Overview

Useful For
Evaluation of loss of response to therapy
Quantification of ustekinumab in human serum
Trough level quantitation for evaluation of patients treated with ustekinumab
Detection of antibodies to ustekinumab in human serum

Profile Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>USQN</td>
<td>Ustekinumab QN, S</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>USTAB</td>
<td>Ustekinumab Ab, S</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Method Name
Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available
Yes

Specimen

Specimen Type
Serum

Specimen Required

Patient Preparation: Collect immediately before the next dose of drug administration (trough level)

Container/Tube:
Preferred: Serum gel
Acceptable: Red top

Specimen Volume: 0.5 mL

Forms
If not ordering electronically, complete, print, and send a Gastroenterology and Hepatology Client Test Request (T728) with the specimen.

Specimen Minimum Volume
0.35 mL
Test Definition: USTEK
Ustekinumab QN with Antibodies, S

Reject Due To

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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</thead>
<tbody>
<tr>
<td>Gross hemolysis</td>
<td>Reject</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gross lipemia</td>
<td>Reject</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heat-inactivated specimen</td>
<td>Reject</td>
<td></td>
<td></td>
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</tbody>
</table>

Specimen Stability Information

Clinical and Interpretive

Clinical Information

Ustekinumab (UTK) is a fully human IgG1 kappa monoclonal antibody (1) that binds with high affinity to the p40 subunit of human interleukin (IL)12 and IL23 and has been approved for the treatment of patients with moderate to severe Crohn disease (CD), moderate to severe ulcerative colitis (UC), psoriatic arthritis, and plaque psoriasis. The drug prevents IL12 and IL23 bioactivity by binding and neutralizing the shared p40 subunit, preventing interaction with the cell surface receptor protein IL12Rbeta1. Through this mechanism of action, UTK effectively neutralizes IL12 and IL23, proteins that are thought to be associated with gastrointestinal inflammation in CD and UC. In the setting of the inflammatory bowel diseases (IBD), CD and UC, the treatment regimen is started with a single weight-based loading dose of the t-mab administered intravenously (IV), and a maintenance regimen with standard (non-weight based) subcutaneous administration of ustekinumab 8 weeks after induction dose, and every 8 weeks thereafter. There is very little data supporting proactive therapeutic drug monitoring for ustekinumab.

The test is most useful in the evaluation of loss of response to therapy. A gradual decrease in efficacy over time following an initial response to biologics is common. In many cases, antibodies generated to the biologic are responsible for treatment failure, as they bind to the drug creating an immunocomplex and clearing the drug faster from circulation.

For IBD, measurements in nonresponders are indicated at post-induction (week 8) and concentrations of ustekinumab associated with favorable outcomes are greater than 3.5 mcg/mL. In addition, for measurements during maintenance stages of therapy, ustekinumab concentrations > or =1 mcg/mL are associated with clinical response and clinical remission. At maintenance stages, ustekinumab concentrations > or =4.5 mcg/mL are associated with mucosal healing.

In clinical trials, 6% to 12.4% of patients using ustekinumab for psoriasis or psoriatic arthritis developed antibodies-to-ustekinumab (ATU) over time. For IBD, between 2.9% and 4.6% of patients developed ATU when treated with ustekinumab for one year.(1) Therefore, it is important to monitor trough concentrations of serum UTK to correlate drug levels with loss of response to therapy. ATU may increase drug clearance in treated patients or neutralize the drug effect, thereby potentially contributing to the loss of response. ATU could also cause adverse events such as serum sickness and hypersensitivity reactions.

Currently, ustekinumab quantitation is performed in conjunction with immunogenicity assessment for ATU.
**Reference Values**

**USTEKINUMAB QN, S:**

Limit of quantitation is 0.3 mcg/mL

In inflammatory bowel disease, at post-induction measurement (week 8), concentrations above 3.5 mcg/mL are associated with good outcomes

For maintenance stages:

Concentrations > or =1.0 mcg/mL are associated with clinical response and clinical remission

Concentrations > or =4.5 mcg/mL are associated with mucosal healing

**USTEKINUMAB AB, S:**

Limit of quantitation is 10 AU/mL

Absent: <10 AU/mL

Present: > or =10 AU/mL

**Interpretation**

<table>
<thead>
<tr>
<th>Antibodies to ustekinumab (ATU) absent</th>
<th>ATU present</th>
</tr>
</thead>
<tbody>
<tr>
<td>For nonresponders: Insufficient ustekinumab is present. In the absence of ATU, consider optimizing therapy by increasing the dose or shortening the administration intervals, or by adding an immunomodulator to the therapeutic regimen.</td>
<td>For nonresponders: Insufficient ustekinumab is present. Antibodies-to-ustekinumab detected can contribute to faster clearance of ustekinumab and treatment failure. Clinical evaluation is recommended.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ustekinumab quantification &lt;1.0 mcg/mL</th>
<th>For nonresponders: If the sample was collected at trough ie, immediately before the next infusion, the results could suggest a mechanistic failure of ustekinumab. The provider may consider switching therapeutic regimen outside of the drug class.</th>
</tr>
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<tr>
<th>Ustekinumab quantification &gt; or =1.0 mcg/mL</th>
<th>For nonresponders:</th>
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<td>If the sample was collected at trough ie, immediately before the next infusion, the results could suggest a mechanistic failure of ustekinumab. The provider may consider switching therapeutic regimen outside of the drug class.</td>
<td></td>
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**Cautions**

This assay measures free ustekinumab. This assay does not measure ustekinumab bound to anti-ustekinumab antibodies (immunocomplexes).
Presence of ustekinumab at concentrations greater than 1 mcg/mL may impair detection of antibodies to ustekinumab (ATU), as the ATU assay is not drug tolerant. This assay measures free ATU. This assay does not measure ATU bound to UTK (immunocomplexes).

Elevated rheumatoid factor (RF) may falsely increase results of ATU. During validation studies, negative ATU samples remained negative and positive ATU samples remained positive; however the quantitative result differed by more than 20% when compared to the non-RF spiked original samples. If patients are positive for RF, clinical correlation is recommended for ATU test interpretation.

Clinical Reference

Performance

Method Description
Ustekinumab quantitation and anti-ustekinumab antibody measurements are performed using enzyme-linked immunosorbent assay (ELISA). Microwell strips are coated with a target antigen. Calibrators, controls, and patient samples are added to separate wells, allowing ustekinumab (UTK), or antibodies to ustekinumab (ATU), to bind to immobilized antigen. Unbound sample is washed away, and a conjugate is added to each well. A second incubation step allows the conjugate to bind to the UTK or ATU that has become attached to the microwells. After washing away the excess of unbound conjugate, the remaining enzyme activity is determined by adding a substrate and measuring the intensity of the color that develops in a spectrophotometer. The signal obtained is proportional to the amount of UTK or ATU in the patient sample.(Package inserts: Promonitor-UTK, Kit Product Number: 5371430000. Progenika Biopharma SA; Rev. 2, 4/2019; Promonitor-ANTI-UTK, Kit Product Number: 5381430000. Progenika Biopharma SA; Rev. 3, 4/2019)

PDF Report
No

Day(s) and Time(s) Test Performed
Tuesday, Friday; 11:00 a.m.

Analytic Time
1 day

Maximum Laboratory Time
4 days

Specimen Retention Time
14 days

Performing Laboratory Location
Rochester

Fees and Codes

Fees
Test Definition: USTEK
Ustekinumab QN with Antibodies, S

- 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
80299
83520

LOINC® Information

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<th>Test Order Name</th>
<th>Order LOINC Value</th>
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<td>USTEK</td>
<td>Ustekinumab QN with Antibodies, S</td>
<td>In Process</td>
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<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
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<td>Ustekinumab QN, S</td>
<td>87408-1</td>
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<tr>
<td>USTAB</td>
<td>Ustekinumab Ab, S</td>
<td>87409-9</td>
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