

Uniquely measures serum infliximab (IFX) and antibodies to infliximab (ATI) levels at any time¹

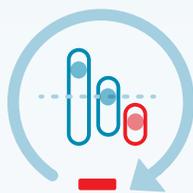
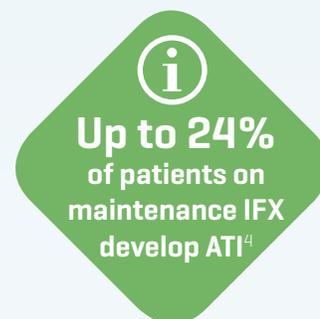
PROMETHEUS®
Anser® IFX

Monitoring your inflammatory bowel disease (IBD) patients may help you address IFX therapy challenges



Development of ATI has been associated with poor clinical outcomes

- 60% of IFX-treated pediatric IBD patients who underwent bowel surgery were ATI-positive (≥ 12 U/mL) vs only 8% positivity in patients who did not have surgery ($P = 0.01$)^{2,*}
- ATI-positive IBD patients had higher likelihood of losing response to IFX than patients without ATI (pooled risk ratio = 3.2; $P < 0.0001$)^{3,**}



IFX drug level may affect outcomes

- IFX level of ≥ 5 $\mu\text{g/mL}$ was associated with a longer duration on maintenance IFX therapy without flares ($P < 0.0001$)^{5,***}
- Recent American Gastroenterological Association guidelines recommend using therapeutic drug monitoring for patients who have lost response to IFX (therapeutic target for IFX: ≥ 5 $\mu\text{g/mL}$)⁶

The PROMETHEUS® Anser® Test heritage of excellence



Proven use in multiple clinical studies^{5,7-13}



More cost-effective than empiric management for managing loss of response to IFX¹⁴



Confidence of over 100,000 patient experiences since 2012

Validated for use with IFX biosimilars¹⁵

¹In a cross-sectional study of 134 pediatric and young adult patients where serum IFX and ATI levels were reported based off PROMETHEUS® Anser® IFX Test.

²From a meta-analysis of 13 studies with reported results from 1,378 patients where serum IFX and ATI levels were reported based off enzyme-linked immunosorbent assays (ELISA).

³In a retrospective, dose-adjustment study of 126 IBD patients where serum IFX levels were reported based off Anser® IFX and ELISA.

► Learn more at anserifx.com

Uniquely measures serum adalimumab (ADA) and antibodies to ADA (ATA) levels at any time¹⁶

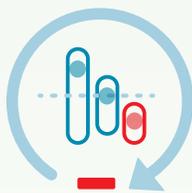
PROMETHEUS®
Anser® ADA

Monitoring your IBD patients may help you address ADA therapy challenges



Development of ATA has been associated with poor clinical outcomes

- A significantly higher proportion of ADA patients who did not achieve mucosal healing (MH) had high-titer ATA (> 1 U/mL)^{9,*}
- The presence of ATA > 0.55 U/mL has been associated with lower ADA and higher C-reactive protein (CRP) levels^{17,**}
 - ATA were more likely to be present when ADA levels were < 7.5 $\mu\text{g/mL}$ ^{17,**}



ADA drug level may affect outcomes

- ADA level of 7.5 $\mu\text{g/mL}$ has been associated with endoscopic healing (EH)^{17,**}
- Recent American Gastroenterological Association guidelines recommend using therapeutic drug monitoring for patients who have lost response to ADA (therapeutic target for ADA: ≥ 7.5 $\mu\text{g/mL}$)



*In a cross-sectional study of 60 CD patients on ADA maintenance therapy where serum ADA and ATA levels were reported based off PROMETHEUS® Anser® ADA Test. MH was defined as the absence of any ulceration in all ileocolonic segments and clinical remission was defined as Harvey-Bradshaw index < 5 . Twenty-eight percent in the group without MH were ATA+ vs 2.9% in the MH group ($P = 3 \times 10^{-2}$).

**In a cross-sectional study of 66 patients (59 CD, 7 UC) on ADA maintenance therapy for at least 12 weeks where serum ADA and ATA levels were reported based off Anser® ADA. EH was defined as the lack of any inflammatory findings in the intestinal mucosa ($P = 0.02$).

References: 1. Wang SL, Ohrmund L, Hauenstein S, et al. Development and validation of a homogeneous mobility shift assay for the measurement of infliximab and antibodies-to-infliximab levels in patient serum. *J Immunol Methods*. 2012;382(1-2):177-188. 2. Zitomersky NL, Atkinson BJ, Fournier K, et al. Antibodies to infliximab are associated with lower infliximab levels and increased likelihood of surgery in pediatric IBD. *Inflamm Bowel Dis*. 2015;21(2):307-314. 3. Nanda KS, Cheifetz AS, Moss AC. Impact of antibodies to infliximab on clinical outcomes and serum infliximab levels in patients with inflammatory bowel disease (IBD): a meta-analysis. *Am J Gastroenterol*. 2013;108(1):40-47. 4. Vande Castele N, Khanna R, Levesque BG, et al. The relationship between infliximab concentrations, antibodies to infliximab and disease activity in Crohn's disease. *Gut*. 2015;64(10):1539-1545. 5. Vaughn BP, Martinez-Vazquez M, Patwardhan VR, Moss AC, Sandborn WJ, Cheifetz AS. Proactive therapeutic concentration monitoring of infliximab may improve outcomes for patients with inflammatory bowel disease: results from a pilot observational study. *Inflamm Bowel Dis*. 2014;20(11):1996-2003. 6. Feuerstein JD, Nguyen GC, Kupfer SS, Falck-Ytter Y, Singh S; American Gastroenterological Association Institute Clinical Guidelines Committee. American Gastroenterological Association Institute guideline on therapeutic drug monitoring in inflammatory bowel disease. *Gastroenterology*. 2017;153(3):827-834. 7. Papamichael K, Chachu KA, Vajravelu RK, et al. Improved long-term outcomes of patients with inflammatory bowel disease receiving proactive compared with reactive monitoring of serum concentrations of infliximab. *Clin Gastroenterol Hepatol*. 2017;15(10):1580-1588. 8. Singh N, Rosenthal CJ, Melmed GY, et al. Early infliximab trough levels are associated with persistent remission in pediatric patients with inflammatory bowel disease. *Inflamm Bowel Dis*. 2014;20(10):1708-1713. 9. Zittan E, Kabakchiev B, Milgrom R, et al. Higher adalimumab drug levels are associated with mucosal healing in patients with Crohn's disease. *J Crohns Colitis*. 2016;10(5):510-515. 10. Velayos FS, Sheibani S, Lockton L, et al. Prevalence of antibodies to adalimumab (ATA) and correlation between ATA and low serum drug concentration on CRP and clinical symptoms in a prospective sample of IBD patients. *Gastroenterology*. 2013;144(5 suppl 1):S-91. 11. Chaparro M, Guerra I, Iborra M, et al. Correlation between adalimumab serum levels and remission after the induction phase in Crohn's disease patients. *Gastroenterology*. 2015;148(4 suppl 1):S107-S108. 12. Baert F, Kondragunta V, Lockton S, et al. Antibodies to adalimumab are associated with future inflammation in Crohn's patients receiving maintenance adalimumab therapy: a post hoc analysis of the Karmiris trial. *Gut*. 2016;65(7):1126-1131. 13. Yarur AJ, Deshpande AR, Sussman DA, et al. Serum adalimumab levels and antibodies correlate with endoscopic intestinal inflammation and inflammatory markers in patients with inflammatory bowel disease. *Gastroenterol Hepatol*. 2013;9(8 suppl 4):6. 14. Velayos FS, Kahn JG, Sandborn WJ, Feagan BG. A test-based strategy is more cost effective than empiric dose escalation for patients with Crohn's disease who lose responsiveness to infliximab. *Clin Gastroenterol Hepatol*. 2013;11(6):654-666. 15. Data on file. Prometheus Laboratories Inc. 16. Wang SL, Hauenstein S, Ohrmund L, et al. Monitoring of adalimumab and antibodies-to-adalimumab levels in patient serum by the homogeneous mobility shift assay. *J Pharm Biomed Anal*. 2013;78-79:39-44. 17. Yarur AJ, Jain A, Hauenstein SI, et al. Higher adalimumab levels are associated with histologic and endoscopic remission in patients with Crohn's disease and ulcerative colitis. *Inflamm Bowel Dis*. 2016;22(2):409-415. 18. Dreesen E, Bossuyt P, Mulleman D, Gils A, Pascual-Salcedo D. Practical recommendations for the use of therapeutic drug monitoring of biopharmaceuticals in inflammatory diseases. *Clin Pharmacol*. 2017;9:101-111. 19. Billioud V, Sandborn WJ, Peyrin-Biroulet L. Loss of response and need for adalimumab dose intensification in Crohn's disease: a systematic review. *Am J Gastroenterol*. 2011;106(4):674-684.

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