*Dose*ASSURE™

OPTIMIZING INFLAMMATORY BOWEL DISEASE TREATMENT THROUGH BIOLOGICS

*Dose*ASSURE™, 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[1-3]
- May help avoid lack of response due to under-treatment[1]
- Assist in preventing and managing loss of response due to immunogenicity[4-5]
- Minimize cost to patient by avoiding unhelpful dose escalation, especially in the setting of immunogenicity[1,6]

Biologic Drug Name	Primary Target	*Clinical Indications	Test Name	Test No.
Infliximab Remicade®; Inflectra®, Renflexis®	TNF	CD, UC **	Infliximab and Anti-Infliximab Antibody (Serial Monitor), *Dose*ASSURE™ IFX	503870
Adalimumab Humira®	TNF	CD, UC, RA	Adalimumab and Anti-Adalimumab Antibody (Serial Monitor), *Dose*ASSURE™ ADL	503890
Vedolizumab Entyvio®	α4β7 integrin	CD, UC	Vedolizumab and Anti-Vedolizumab Antibody, *Dose*ASSURE™ VDZ	504567
Golimumab Simponi®	TNF	UC, RA	Golimumab and Anti-Golimumab Antibody, *Dose*ASSURE™ GOL	504563
Ustekinumab Stelara®	IL23, IL12	CD, PA, PP	Ustekinumab and Anti-Ustekinumab Antibody, *Dose*ASSURE™ UST	504594
Certolizumab Cimzia®	TNF	CD, RA, PA, PP	Certolizumab and Anti-Certolizumab Antibody, *Dose*ASSURE™ CTZ	504627

*Partial listing of FDA-approved indications. TNF: tumor necrosis factor, IL: interleukin, CD: Crohn's Disea Ulcerative Colitis, RA: Rheumatoid Arthritis, PA: Psoriatic Arthritis, PP: Plaque Psoriasis
**Also approved for pediatric forms of CD & UC

*Dose*ASSURE 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.[16]

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.[8]
- 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.[17-19]

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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]

Drug	Normal half-life	Proposed Target Trough Concentrations§
Infliximab	7.7 to 9.5 days	3 – 7 µg/mL[1]; 5 -10 µg/mL[2]; >4.0 µg/mL for mucosal healing[12]; ≥10.0 µg/mL may be required for fistula healing[20]
Adalimumab	Approx 2 weeks	≥ 7.5 µg/mL[13] > 5.85 µg/mL[14]
Vedolizumab	Approx 25 days	>30 µg/mL at week 6[13] >14 µg/mL during maintenance[24]
Golimumab	Approx 2 weeks	≥ 4.27 µg/mL correlated with greater response and remission[22]
Ustekinumab	Approx 3 weeks	>4.5 µg/mL has been associated with greater rate of endoscopic response[23]
Certolizumab	Approx 2 weeks	≥20 µg/mL correlated to higher remission rate[13]

§Note: These targets 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.[9,15]
- Anti-drug antibody positivity should be interpreted in the context of the concomitant free drug level.

Anti-Drug Antibodies	Quantitative Range	Result Interpretation
Anti-Infliximab Abs	22- 10,000+ng/mL	Antibodies are reported as Low, Intermediate or High Titer
Anti-Adalimumab Abs	25-10,000+ ng/mL	Antibodies are reported as Low, Intermediate or High Titer
Anti-Vedolizumab Abs	25-10,000+ ng/mL	Stratification into low to high titer has yet to be determined.
Anti-Golimumab Abs	20-10,000+ ng/mL	Stratification into low to high titer has yet to be determined.
Anti-Ustekinumab Abe	40-10,000+ ng/mL	Stratification into low to high titer has yet to be determined.
Anti-Certolizumab Abs	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

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.

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