**DoseASSURE™**, LabCorp’s portfolio of biologics monitoring assays, may help physicians maximize treatment response using a personalized, patient-specific approach

- Help aid in titrating doses or adjusting frequency to optimize effectiveness\(^1^\text{-}^3\)
- May help avoid lack of response due to under-treatment\(^1\)
- Assist in preventing and managing loss of response due to immunogenicity\(^4^\text{-}^5\)
- Minimize cost to patient by avoiding unhelpful dose escalation, especially in the setting of immunogenicity\(^1^,^6\)

**DoseASSURE test portfolio provides tests for both drug concentration (TDM) & anti-drug antibody (immunogenicity)**

### Therapeutic Drug Monitoring (TDM)

- Biologics have variable pharmacokinetics.\(^3^,^7\)
- Dosing by weight and empiric dose adjustment are inefficient and suboptimal.\(^3^,^7\)
- TDM for Biologics is a valuable tool to evaluate doses and to tailor dose adjustments to your individual patient.\(^3^,^7\)
- TDM can help differentiate under-treatment from other causes of lack of response.
- Proactive dose optimization using TDM may improve clinical scores and prolong duration of anti-TNF therapy.\(^1\)
- TDM has been shown to be cost-effective and may direct more appropriate care.\(^1^6\)

### Immunogenicity Testing (Anti-drug Antibody level)

- All biologics have the potential to induce an antibody-mediated immune response.
- Close to half of IBD patients on biologic therapy may develop anti-drug antibodies.\(^4^,^8^,^9\)
- Anti-drug antibodies may appear as early as after the first infusion and persist for years.\(^8\)
- Anti-drug antibodies can adversely affect the amount of drug in the body.\(^9\)
- Sufficient drug levels (e.g. infliximab >3ug/mL), concomitant use of immunomodulating agents, and regular dosing may protect against the risk of developing anti-drug antibodies.\(^1^7^,^19\)

<table>
<thead>
<tr>
<th>Biologic Drug Name</th>
<th>Primary Target</th>
<th><em>Clinical Indications</em></th>
<th>Test Name</th>
<th>Test No.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infliximab</strong></td>
<td>TNF</td>
<td>CD, UC **</td>
<td>Infliximab and Anti-Infliximab Antibody (Serial Monitor), DoseASSURE™ IFX</td>
<td>503870</td>
</tr>
<tr>
<td>Remicade®, Inflectra®, Renflexis®</td>
<td></td>
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</tr>
<tr>
<td><strong>Adalimumab</strong></td>
<td>TNF</td>
<td>CD, UC, RA</td>
<td>Adalimumab and Anti-Adalimumab Antibody (Serial Monitor), DoseASSURE™ ADL</td>
<td>503890</td>
</tr>
<tr>
<td>Humira®</td>
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<tr>
<td><strong>Vedolizumab</strong></td>
<td>α4B7 integrin</td>
<td>CD, UC</td>
<td>Vedolizumab and Anti-Vedolizumab Antibody, DoseASSURE™ VDZ</td>
<td>504567</td>
</tr>
<tr>
<td>Entyvio®</td>
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</tr>
<tr>
<td><strong>Golimumab</strong></td>
<td>TNF</td>
<td>UC, RA</td>
<td>Golimumab and Anti-Golimumab Antibody, DoseASSURE™ GOL</td>
<td>504563</td>
</tr>
<tr>
<td>Simponi®</td>
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<tr>
<td><strong>Ustekinumab</strong></td>
<td>IL23, IL12</td>
<td>CD, PA, PP</td>
<td>Ustekinumab and Anti-Ustekinumab Antibody, DoseASSURE™ UST</td>
<td>504594</td>
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<tr>
<td>Stelara®</td>
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<tr>
<td><strong>Certolizumab</strong></td>
<td>TNF</td>
<td>CD, RA, PA, PP</td>
<td>Certolizumab and Anti-Certolizumab Antibody, DoseASSURE™ CTZ</td>
<td>504627</td>
</tr>
<tr>
<td>Cimzia®</td>
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</tbody>
</table>


\(^**\)Also approved for pediatric forms of CD & UC
Interpreting Drug Concentrations

- Detectable drug levels are associated with better clinical outcome as measured by mucosal healing, lower C-reactive protein, higher remission rate, and less relapse.1,2,10,11
- Target ranges and maximally effective concentrations have not been established.3
- Optimal drug concentration depends on the desired therapeutic endpoint and may differ case by case.12

<table>
<thead>
<tr>
<th>Drug</th>
<th>Normal half-life</th>
<th>Proposed Target Trough Concentrations$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab</td>
<td>7.7 to 9.5 days</td>
<td>3–7 µg/mL; 5–10 µg/mL; &gt;4.0 µg/mL for mucosal healing21; ≥10.0 µg/mL may be required for fistula healing20</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>Approx 2 weeks</td>
<td>≥7.5 µg/mL13; ≥8.85 µg/mL14</td>
</tr>
<tr>
<td>Vedolizumab</td>
<td>Approx 25 days</td>
<td>&gt;30 µg/mL at week 613; &gt;14 µg/mL during maintenance24</td>
</tr>
<tr>
<td>Golimumab</td>
<td>Approx 2 weeks</td>
<td>≥4.27 µg/mL correlated with greater response and remission22</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>Approx 3 weeks</td>
<td>&lt;4.5 µg/mL has been associated with greater rate of endoscopic response23</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>Approx 2 weeks</td>
<td>≥20 µg/mL correlated to higher remission rate13</td>
</tr>
</tbody>
</table>

$Note: These target ranges were those used in landmark studies and do not necessarily translate into general recommendations for individual patients.

Interpreting Anti-Drug Antibody Levels

- Anti-drug antibodies can impact pharmacokinetics, efficacy, and the cost effectiveness of biologics.
- Low titer antibodies may have little to no effect on drug levels or clinical outcome but evidence suggests they may lead to later development of higher titers.9
- In contrast, high titers of antibodies are likely to be more consequential, leading to loss of drug efficacy by preventing drug binding to TNF and/or increasing drug clearance.5,15
- Anti-drug antibody positivity should be interpreted in the context of the concomitant free drug level.

When & where to collect blood on my patients?

- The timing of sample collection is important because the drug concentration will change during the dosing interval.
- The Trough Concentration (TC) is measured at the least variable time in the dosing interval, just before the next dose (same day to within <7 days depending on the drug’s normal half-life).
- During induction and maintenance phases, trough collections are usually recommended because target ranges are defined using TC.
- Blood can be drawn at any of LabCorp’s nearly 2000 patient service centers located nationwide.

References