

REQUESTING PHYSICIAN

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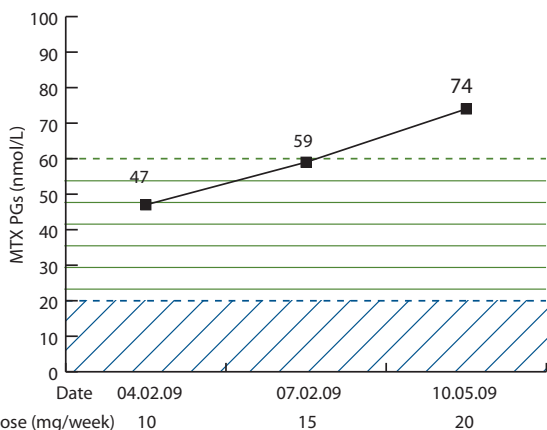
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PATIENT AND ORDER INFORMATION

Order ID: 9999999A
Patient Name: Susan S. Sample
DOB: 01.01.60 Gender: Female
Patient ID / Medical Record #: 7777777B
Sample ID: 3333333C
Date of Collection: Date Received: Date Reported:
10.05.09 10.07.09 10.09.09

AVISE PG TEST RESULTS

CURRENT DOSE MTX (mg/week)	DATE CURRENT DOSE INITIATED	DATE MTX INITIATED	RESULTS (nmol/L)	RESULT ASSESSMENT
20	07.02.09	01.01.09	74	Therapeutic levels of MTX PGs



The Avise PG test measures red blood cell methotrexate polyglutamates (MTX PGs), the active metabolites of methotrexate

In a cohort of 256 rheumatoid arthritis patients taking methotrexate (range 5-25 mg/wk, median 15 mg/wk) for more than 3 months:^{1-3,5}

- Those with MTX PG levels below 20 nmol/L were 3 fold more likely to have a poor response to methotrexate vs. those with levels ≥ 20 nmol/L (OR = 2.9; 95% CI: 1.4-5.9)
- Those with MTX PG levels above 60 nmol/L were more than 5 fold more likely to have a good response to methotrexate vs. those with levels ≤ 60 nmol/L (OR=5.5; 95% CI: 2.5-12.0)

ADDITIONAL INFORMATION

CAUTION: Studies supporting the clinical utility of this test are based on patients receiving methotrexate for at least three months. Caution should be used in interpreting results for patients on therapy for less than three months.

REFERENCES

1) Dervieux T, Furst D, et al. Polyglutamation of Methotrexate With Common Polymorphisms in Reduced Folate Carrier, Aminoimidazole Carboxamide Ribonucleotide Transformylase, and Thymidylate Synthase Are Associated With Methotrexate Effects in Rheumatoid Arthritis, *Arthritis Rheum.* 2004; 50(9):2766-2774. 2) Dervieux T, Furst D, et al. Pharmacogenetic and metabolite measurements are associated with clinical status in patients with rheumatoid arthritis treated with methotrexate: results of a multicentred cross sectional observational study, *Ann Rheum Dis* 2005;64(8):1180-1185. 3) Dervieux T, Greenstein N, et al. Pharmacogenomic and Metabolic Biomarkers in the Folate Pathway and Their Association With Methotrexate Effects During Dosage Escalation in Rheumatoid Arthritis., *Arthritis Rheum.* 2006; 54(10):3095-3103. 4) Kremer J. Toward a Better Understanding of Methotrexate, *Arthritis Rheum.* 2004; 50(5):1370-1382. 5) Data on file.

ASSAY DESCRIPTION AND METHODOLOGY

Results were obtained by a proprietary liquid chromatographic method with post column photo-oxidation technique (US patent 6,921,667 and patents pending).

INTENDED USE

Avise PG, in conjunction with other laboratory and clinical findings, is an aid for optimizing methotrexate therapy in the treatment of rheumatoid arthritis.

CLINICAL LABORATORY INFORMATION

Cypress Bioscience, Inc. Laboratory Director: Curtis McGuyer, M.D. CLIA# 05D1075048 CAP# 7201051 CA# CLF334804

Diagnostic testing should be interpreted in the context of additional clinical findings. How this information is used to guide patient care is the responsibility of the physician. This test was developed and its performance characteristics determined by Cypress Bioscience. It has not been approved by the U.S. Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under CLIA-88 as qualified to perform high complexity clinical laboratory testing. © Cypress Bioscience, Inc. 2008-2010. All rights reserved. Avise PG and the Avise PG logo are service marks of Cypress Bioscience, Inc. The Cypress Bioscience, Inc. logo is a registered trademark of Cypress Bioscience, Inc.