INFLAMMATORY BOWEL DISEASE
Inflammatory Bowel Disease (IBD) is a chronic disease impacting nearly 1.2 million Americans.\(^1\) Developments in treatment, such as biologics, have greatly improved quality of life for patients and advancements in laboratory testing are helping to support diagnosis and optimize therapy. LabCorp offers leading expertise and comprehensive testing services to support physicians in the management of IBD patients.

**LabCorp’s IBD test offering supports complete care decisions**

**Inflammation Status**
- CBC
- Metabolic Panel
- C-Reactive Protein
- Sed Rate
- Calprotectin, Fecal
- Stool Lactoferin

**IBD Diagnosis**
- GI Pathology
  - Colonoscopy or Other Endoscopy
- Indeterminate or Patient non-compliance

**Risk Assessment**
- Co-Morbidity
  - Clostridium difficile
  - Stool Culture
  - CMV
- Crohn’s Prognostic
  - Anti-Glycan Antibodies

**Treatment Decision**
- Biologic
- Thiopurine
- Methotrexate

**Non-Responder**
- Switch treatment
- Add co-therapy
Single-Source Laboratory Solution for the Gastroenterology Specialist

Through specialized GI testing, a national service network, and multiple connectivity options, LabCorp makes it easier for gastroenterologists to manage their laboratory needs.

- Expansive network of managed care health plans
- Nearly 2000 patient service centers located nationwide
- Integrations with more than 700 EMR/EHRs, PWS, and HIE systems
- PhD and MD level client consultation
- Specialized service offerings for IBD, HCV, Celiac Disease, and Pathology

Pre-Treatment Testing
- CBC
- Metabolic Panel
- QuantiFERON Gold TB
- Hepatitis B Screening
- CBC
- TPMT Enzymes and/or TPMT Genetics
- CBC
- Metabolic Panel

Disease Activity
- C-Reactive Protein
- Stool Lactoferin
- Calprotectin, Fecal

Responder
Monitor progress
Adjust dosing if indicated

Treatment Monitoring
- Thiopurine Metabolites
- MTX Polyglutamates
- Biologic Drug Concentration and Antibody Testing (DoseASSURE™)

Quantify active drug levels,
Identify immunogenicity,
Adjust dosing and frequency,
Consider co-therapy,
Switch Treatment

Indeterminate or Patient non-compliance

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Quantify active drug levels,
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Evaluate Immunogenicity (Anti-drug Antibody level)

- Close to half of IBD patients on biologic therapy may develop anti-drug antibodies.23,28,29
- Anti-drug antibodies can adversely affect the amount of drug in the body.28
- Sufficient drug levels (e.g. infliximab >3μg/mL), concomitant use of immunomodulating agents, and regular dosing may protect against the risk of developing anti-drug antibodies.30–32

Optimize Biologics Drug Concentrations

- Dosing by weight and empiric dose adjustments are inefficient and suboptimal.19,20
- TDM for Biologics is a valuable tool to evaluate doses and to tailor adjustments to your individual patient.19,20
- 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.21

Trough collections are recommended in most cases.

<table>
<thead>
<tr>
<th>Biologic Drug Name</th>
<th>LabCorp Test</th>
<th>LabCorp Test No.</th>
<th>Proposed Target Trough Concentrations</th>
<th>Anti-Drug Antibodies Quantitative Range/Result Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab Remicade® Inflectra® Renflexis®</td>
<td>Infliximab and Anti-Infliximab Antibody (Serial Monitor), DoseASSURE™ IFX</td>
<td>503870</td>
<td>3–7 μg/mL; &gt;4.0 μg/mL for mucosal healing; ≥10.0 μg/mL may be required for fistula healing25</td>
<td>≥10,000+ ng/mL Reported as Low, Intermediate, or High Titer</td>
</tr>
<tr>
<td>Adalimumab Humira®</td>
<td>Adalimumab and Anti-Adalimumab Antibody (Serial Monitor), DoseASSURE™ ADL</td>
<td>503890</td>
<td>≥7.5 μg/mL26 &gt;5.85 μg/mL27</td>
<td>25–10,000+ ng/mL Reported as Low, Intermediate, or High Titer</td>
</tr>
<tr>
<td>Vedolizumab Entyvio®</td>
<td>Vedolizumab and Anti-Vedolizumab Antibody, DoseASSURE™ VDZ</td>
<td>504567</td>
<td>≥30 μg/mL at week 626 &gt;14 μg/mL during maintenance26</td>
<td>25–10,000+ ng/mL Stratification into low to high titer has yet to be determined.</td>
</tr>
<tr>
<td>Golimumab Simponi®</td>
<td>Golimumab and Anti-Golimumab Antibody, DoseASSURE™ GOL</td>
<td>504563</td>
<td>≥4.27 μg/mL correlated with greater response and remission26</td>
<td>20–10,000+ ng/mL Stratification into low to high titer has yet to be determined.</td>
</tr>
<tr>
<td>Ustekinumab Stelara®</td>
<td>Ustekinumab and Anti-Ustekinumab Antibody, DoseASSURE™ UST</td>
<td>504594</td>
<td>≥4.5 μg/mL has been associated with greater rate of endoscopic response26</td>
<td>40–10,000+ ng/mL Stratification into low to high titer has yet to be determined.</td>
</tr>
<tr>
<td>Certolizumab Cimzia®</td>
<td>Certolizumab and Anti-Certolizumab Antibody, DoseASSURE™ CTZ</td>
<td>504627</td>
<td>≥20 μg/mL correlated to higher remission rate26</td>
<td>40–10,000+ ng/mL Stratification into low to high titer has yet to be determined.</td>
</tr>
</tbody>
</table>

Patient-specific clinical context must be taken into account when evaluating drug and anti-drug antibody. Serial measurements over time may be helpful.

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

Monitoring drug levels for Immunomodulators supports dosing decisions, assessing patient compliance, and determining effectiveness of treatment.

- Utilize during treatment to help reach and maintain therapeutic goal
- Assists with evaluating unresponsive patients
- Thiopurine drugs monitoring helps avoid potential toxicity in responsive patients
- Approximately 30% – 40% of RA patients do not adequately respond to methotrexate treatment

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>LabCorp Test</th>
<th>LabCorp Test No</th>
<th>Target Concentrations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purinethol®</td>
<td>Thiopeurine Metabolites</td>
<td>503800</td>
<td>Suboptimal dosing: &lt;235 pmol 6-TG/8x10⁸ RBC&lt;br&gt;Optimal dosing: 235-450 pmol 6-TG/8x10⁸ RBC&lt;br&gt;Increasing risk for myelotoxicity and leukopenia: &gt;450 pmol 6-TG/8x10⁸ RBC&lt;br&gt;Hepatotoxicity risk: &gt;5700 pmol 6-MMP/8x10⁸ RBC</td>
</tr>
<tr>
<td>Azasan®</td>
<td>Thiopurine Metabolites</td>
<td>6-MMPN</td>
<td></td>
</tr>
<tr>
<td>Imuran®</td>
<td>Thiopurine Metabolites</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tabloid®</td>
<td>Thiopurine Metabolites</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rasuvo®</td>
<td>Methotrexate Polyglutamates</td>
<td>504104</td>
<td>The minimal concentrations of MTX-polyglutamates associated with a significantly decreased disease activity score (DAS28) at three months were:&lt;br&gt;– 20 nmol/L MTX-PG3&lt;br&gt;– 50 nmol/L Total-PGS (MTX-PG 1–5)&lt;br&gt;85% of patients having a significant reduction (-2) grades of their DAS did so prior to reaching a:&lt;br&gt;– Total MTX-PG (1–5) of 150 nmol/L&lt;br&gt;– MTX-PG2 of 22 nmol/L&lt;br&gt;– MTX-PG3 of 60 nmol/L&lt;br&gt;15% of eventual responders required higher levels.</td>
</tr>
<tr>
<td>Rheumatrex®</td>
<td>Methotrexate Polyglutamates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DosePack®</td>
<td>Methotrexate Polyglutamates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Otrexup®</td>
<td>Methotrexate Polyglutamates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trexall®</td>
<td>Methotrexate Polyglutamates</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

TPMT genetic and TPMT activity testing is additionally available to assess dosing prior to Thiopurine treatment, as well as to identify patients who may be at risk for drug toxicity.
IBD Diagnosis
A combination of clinical findings, endoscopic, histopathologic, radiologic, and laboratory testing is used to establish the diagnosis of IBD.

Diagnostic challenges arise when clinical presentation is indolent, invasive procedures are not obtainable, or results are inconclusive. Novel serological markers for IBD offer improved sensitivity and specificity to aid in differential diagnosis and provide valuable prognostic information about disease behavior.

**IBD Expanded Diagnostic Profile (LabCorp Test No: 162045)**

<table>
<thead>
<tr>
<th>Testing includes five IBD specific antibody markers*</th>
</tr>
</thead>
<tbody>
<tr>
<td>gASCA</td>
</tr>
<tr>
<td>ACCA</td>
</tr>
<tr>
<td>ALCA</td>
</tr>
<tr>
<td>AMCA</td>
</tr>
<tr>
<td>pANCA</td>
</tr>
</tbody>
</table>

**Overcome Diagnostic Challenges**
The markers examined in LabCorp’s IBD Expanded Diagnostic Profile may help clarify diagnosis and expedite therapeutic decisions.2-7

- Aid in the prompt recognition of IBD
- Aid in differentiating between IBD and non-IBD forms of colitis
- Assist in the differential diagnosis of UC vs CD in both adults and children
- Assist in the evaluation of patients with indeterminate colitis or IBD unclassified

**Support Crohn’s Disease Prognosis and Treatment Decisions**
The markers examined in LabCorp’s IBD Expanded Diagnostic profile have been shown to be highly specific predictors of aggressive disease behavior in Crohn’s Disease.2,3,6,10-17 Our profile may help physicians:

- Gain prognostic insight by identifying CD patients at risk for progression to complicated disease
- Stratify patients into disease severity/phenotypic subtypes
- Evaluate candidates for colectomy or IPAA and their post-surgical prognosis
A meta-analysis of CRP, fecal calprotectin and stool lactoferrin yielded the pooled sensitivities and specificities, odds ratios, and positive and negative predictive values listed in the chart below. Based on these findings, a negative fecal calprotectin in patients with symptoms consistent with IBD may rule out endoscopically active disease with a NPV of 86%. Conversely, a positive CRP result may rule in endoscopically active disease with a PPV of 86%.

### Diagnostic Accuracy for Endoscopically Active Disease

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>LabCorp Test No</th>
<th>Optimum Cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV*</th>
<th>NPV*</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-reactive Protein (CRP), quant.</td>
<td>006627</td>
<td>5.0 mg/L</td>
<td>0.49</td>
<td>0.92</td>
<td>0.86</td>
<td>0.64</td>
</tr>
<tr>
<td>Calprotectin, fecal</td>
<td>123255</td>
<td>50 μg/g</td>
<td>0.88</td>
<td>0.73</td>
<td>0.76</td>
<td>0.86</td>
</tr>
<tr>
<td>Lactoferrin, fecal quant.</td>
<td>123016</td>
<td>7.25 mg/L</td>
<td>0.82</td>
<td>0.79</td>
<td>0.80</td>
<td>0.82</td>
</tr>
</tbody>
</table>

*where average pre-test probabilities of endoscopically active disease are 50%.

#### IBD and Related Testing

<table>
<thead>
<tr>
<th>Test No.</th>
<th>Test Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>503890</td>
<td>Adalimumab and Anti-Adalimumab Antibody (Serial Monitor), DoseASSURE™ ADL</td>
</tr>
<tr>
<td>006627</td>
<td>C-Reactive Protein (CRP), Quantitative</td>
</tr>
<tr>
<td>123255</td>
<td>Calprotectin, Fecal</td>
</tr>
<tr>
<td>504627</td>
<td>Certolizumab and Anti-Certolizumab Antibody, DoseASSURE™ CTZ</td>
</tr>
<tr>
<td>183988</td>
<td>Clostridium difficile Toxin Gene, NAA</td>
</tr>
<tr>
<td>005009</td>
<td>Complete Blood Count (CBC) With Differential</td>
</tr>
<tr>
<td>162020</td>
<td>Crohn's Prognostic Profile</td>
</tr>
<tr>
<td>504563</td>
<td>Golimumab and Anti-Golimumab Antibody, DoseASSURE™ GOL</td>
</tr>
<tr>
<td>006510</td>
<td>Hepatitis B Surface Antigen</td>
</tr>
<tr>
<td>016881</td>
<td>Hepatitis B Core Antibody, IgM</td>
</tr>
<tr>
<td>162045</td>
<td>IBD Expanded Diagnostic Profile</td>
</tr>
<tr>
<td>503870</td>
<td>Infliximab and Anti-Infliximab Antibody (Serial Monitor), DoseASSURE™ IFX</td>
</tr>
<tr>
<td>322000</td>
<td>Metabolic Panel (14), Comprehensive</td>
</tr>
<tr>
<td>504104</td>
<td>Methotrexate Polyglutamates</td>
</tr>
<tr>
<td>182873</td>
<td>QuantiFERON®-TB Gold</td>
</tr>
<tr>
<td>005215</td>
<td>Sedimentation Rate, Modified Westergren</td>
</tr>
<tr>
<td>008144</td>
<td>Stool Culture</td>
</tr>
<tr>
<td>503800</td>
<td>Thiopurine Metabolites</td>
</tr>
<tr>
<td>510750</td>
<td>Thiopurine Methyltransferase (TPMT), Enzyme Activity</td>
</tr>
<tr>
<td>504142</td>
<td>Thiopurine Methyltransferase (TPMT) Genotyping</td>
</tr>
<tr>
<td>504594</td>
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References