



LABCORP DIAGNOSTICS

Inflammatory Bowel Disease



Labcorp's IBD test offerings support complete care decisions

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.



INFLAMMATION STATUS

CBC
Metabolic Panel
C-Reactive Protein
Sed Rate
Calprotectin, Fecal
Stool Lactoferrin



IBD DIAGNOSIS

GI Pathology
Colonoscopy or Other
Endoscopy

*Indeterminate
or Patient
non-compliance*

IBD Specific Serology

- ASCA
- ANCA
- Anti-Glycan Antibodies



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
- More than 2,000 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; Pre-Biologic Screening Profile; Hepatitis C Virus (HCV) Antibody Cascade to Quantitative PCR and Genotyping; Hepatitis B Surface Antigen (HBsAg) Screen, Qualitative; Hepatitis B Surface Antibody, Quantitative; Hepatitis B Core Antibody with Reflex; QuantiFERON®-TB Gold Plus; HLA-DQA1*05

CBC, TPMT Enzyme Activity, and/or *TPMT* and *NUDT15* Genotyping

CBC
Metabolic Panel



DISEASE ACTIVITY

C-Reactive Protein
Stool Lactoferrin
Calprotectin, Fecal



TREATMENT MONITORING

Thiopurine Metabolites

MTX Polyglutamates

Biologic Drug
Concentration and
Antibody Testing
(DoseASSURE™)



TREATMENT MANAGEMENT

Adjust dosing and
frequency

Identify high and
low immunogenicity

Consider co-therapy

Switch Treatment

Responder
Monitor progress
Adjust dosing if indicated

IBD Treatment Monitoring

Patient response to IBD treatments may be highly variable but new therapeutic drug monitoring (TDM) assays can help optimize therapy using a personalized, patient-specific approach.

Monitoring Biologics—DoseASSURE™ Portfolio

Biologic therapeutic drug monitoring (TDM) consists of tandem assays measuring drug and anti-drug antibody concentrations to support improved clinical outcomes and help identify the underlying mechanism of diminished response to therapy.²⁻⁵ DoseASSURE™, Labcorp's portfolio of biologic monitoring assays, may help physicians optimize biological therapy using a personalized, patient-specific approach.

- All biologics have variable pharmacokinetics and the potential to induce an antibody-mediated immune response^{6,7}
- TDM helps optimize dosing and frequency of treatment^{7,8}
- TDM assists in preventing and managing loss of response due to immunogenicity^{9,10}
- TDM can elucidate poor response as due to undertreatment (pharmacokinetic), mechanistic mismatch (pharmacodynamic) or development of anti-drug antibodies (immunogenic)

Biologic Drug Name	Labcorp Test Name	Test No.	Proposed Target Trough Concentrations	Anti-Drug Antibodies Quantitative Range/Result Interpretation
Infliximab Remicade® Avsola™ Renflexis®	Infliximab and Anti-Infliximab Antibody, DoseASSURE™ IFX	503870	3 – 7 µg/mL ⁷ ; 5 -10 µg/mL ⁸ ; >4.0 µg/mL for mucosal healing ¹¹ ; ≥10.0 µg/mL may be required for fistula healing ¹²	22-10,000+ng/mL Reported as Low, Intermediate, or High Titer
Adalimumab Humira®	Adalimumab and Anti-Adalimumab Antibody, DoseASSURE™ ADL	503890	≥7.5 µg/mL ¹³ >5.85 µg/mL ⁴	25-10,000+ ng/mL Reported as Low, Intermediate, or High Titer
Vedolizumab Entyvio®	Vedolizumab and Anti-Vedolizumab Antibody, DoseASSURE™ VDZ	504567	>30 µg/mL at week 6 ¹³ >14 µg/mL during maintenance ¹⁴	25-10,000+ ng/mL Stratification into low to high titer has yet to be determined.
Ustekinumab Stelara®	Ustekinumab and Anti-Ustekinumab Antibody, DoseASSURE™ UST	504594	>4.5 µg/mL has been associated with greater rate of endoscopic response ¹⁵	40-10,000+ ng/mL Stratification into low to high titer has yet to be determined.
Golimumab Simponi®	Golimumab and Anti-Golimumab Antibody, DoseASSURE™ GOL	504563	≥4.27 µg/mL correlated with greater response and remission ¹⁶	20-10,000+ ng/mL Stratification into low to high titer has yet to be determined.
Certolizumab Cimzia®	Certolizumab and Anti-Certolizumab Antibody, DoseASSURE™ CTZ	504627	≥20 µg/mL correlated to higher remission rate ¹³	40-10,000+ ng/mL Stratification into low to high titer has yet to be determined.

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.

Trough collections are recommended in most cases.

Optimize Biologics Drug Concentrations

- Dosing by weight and empiric dose adjustments are inefficient and suboptimal^{6,7}
- TDM for Biologics is a valuable tool to evaluate doses and to tailor adjustments to your individual patient^{6,7}
- 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 therapy³

Evaluate Immunogenicity (Anti-drug Antibody level)

- Close to half of IBD patients on biologic therapy may develop anti-drug antibodies^{5,9,17}
- Anti-drug antibodies can adversely affect the amount of drug in the body¹⁷
- 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 antibodies¹⁸⁻²⁰

HLA-DQA1*05 Variant Associated with Immunogenicity Risk for IFX/ADL Antibodies [167680]

- HLA-DQA1*05 genotype is associated with a 75% higher risk of anti-infliximab or anti-adalimumab antibodies and a 67% risk of loss of response compared to non-carriers²¹
- Informs treatment decisions when immunomodulators may pose a risk for adverse events or there is consideration to de-escalate combination therapy
- Aids in ruling out the risk of immunogenicity

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 goal²²
- Assists with evaluating unresponsive patients²²
- Thiopurine drug monitoring helps avoid potential toxicity in responsive patients²²
- Approximately 30% – 40% of RA patients do not adequately respond to methotrexate treatment²³

Drug Name	Labcorp Test	Test No.	Target Concentrations
Purinethol® Azasan® Imuran® Tabloid®	Thiopurine Metabolites	503800	6-TGN Suboptimal dosing: <235 pmol 6-TG/8x108 RBC Optimal dosing: 235-450 pmol 6-TG/8x108 RBC Increasing risk for myelotoxicity and leukopenia: >450 pmol 6-TGN/8x108 RBC 6-MMPN Hepatotoxicity risk: >5700 pmol 6-MMP/8x108 RBC
Rasuvo® Rheumatrex® DosePack® Otrexup® Trexall®	Methotrexate Polyglutamates	504104	Total MTX PG is the sum of Methotrexate PG1 through PG5. Total MTX PG greater than 74 nmol/L at 3 months is consistent with therapeutic efficacy. ²⁴ MTX PG1 is the unmodified/native circulating parent drug. MTX PG2 and long-chain MTX polyglutamates (MTX PG3, MTX PG4, MTX PG5) are formed and retained intracellularly. ²⁴ Clinical response may be mediated by long-chain MTX PGs. ²⁵

TPMT genetic and TPMT enzyme activity testing are available prior to Thiopurine treatment to identify patients who may be at risk for drug toxicity and to determine patient-specific dosing.

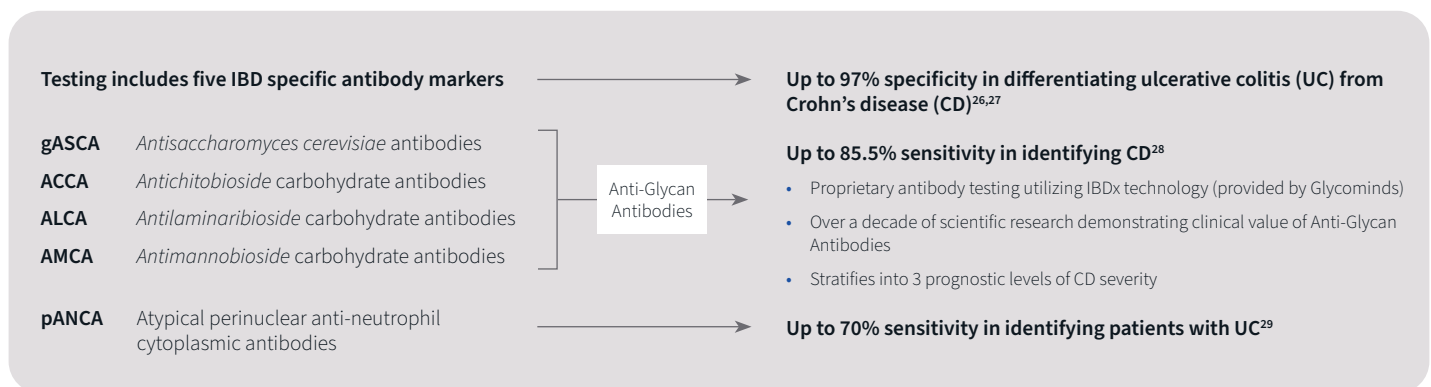


IBD Diagnosis

A combination of clinical findings and 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)



Overcome Diagnostic Challenges

The markers examined in Labcorp's IBD Expanded Diagnostic Profile may help clarify diagnosis and expedite therapeutic decisions.²⁶⁻³¹

- Aid in the prompt recognition of IBD³⁰
- Aid in differentiating between IBD and non-IBD¹ forms of colitis
- Assist in the differential diagnosis of UC vs CD in both adults and children³⁰
- Assist in the evaluation of patients with indeterminate colitis or IBD unclassified^{32,33}

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.^{2,26,27,30,34-40} Our profile may help physicians:

- Gain prognostic insight by identifying CD patients at risk for progression to complicated disease^{2,26,27,30,34-40}
- Stratify patients into disease severity/phenotypic subtypes^{2,26,27,30,34-40}
- Evaluate candidates for colectomy or IPAA and their post-surgical prognosis^{33,41}



IBD Expanded Diagnostics Profile was developed to be both clinically useful and cost-effective for patients.

IBD Disease Activity

Non-invasive biomarkers may be useful in assessing and monitoring disease activity in Inflammatory Bowel Disease.

A meta-analysis of C-Reactive Protein (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.⁴² 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

Biomarker	Test No.	Optimum Cut-off	Sensitivity ⁴²	Specificity ⁴²	PPV ^{*42}	NPV ^{*42}
C-Reactive Protein (CRP), Quantitative	006627	5.0 mg/L	0.49	0.92	0.86	0.64
Calprotectin, Fecal	123255	50 µg/g	0.88	0.73	0.76	0.86
Lactoferrin, Fecal, Quantitative	123016	7.25 mg/L	0.82	0.79	0.80	0.82

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

IBD and Related Testing

Test Name	Test No.	Test Name	Test No.
Adalimumab and Anti-Adalimumab Antibody, <i>DoseASSURE™</i> ADL	503890	Infliximab and Anti-Infliximab Antibody, <i>DoseASSURE™</i> IFX	503870
C-Reactive Protein (CRP), Quantitative	006627	Lactoferrin, Fecal, Quantitative	123016
Calprotectin, Fecal	123255	Metabolic Panel (14), Comprehensive	322000
Certolizumab and Anti-Certolizumab Antibody, <i>DoseASSURE™</i> CTZ	504627	Methotrexate Polyglutamates	504104
<i>Clostridioides difficile</i> Toxin Gene, NAA	183988	Pre-Biologic Screening Profile	144441
Complete Blood Count (CBC) With Differential	005009	QuantiFERON®-TB Gold Plus	182879
Crohn's Prognostic Profile	162020	Sedimentation Rate, Modified Westergren	005215
Golimumab and Anti-Golimumab Antibody, <i>DoseASSURE™</i> GOL	504563	Stool Culture	008144
Hepatitis B Surface Antigen	006510	Thiopurine Metabolites	503800
Hepatitis B Core Antibody, IgM	016881	Thiopurine Methyltransferase (TPMT), Enzyme Activity, Erythrocytes	510750
HLA-DQA1*05 Variant Associated With Immunogenicity Risk for IFX/ADL Antibodies	167680	<i>TPMT</i> and <i>NUDT15</i> Genotyping	512300
Inflammatory Bowel Disease (IBD) Expanded Profile	162045	Ustekinumab and Anti-Ustekinumab Antibody, <i>DoseASSURE™</i> UST	504594
		Vedolizumab and Anti-Vedolizumab Antibody, <i>DoseASSURE™</i> VDZ	504567



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