| Patient | | Sample | | Physician | |
|---|---|---|---|---|---|
| Name | **Patient Doe** | Specimen Type | **Blood** | Ordering Physician | **Dr. Jane Smith** |
| Date of Birth (Age) | **09/02/1947 (78 yrs)** | Collection Date | **01/03/2026** | Medical Facility | **BillionToOne, Inc.** |
| Assigned Sex at Birth | **Female** | Receipt Date | **01/04/2026** | Address | **1035 O'Brien Drive Menlo Park, California 94025** |
| Diagnosis | **Colorectal Adenocarcinoma** | Accession ID | **TEST100100001-1** | Phone | **(833) 537-1819** |
| Medical Record # | **MRN12345** | Report Date | **01/10/2026** | Fax | **(833) 874-0918** |
| Internal Patient ID | **ID12345** | | | | |

# Northstar Pharmacogenomics (PGx) Results

## Tested Genes

### DPYD

Metabolizer status

**Normal**

Genotype

Allele 1: *1 (reference)

Allele 2: *1 (reference)

**No indication to change the dose of 5-fluorouracil or capecitabine.**

This patient is predicted to be a DPYD normal metabolizer, suggestive of typical DPD enzyme activity. Please refer to the drug label for recommended dosage and administration. This result does not rule out the possibility of additional rare variants that may impact the metabolism of 5-fluorouracil or 5-fluorouracil prodrug-based medications like capecitabine. Note that drug-drug interactions and other non-genetic factors may impact phenotype.

### UGT1A1

Metabolizer status

**Intermediate**

Genotype

Allele 1: *28

Allele 2: *1 (reference)

**Consider dose reduction before administering irinotecan-based therapies.**

This patient is predicted to be a UGT1A1 intermediate metabolizer, suggestive of mildly reduced UGT1A1 enzyme activity. Please refer to the drug label for recommended dosage and administration. This result does not rule out the possibility of additional rare variants that may impact the metabolism of irinotecan-based medications. Note that drug-drug interactions and other non-genetic factors may impact phenotype.

| | | | | | |
|---|---|---|---|---|---|
| Patient Name | **Patient Doe** | Date of Birth (Age) | **09/02/1947 (78 yrs)** | Assigned Sex at Birth | **Female** |
| Diagnosis | **Colorectal Adenocarcinoma** | Internal Patient ID | **ID12345** | Report Date | **01/10/2026** |

## Methods and Limitations

Northstar PGx™ is an in vitro diagnostic test utilizing next-generation sequencing (NGS) to detect substitutions (SNVs) and small insertions and deletions (indels) in the pharmacogenes DPYD and UGT1A1.

Northstar PGx is performed using cell-free DNA (cfDNA) extracted from patient plasma. The targeted regions are then amplified, sequenced, and aligned to the hg19 reference genome. The assay is validated to report the following SNVs and indels in DPYD (NM_000110): c.299_302del (*7), c.557A>G, c.703C>T (*8), c.868A>G, c.1129-5923C>G (HapB3), c.1314T>G, c.1475C>T, c.1679T>G (*13), c.1774C>T, c.1905+1G>A (*2A), c.2279C>T, c.2639G>T, and c.2846A>T and in UGT1A1 (NM_000463): (TA)5 (*36), (TA)7 (*28), (TA)8 (*37), and c.211G>A (*6). The absence of detected variants in a gene is reported as *1. Other findings involving these genes are outside the scope of the current test design and therefore will not be analyzed or included in this report.

Northstar PGx analytical sensitivity is 100% (95% CI: 93%–100.00%) for heterozygous and homozygous variant alleles, and accuracy is 100% (95% CI: 94.5%–100.00%) for detection of the SNVs and indels mentioned above. This assay is optimized for germline PGx variants detected in cfDNA, which typically occur at allele frequencies near 50% (heterozygous) or 100% (homozygous). Analytical sensitivity may be reduced by low cfDNA input, mixed chimerism, or significant chromosomal copy number abnormalities, including loss of heterozygosity (LOH), which can skew allele fractions away from expected germline distributions.

Northstar PGx is validated for the detection of presumed germline (inherited) pharmacogenomic variants, but cannot distinguish these from somatic (acquired) variants. Patients who have received frequent or recent blood transfusions may have donor-derived cfDNA that is unable to be separated from native patient cfDNA, which may complicate PGx metabolizer determination yielding a Not Determined result. Exercise caution prior to basing current therapy decisions on PGx results that were completed prior to organ transplant (especially liver transplant) or allogeneic stem cell transplant, as the donor-derived DNA may have a differing metabolizer status. Several pharmacogenomic genes are associated with clinical genetic conditions. This assay is not validated to provide information regarding these conditions or their diagnosis. Further germline testing may be warranted to identify and characterize variants that have hereditary implications. Metabolizer status is assigned based on the Clinical Pharmacogenetics Implementation Consortium (CPIC) variant activity scores in conjunction with supporting medical literature [1-6]. In the event that more than two variants are detected, the activity scores of the two most deleterious variants will be used to determine metabolizer status as recommended by CPIC [2].

Pharmacogenomic variants detected by this assay are reported for informational purposes and do not by themselves mandate a change in treatment, dose, or clinical management. PGx-guided treatment decisions require integration of multiple factors, including patient comorbidities, concomitant medications, organ function, treatment intent, and the therapeutic index of the drug being considered. The interpretation of PGx results should be made within the full clinical context.

Recommendations for drug selection and dosing may evolve as new evidence becomes available. Clinicians should consult professional practice guidelines, such as those published by CPIC (cpicpgx.org) as well as the FDA's drug safety-related labeling resource for the most current recommendations. These sources provide validated frameworks for interpreting PGx variants in relation to specific therapeutics. This laboratory does not independently determine or assign clinical dosing recommendations. Final prescribing decisions remain the responsibility of the treating provider.

## References

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This NGS-based assay was developed and its performance characteristics determined by BillionToOne, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration. BillionToOne, Inc. is regulated under CLIA. This test is used for clinical purposes. It should not be regarded as investigational or for research. This test was performed using BillionToOne's patented technology (www.billiontoone.com/patents).

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