PROMETHEUS®

7C4 Diagnostic Test

Nonfasting PROMETHEUS® 7C4 Diagnostic Test for bile acid malabsorption (BAM)[1]

Helps determine if BAM may be a cause of gastrointestinal-related symptoms in patients with inflammatory bowel disease (IBD), or diarrhea-predominant irritable bowel syndrome (IBS-D)

- Serum test measures 7α-hydroxy-4-cholesten-3-one (7C4) levels with liquid chromatography-tandem mass spectrometry
  - 7C4 is a biomarker for measuring the activity of the major rate-limiting enzyme in the hepatic bile acid biosynthesis pathway[2]
  - Correlation of 7C4 with bile acid synthesis has been validated in multiple studies[3,4]
  - Increased 7C4 serum levels can be used to help diagnose BAM[3]
- In validation testing, the 7C4 Diagnostic test demonstrated[1,*]:
  - 94% specificity, 65% sensitivity, and 71% positive predictive value
  - No reported interference**
- In a clinical study, 7C4 concentrations were associated with bile acid diarrhea regardless of IBD disease activity or length of ileal resection[5,***]

BAM—or the failure of absorption of bile acids by the distal ileum—leads to increased colonic secretion and diarrhea[3]

The high specificity suggests the test will be useful to rule in BAM[1]

*In laboratory testing using a cutoff of 55 ng/mL 7C4.

**When the 7C4 analyte was tested with multiple cross-reactants and interfering substances, all test samples recovered below the lower limit of quantitation (< 1.5 ng/mL) with no spiked 7C4 and recovered within 15% bias (85%-115% recovery) when 7C4 was spiked at target concentrations.

***In a prospective study of IBD patients where serum samples from 26 Crohn's disease patients with ileal resection (97 serum samples) and 11 ulcerative colitis patients (13 serum samples, no ileal resection) were analyzed with the 7C4 Diagnostic test. Diarrhea was defined as > 3 bowel movements a day.

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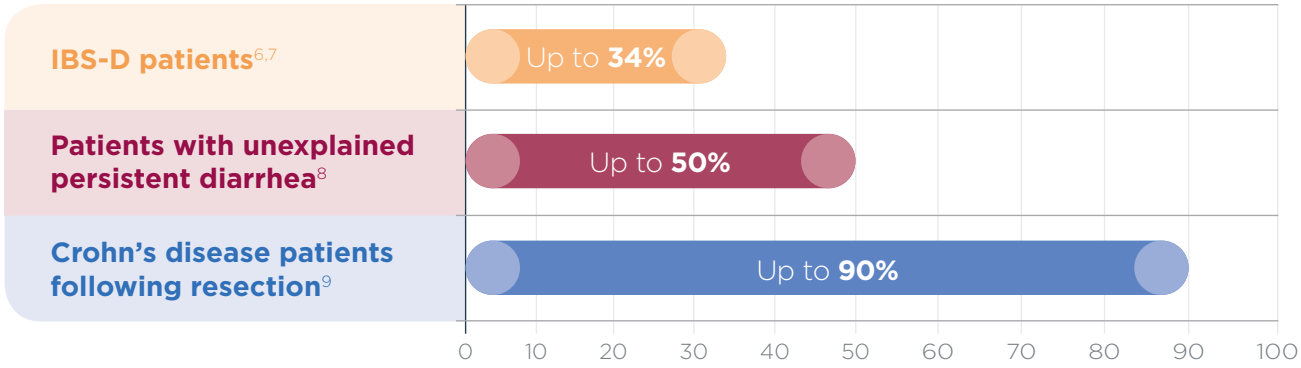
Prevalence of BAM[6-9]

Percentage of Patients With BAM Across Different Conditions[6-9,*]



*Graphic depicts data compiled from separate studies.

Ordering the PROMETHEUS® 7C4 Diagnostic Test:

- Catalog number: #8205
- CPT® Code (as applied by Prometheus): 82542
- Specimen requirements: Serum separator tube or red top tube. Cold pack required
- Storage: Room temperature or refrigerated
- Stability:
  - Room temperature: 3 days
  - Refrigerated: 7 days
- Turnaround time: 3-4 business days from receipt of sample

References: 1. Data on file. Prometheus Laboratories Inc. **2.** Russell DW. The enzymes, regulation, and genetics of bile acid synthesis. *Annu Rev Biochem.* 2003;72:137-174. **3.** Hofmann AF, Mangelsdorf DJ, Kliewer SA. Chronic diarrhea due to excessive bile acid synthesis and not defective ileal transport: a new syndrome of defective fibroblast growth factor 19 release. *Clin Gastroenterol Hepatol.* 2009;7(11):1151-1154. **4.** Axelson M, Mörk B, Sjövall J. Ethanol has an acute effect on bile acid biosynthesis in man. *FEBS Lett.* 1991;281(1-2):155-159. **5.** Battat R, Duijvestein M, Vande Casteele N, et al. The association of serum 7α-hydroxy-4-cholesten-3-one (7C4) with bile acid diarrhea in patients with inflammatory bowel disease. Poster presented at: 13th Congress of European Crohn's and Colitis Organisation; February 14-17, 2018; Vienna, Austria. **6.** Slattery SA, Niaz O, Aziz Q, Ford AC, Farmer AD. Systematic review with meta-analysis: the prevalence of bile acid malabsorption in the irritable bowel syndrome with diarrhoea. *Aliment Pharmacol Ther.* 2015;42(1):3-11. **7.** Kurien M, Evans KE, Leeds JS, Hopper AD, Harris A, Sanders DS. Bile acid malabsorption: an under-investigated differential diagnosis in patients presenting with diarrhea predominant irritable bowel syndrome type symptoms. *Scand J Gastroenterol.* 2011;46(7-8):818-822. **8.** Pattni S, Walters JR. Recent advances in the understanding of bile acid malabsorption. *Br Med Bull.* 2009;92:79-93. **9.** Barkun AN, Love J, Gould M, Pluta H, Steinhart H. Bile acid malabsorption in chronic diarrhea: pathophysiology and treatment. *Can J Gastroenterol.* 2013;27(11):653-659.

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Prometheus diagnostic services provide important information to aid in the diagnosis and management of certain diseases and conditions. How this information is used to guide patient care is the responsibility of the physician.

Assays and methods within this test may be covered by one or more US pending or issued patents. For details, please go to www.prometheuslabs.com.

PROMETHEUS® Therapeutics & Diagnostics

For the person in every patient®

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