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## 1 Intended Use and Indications for Use

The Cologuard Plus™ test is a qualitative in vitro diagnostic test intended for the detection of colorectal neoplasia-associated DNA markers and for the presence of occult hemoglobin in human stool. The Cologuard Plus test is performed on samples collected using the Cologuard Plus Collection Kit. A positive result may indicate the presence of colorectal cancer (CRC) or advanced precancerous lesions (APL) and should

be followed by colonoscopy. The Cologuard Plus test is indicated to screen adults 45 years or older, who are at average risk for CRC. The Cologuard Plus test is not a replacement for diagnostic colonoscopy or surveillance colonoscopy in high-risk individuals.

The Cologuard Plus test is performed at Exact Sciences, Madison, WI.

## 2 Contraindications

The Cologuard Plus test is not indicated for use in patients that have the following:

- A personal history of colorectal cancer or advanced precancerous lesions.
- A positive result from another colorectal cancer screening method within the last 6 months, or:
  - 12 months for a fecal occult blood test (FOBT) or a fecal immunochemical test (FIT).
  - 36 months for a FIT-DNA test.
- A family history of CRC, defined as having a first-degree relative (parent, sibling, or child) with a CRC diagnosis at any age.
- Personal history of any of the following high-risk conditions for colorectal cancer:
  - A diagnosis of Inflammatory Bowel Disease (Chronic Ulcerative Colitis, Crohn’s Disease).
  - A diagnosis of a relevant familial (hereditary) cancer syndrome or other polyposis syndrome, including but not limited to: Familial adenomatous polyposis (FAP or Gardner’s), Hereditary non-polyposis colorectal cancer syndrome (HNPCC or Lynch), Peutz-Jeghers, MYH-Associated Polyposis (MAP), Turcot’s (or Crail’s), Cowden’s, Juvenile Polyposis, Cronkhite- Canada, Neurofibromatosis, or Serrated Polyposis.

## 3 Warnings and Precautions

- Patients should not provide a sample if they are experiencing diarrhea or have known blood in their urine or stool (e.g., from bleeding hemorrhoids,

bleeding cuts or wounds on their hands, rectal bleeding, or menstrual bleeding). Unexpected bleeding should be discussed with your healthcare provider.

- Reference national guidelines for the recommended screening ages for colorectal cancer. The decision to screen persons over the age of 75 should be made on an individualized basis in consultation with your healthcare provider. Cologuard Plus test results should be interpreted with caution in older patients as the rate of false positive results increases with age.
- The Cologuard Plus test may produce false negative or false positive results. A false positive result occurs when the Cologuard Plus test produces a positive result, even though a colonoscopy will not find CRC or APL. A false negative result occurs when the Cologuard Plus test does not detect an advanced precancerous lesion or colorectal cancer even when a colonoscopy identifies either of these findings.
- A negative Cologuard Plus test result does not guarantee the absence of cancer or advanced precancerous lesions. Patients with a negative Cologuard Plus test result should continue participating in colorectal screening programs at the appropriate guideline recommended levels.
- The performance of the Cologuard Plus test has been established in a cross-sectional study (i.e., single point in time). Programmatic performance of the Cologuard Plus test (i.e., benefits and risks with repeated testing over an established period of time) has not been studied. Non-inferiority or superiority of the Cologuard Plus test's programmatic sensitivity as compared to other recommended screening methods for CRC and APL has not been established.
- Patients should initiate the return process when they can get the Cologuard Plus Collection Kit back to UPS the same day they collect or the next day. Patients should refer to the shipping instructions provided in with the Cologuard Plus Collection Kit or ask their prescribers for more information.
- Patients should be advised of the caution listed in the Cologuard Plus Collection Kit instructions. Patients should NOT drink the preservative liquid.
- The risks related to using the Cologuard Plus Collection Kit are low, with no serious adverse events reported among people in a clinical trial. Patients should be careful when opening and closing the lids to avoid the risk of hand strain.

## 4 What is cancer screening?

Some types of cancer can be found before warning signs are present. Or they can be found when the disease is in an early stage of growth. Screening checks for cancer (or

for conditions that may lead to cancer) in people who have no warning signs. Screening can help doctors find and treat some types of cancer early. Generally, the earlier colon cancer is detected, the easier it is to treat.

Screening for colorectal cancer (CRC) or colon cancer is the first and most crucial step in finding and preventing colon cancer for adults who are at average risk for colon cancer.

## 5 Key facts about colon cancer

**Many people do not know that colon cancer can be avoided.**<sup>1</sup> It is the third most common cancer. It is the second leading cause of cancer deaths in both men and women in the US.<sup>2</sup> Despite these facts, colon cancer can be treated if it is found early through screening.<sup>1</sup> Yet, about 40% of adults ages 45-75 years are not getting screened.<sup>3</sup>

**Colorectal cancer can be found early, if you are looking for it.**<sup>1</sup> Colon cancer grows slowly. It generally starts from small polyps in the colon or rectum.<sup>1</sup> A polyp is a growth on the inside wall of your colon or rectum.<sup>1</sup> Polyps are found in adults younger than 45 and in older adults, too.<sup>4</sup> While polyps are common and do not usually cause symptoms, some are harmful and can turn into cancer over time.<sup>2</sup> If polyps are found and removed early, the chances of getting colon cancer can be lowered.<sup>5</sup> If colon cancer is found early through screening, treatment is most likely to be successful.<sup>1</sup>

## 6 Why should I get screened for colon cancer?

It is easier to treat colon cancer if it is found early. National guidelines recommend that screening starts at age 45.<sup>1</sup> There are different ways of screening for colon cancer. Choosing a colon cancer screening test isn't always an easy decision. It is important to talk to your healthcare provider about when to begin screening for colon cancer and how to choose among the different tests.

## 7 Choosing the best colon cancer screening test for you

Talk to your healthcare provider. They can help you choose a colon cancer screening test that is right for you. You have options. Here are some of the questions to ask:

- Is the test right for your age, medical history, family history, and general health?

- Can the test find both precancer and cancer?
- How is the test performed?
- Will you need to be sedated?
- How much time will the test take?
- Is the test easy to use?
- Are there any potential harms of the test?
- What care is needed after the test?

## **8 What is the Cologuard Plus test? Why is it different?**

- The Cologuard Plus test is an accurate noninvasive colon cancer screening test.
- It is for patients who are at average risk for colon cancer.
- Patients collect a sample at home.
- The Cologuard Plus test is the colon screening test that uses a stool DNA technology. It is effective in finding both precancer and cancer.

## **9 What is stool DNA technology?**

Every day, your colon sheds cells that line the colon. As part of this process, normal cells along with abnormal cells from precancer or cancers are shed into the colon. Your stool picks up those cells as it passes through your colon. The Cologuard Plus test is designed to detect the DNA and hemoglobin (blood) released from these abnormal cells in your stool.

## **10 The Cologuard Plus test is easy to use:**

Use the Cologuard Plus Collection Kit to collect a stool sample. The kit comes with easy-to-use instructions. You ship your sample back to Exact Sciences Laboratories. The laboratory tests your stool sample and sends the results back to your healthcare provider who prescribed your test. Your results will be shared with you.

You do not need to change your diet or medications to use this screening test.

## **11 Is the Cologuard Plus test accurate and effective in finding precancer and cancer?**

- The Cologuard Plus test finds 95% of colon cancers.
- The Cologuard Plus test is effective because it finds both precancer and cancer.
- In a large clinical study, the Cologuard Plus test found more cancers and precancers than an ordinary fecal blood test (FIT).

The Cologuard Plus test does produce some false positive results. Any positive result should be discussed

with your doctor and followed by a colonoscopy. In the clinical study of the Cologuard Plus test, the Cologuard Plus test detected 95% of colorectal cancers and 43% of precancers. An ordinary fecal blood test (FIT) detected 71% of cancers and 23% of precancers.

## **12 How do we know the Cologuard Plus test is effective?**

The effectiveness of the Cologuard Plus test was proven in a large clinical study. The trial included more than 18,000 patients at 186 sites in the U.S. Each person completed the Cologuard Plus test before having a standard colonoscopy. The main purpose of the study was to find out the performance of the Cologuard Plus test for finding cancer and precancer compared to a colonoscopy.

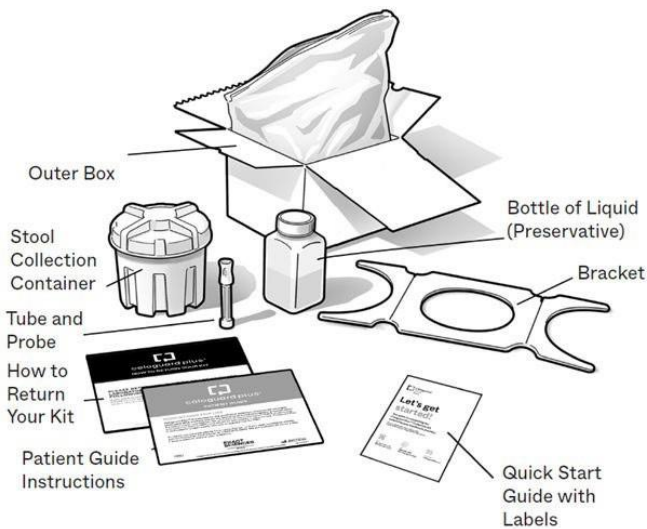
In the study, the Cologuard Plus test:

- Correctly detected 95% of colon cancers and 43% of advanced precancerous lesions in the patients in the study that had disease.
- Correctly gave a negative result for 91% of the study patients that did not have colon cancer or advanced precancer. This means 9% of people without colorectal cancer or advanced precancerous lesions tested positive.

## **13 I want to be screened for colorectal cancer. How do I get the Cologuard Plus test?**

The Cologuard Plus test is prescribed by your healthcare provider. It cannot be purchased over the counter. Once your healthcare provider prescribes the Cologuard Plus test, it is easy to collect a sample.

- A collection kit is sent directly to your preferred mailing address. You can store your kit until you are ready to use it. Store it at room temperature in a cool, dry place. Keep away from heat and direct sunlight and out of reach of children.
- Wait to collect your stool sample until you have no diarrhea. Also wait until you have no blood in your urine or stool (such as from hemorrhoids or menstruation). Contact your healthcare provider if you have unexpected bleeding.
- When you are ready, collect a sample in the privacy of your own home.
- After you collect a stool sample, you drop off the collection kit at any UPS store or call to schedule a pickup. Your sample will be sent directly back to Exact Sciences Laboratories. All postage is pre-paid.
- Exact Sciences Laboratories will test your stool sample and send the result to the provider who ordered your test.



- If you have any questions or concerns, call the Customer Care Center toll free at 1-844-870-8870. Representatives are available 24/7. Or chat with someone and find help at [www.cologuardplus.com](http://www.cologuardplus.com).

## 14 Understanding your results

Your healthcare provider will talk with you about your results. The test result can be **Positive**, **Negative** or **No Result Obtained**.

What does a **Positive** Result mean?

- A Positive Result means the test detected possible signs of precancer or colorectal cancer from your stool sample.
  - Out of 100 patients testing positive, approximately 3 patients will have CRC, 34 will have APL, 33 will have a non-advanced adenoma, and 30 will have no neoplastic findings.
- Talk to your healthcare provider about your test result. Any Positive Result should be followed by a colonoscopy.
- A colonoscopy is recommended to determine if cancer or precancer is present (True Positive) or not (False Positive).
- The test can also have a Positive Result that is incorrect (false positive). This means the test result is Positive, but no cancer or precancer is actually present. Talk about your test result with your doctor to find out if additional testing is needed.

What does a **Negative** Result mean?

- A Negative Result means the test did not detect signs of precancer or colorectal cancer from your stool sample.
  - Out of every 10,000 patients testing negative,

approximately 2 patients will be falsely reassured that they do not have CRC. Out of every 100 patients testing negative, approximately 7 patients will be falsely reassured that they do not have APL.

- The test can also have a Negative Result that is incorrect (False Negative). This means the test missed a potential cancer or precancer.
- Talk to your healthcare provider about your test result. They will recommend a screening schedule that is best for you.

What does **No Result Obtained** mean?

- A “No Result Obtained” means the test was not able to provide a result.
- If this happens, you may be asked to provide another stool sample to test.

## 15 The Cologuard Plus test may not be for everyone

Talk with your healthcare provider about using the Cologuard Plus test if any of the Contraindications apply to you.

## 16 What are the risks associated with using the Cologuard Plus test?

The risks related to using the Cologuard Plus Collection Kit are low. No serious adverse events were reported among 18,911 people in a clinical trial.

- Opening or closing the lids of items in the kit may be difficult for some people. Be careful when opening and closing the lids to avoid the risk of hand strain. Close all sample containers tightly.
- Using this kit requires sitting down on the toilet and standing up from the toilet. Have someone who can help you if needed.
- There is a chance that a stool sample sent to the lab may have no result. If this happens, you will be contacted. You may be asked to provide another sample.

## 17 Cologuard Plus test Precautions

- **Do not drink the bottle of preservative liquid.**
- **Do not let the liquid touch your skin or eyes.**
- If the liquid touches your skin or eyes, wash the area with water.

## 18 Who can I call if I have questions?

If you have questions, please call the Exact Sciences Laboratories Customer Care Center. You may also find helpful resources online (<http://www.cologuardplus.com>).

Phone Number: 1-844-870-8870

Hours of Operations: 24 hours a day, 7 days a week

## 19 References

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## 20 Trademarks and Copyright

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