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COLOGUARD: A NEW SCREENING TEST FOR COLORECTAL CANCER

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Effective June 1, 2015, Marshfield Clinic will make available the Cologuard© test as an option to screen for colorectal cancer (CRC). CRC is the second leading cause of cancer-related deaths in the United States (US). The stepwise histopathologic changes in the development of CRC allow for early detection and surgical cure when caught early. Yet, at least one third of Americans report not being compliant with screening recommendations.

BACKGROUND

CRC arises from accumulated genetic abnormalities. This forms the basis for molecular (DNA-based) testing of stool samples which contain minute numbers of cells shed from pre-cancerous or cancerous lesions. Cologuard© (developed by Exact Sciences, Madison, WI) is a multi-target stool DNA assay for aberrantly methylated BMP3 and NDRG4 promoter regions, mutant KRAS, and beta-actin (a reference gene to control for human DNA quantity), combined with fecal immunochemical testing (FIT) for human hemoglobin. Whereas stool DNA testing can detect conventional adenomas (chromosome instability pathway) and serrated adenomas (microsatellite instability pathway), FIT is ineffective in screening for the latter.

A landmark study (and accompanying editorial) in the April 3, 2014, issue of The New England Journal of Medicine summarized the performance of Cologuard© in nearly 10,000 participants. Although Cologuard©'s sensitivity for detecting CRC was 92%, it was only 42% for precancerous lesions. One-time fecal

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immunochemical testing (FIT) using the Polymedco assay was considerably less sensitive at 74% and 24%, respectively. FIT was slightly more specific at about 95-96% compared with 87-90% for Cologuard©.

TESTING

Cologuard© received Food and Drug Administration (FDA) approval in August, 2014, and in October the Centers for Medicare & Medicaid Services (CMS) issued its coverage decision with a proposed payment of approximately $500. Medicare will cover Cologuard© testing once every three years if patients meet all of the following criteria:

(1) 50-85 years of age
(2) No GI symptoms, previous positive guaiac, or FIT
(3) No personal or family history of adenomatous polyps, CRC, or inflammatory bowel disease.

Colonoscopy, generally starting at age 50 years for patients at average risk, remains the "gold standard" for the screening, diagnosis, and (in cases of small polypoid lesions) treatment of CRC and its precursor lesions. Yearly FIT still remains a less costly (albeit less sensitive) screening option at about $25-40 per test. Comparative effectiveness studies are clearly needed.

Remember that Cologuard© and FIT do not make a definitive diagnosis. The result is binary and will be entered into the combined medical record (CMR) as either POSITIVE or NEGATIVE. In counseling patients regarding CRC screening, patients must understand that if they choose either Cologuard© or FIT, they are obligated to undergo colonoscopy if the result comes back POSITIVE. In the general population, roughly 15% of patients will have a POSITIVE Cologuard screening test with a slightly lower percentage for FIT. Providers will directly contact patients with POSITIVE results to schedule colonoscopy.

HOW TO ORDER THIS TEST

The Cologuard test will be ordered as "ColoGuard DNA Stool Test" in clinical order manager (COM). Exact Sciences will mail out the kits and also receive the completed kits by mail. Sample testing will be performed by Exact Sciences with results transmitted back to Marshfield Labs' Customer Service department for entry into the patient's medical record. (See details on pages 3-4.)

Test Name	ColoGuard DNA Stool Test
Test Code	COLOSO
Keywords	Colorectal Cancer Screen

QUESTIONS

Test information is available in: Marshfield Labs' Test Reference Manual.
For clinical information contact:

- Gene R. Shaw, MD; Jeffrey M. Resnick, MD; or Timothy Uphoff, PhD.

Phone number: 800-222-5835.

REFERENCES

1. Imperiale,T.F., Ransohoff, D.F., et,al. Multitarget Stool DNA Testing for Colorectal-Cancer Screening. N Engl J Med 2014; 370:1287-1297. April 3, 2014.
2. Exact Sciences Corporation, Madison, WI. www.exactsciences.com/

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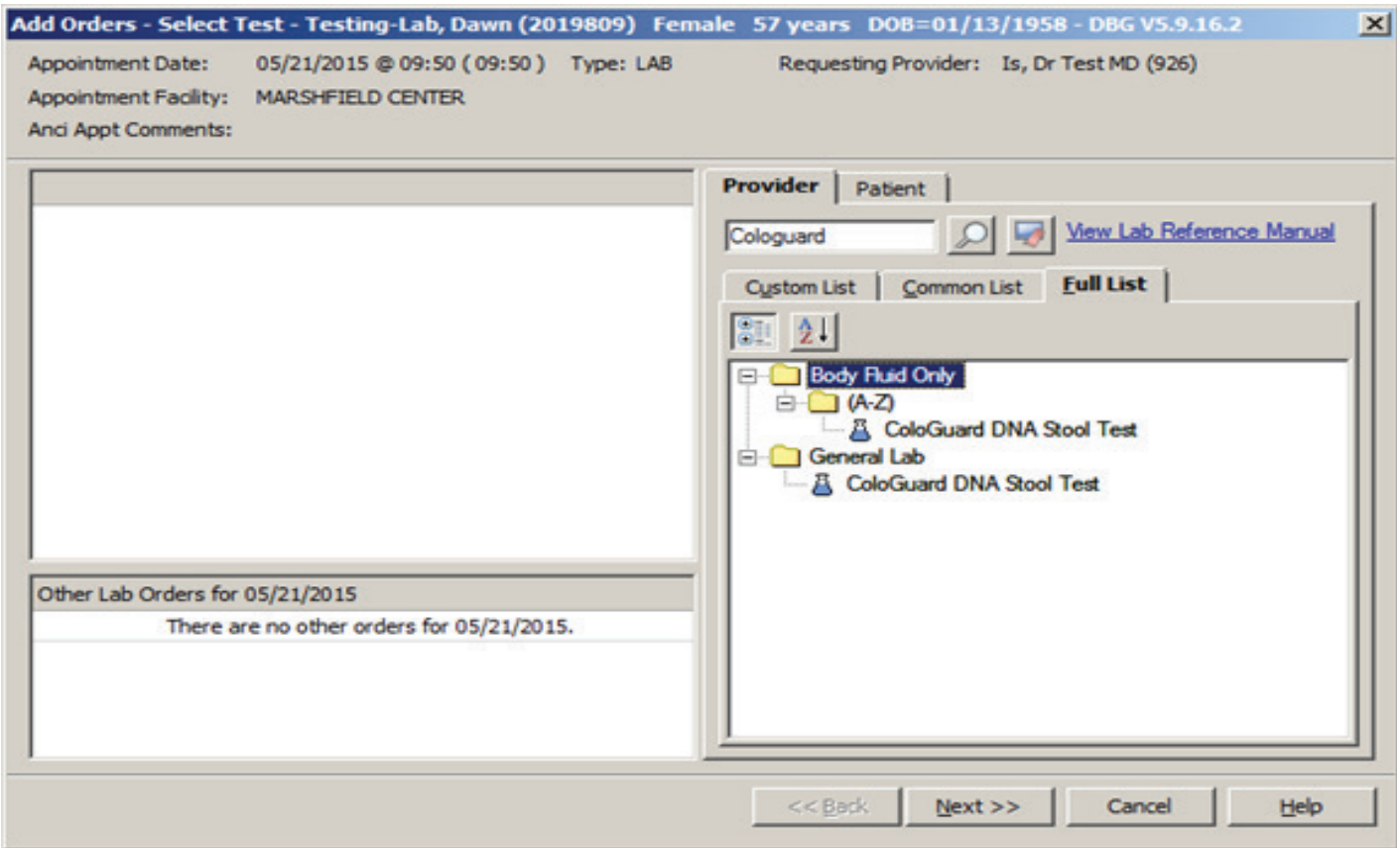
COLOGUARD DNA STOOL TEST: TEST INFORMATION; ORDERING AND VIEWING RESULTS

1. Cologuard is ordered in Clinical Order Manager (COM) as "***ColoGuard DNA Stool Test***".
    a. In COM in the "Full List" tab, the test will reside under both the "Body Fluid" and the "General Lab" folders.
    b. Providers can move the test to their custom lists if they so desire.



2. Marshfield Labs will receive the order and relay it to Exact Sciences.
3. Within a day or two of receiving the Cologuard order from Marshfield Labs, Exact Sciences will telephone the patient directly. The phone call will be for the purposes of:
    a. confirming an address for kit shipment to the patient
    b. discussing insurance coverage.
4. Exact Sciences will ship the collection kit directly to the patient's home.
5. The patient will collect a single stool sample using the kit according to instructions provided by Exact Sciences. A "How To Video" is provided on the Exact Sciences web site.
    a. There are no known dietary issues or restrictions that would interfere with an accurate Cologuard result.
    b. There is no need to stop any medications prior to collecting a sample for Cologuard.
6. The patient will return the sample kit directly to Exact Sciences via prepaid UPS shipping or pick-up. Shipping the sample within 24 hours of collection is recommended.

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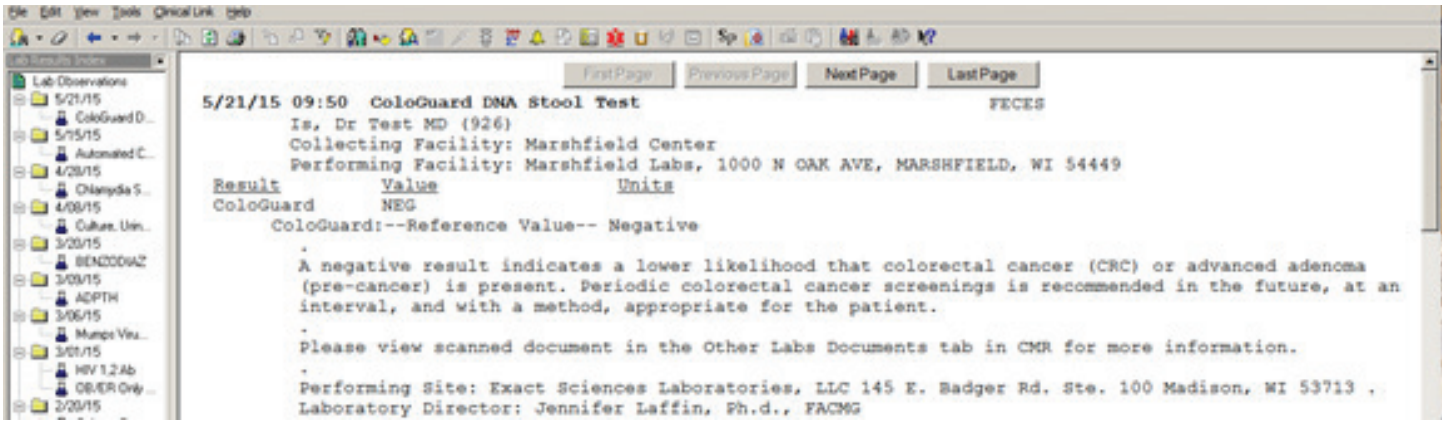
7. If no kit is received at Exact Sciences within 30 days of the order being placed, the test will be cancelled. Exact Sciences will contact the patient twice during this 30 day period to ask if they have questions or need any other information to help them in the specimen collection and shipping process.
8. Expected turnaround time for the assay is 2 weeks after receipt of the specimen at Exact Sciences.
9. Exact Sciences will send results to Marshfield Labs Customer Service who will enter the results in the Combined Medical Record (CMR).
10. Results may be viewed in CMR under "Lab by Date" or "Lab by Panel".

Lab by Date View:



Lab by Panel View