Overview

Useful For
Monitoring whole blood cyclosporine concentration during therapy, particularly in individuals coadministered CYP3A4 substrates, inhibitors, or inducers

Adjusting dose to optimize immunosuppression while minimizing toxicity

Evaluating patient compliance

Method Name
High-Performance Liquid Chromatography-Tandem Mass Spectrometry (HPLC-MS/MS)

NY State Available
Yes

Specimen

Specimen Type
Whole Blood EDTA

Specimen Required

Container/Tube: Lavender top (EDTA)

Specimen Volume: 3 mL

Collection Instructions:
1. Draw specimen immediately before a scheduled dose.

2. Do not centrifuge.

3. Send specimen in original tube.

Additional Information: Therapeutic range applies to trough specimens drawn immediately prior to a.m. dose.

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

- Renal Diagnostics Test Request (T830)

- Therapeutics Test Request (T831)

Specimen Minimum Volume
1 mL

Reject Due To

<table>
<thead>
<tr>
<th>Condition</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross hemolysis</td>
<td>OK</td>
</tr>
<tr>
<td>Gross lipemia</td>
<td>OK</td>
</tr>
</tbody>
</table>
Gross icterus  OK

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Blood EDTA</td>
<td>Refrigerated (preferred)</td>
<td>14 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ambient</td>
<td>14 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td>14 days</td>
<td></td>
</tr>
</tbody>
</table>

Clinical and Interpretive

Clinical Information

Cyclosporine is a lipophilic polypeptide used to prevent rejection after solid organ transplantation; it suppresses T-cell activation by inhibiting calcineurin to decrease interleukin-2 (IL-2) production. There is substantial interpatient variability in absorption, half-life, and other pharmacokinetic parameters. Cyclosporine is extensively metabolized by CYP3A4 to at least 30 less-active metabolites, many of which are detected by immunoassays. Cyclosporine is known for many drug interactions, including increased neuro- and nephrotoxicity when coadministered with antibiotics, antifungals, or other immunosuppressants. Cyclosporine has a narrow therapeutic range with frequent adverse effects making therapeutic drug monitoring essential.

With 80% of cyclosporine sequestered in erythrocytes, whole blood is the preferred specimen for analysis. Dose is adjusted initially (up to 2 months posttransplant) to maintain concentrations generally between 150 and 400 ng/mL. Target trough concentrations vary according to clinical protocol and depend on type of allograft, risk of rejection, concomitant immunosuppressive drugs, and toxicity. After the first 2 postoperative months, the target range is generally lower, between 75 and 300 ng/mL. Conversion between formulations is generally done at the same dose but with drug monitoring.

Reference Values

100-400 ng/mL (Trough)

Target steady-state trough concentrations vary depending on the type of transplant, concomitant immunosuppression, clinical/institutional protocols, and time post-transplant. Results should be interpreted in conjunction with this clinical information and any physical signs/symptoms of rejection/toxicity.

Interpretation

Most individuals display optimal response to cyclosporine with trough whole blood levels 100 to 400 ng/mL. Preferred therapeutic ranges may vary by transplant type, protocol, and comedication. Therapeutic ranges are based on specimens drawn at trough (i.e., immediately before the next scheduled dose). Blood drawn at other times will yield higher results. This test may also be used to analyze cyclosporine levels 2 hours after dosing (C2 concentrations); trough therapeutic ranges do not apply to C2 specimens.

The assay is specific for cyclosporine; it does not cross-react with cyclosporine metabolites, sirolimus, sirolimus metabolites, tacrolimus, or tacrolimus metabolites. Results by liquid chromatography with detection by tandem mass spectrometry are approximately 30% less than by immunoassay.
Cautions
The recommended therapeutic ranges described above apply to trough specimens drawn just before a dose. Blood drawn at other times will yield higher results.

Clinical Reference


Performance

Method Description

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday; Continuous until 3 p.m.
Saturday, Sunday; Continuous until 1 p.m.

Analytic Time
Same day/1 day

Maximum Laboratory Time
1 day

Specimen Retention Time
14 days

Performing Laboratory Location
Rochester

Fees and 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 Regional Manager. For assistance, contact Customer Service.
Test Definition: CYSPR
Cyclosporine, B

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
80158

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYSPR</td>
<td>Cyclosporine, B</td>
<td>3520-4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>35143</td>
<td>Cyclosporine, B</td>
<td>3520-4</td>
</tr>
</tbody>
</table>