up to 10 mcg/mL IFX for ATI <500 U/mL

Cautions

While the immunogenicity rates between reference product and biosimilars are similar, there could be epitope differences in the anti-drug-antibodies for each formulation.

Clinical management decisions for patients receiving infliximab (IFX) treatment should not be based solely on quantitation of IFX or assessment of antibodies-to-infliximab (ATI). Test results must be interpreted within the clinical context of the patient.

Toxicity effects other than acute hypersensitivity infusion reactions have not been described nor correlated with IFX concentrations.(5)

During the initial induction phase of treatment (weeks 0, 2, and 6), steady-state has not yet been achieved and concentrations of IFX may vary significantly between infusions.(9)

Therapeutic concentrations of IFX may vary according to the disease (eg, Crohn disease, ulcerative colitis, or rheumatoid arthritis).

Samples containing more than 12.5 ng/mL biotin (vitamin B7) may interfere (in the form of depressed signal) with INXAB / Infliximab Antibodies, Serum.

For antibodies-to-infliximab (ATI), pediatric and adult reference ranges were validated, and the presence of an ATI is established as greater than or equal to 50 U/mL by our electrochemiluminescent method.

The presence of IFX in a patient's serum is a recognized interference in most ATI methods. This assay includes an acid dissociation step, which partially mitigates this interference.

This test is designed to quantify infliximab and detect anti-drug antibodies specific to it, regardless of formulation. It is suitable for testing both the reference product and all US Food and Drug Administration- and European Medicines Agency-approved biosimilars. The assays do not differentiate between the originator and biosimilar products.

Clinical Reference

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Performance

Method Description

Infliximab Quantitation:
Testing for infliximab quantitation is performed using a laboratory-developed liquid chromatography tandem mass spectrometry assay.(Unpublished Mayo method)

Infliximab Antibodies:
Testing for antibodies to infliximab is performed using a laboratory-developed immunoassay.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available
3 to 6 days

Specimen Retention Time
2 weeks

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

CPT Code Information
80230
82397-(if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
INFXR	Infliximab QN with Reflex to Ab, S	39803-2

Result ID	Test Result Name	Result LOINC® Value
63000	Infliximab, S	39803-2
36847	Interpretation	59462-2