Overview

Useful For
Identifying individuals with genetic variants in *DPYD* who are at increased risk of toxicity when prescribed 5-fluorouracil (5-FU) or capecitabine chemotherapy treatment

Genetics Test Information
This is a pharmacogenomics test associated with 5-fluorouracil and capecitabine drug sensitivity. Biallelic variation in the *DPYD* gene is also associated with dihydropyrimidine dehydrogenase (DPD) deficiency. (1) Individuals who have variations identified in the *DPYD* may benefit from genetic consultation.

Special Instructions
- Informed Consent for Genetic Testing
- Pharmacogenomic Associations Tables
- Multiple Genotype Test List
- Informed Consent for Genetic Testing (Spanish)

Method Name
Real-Time Polymerase Chain Reaction (PCR) with Allelic Discrimination Analysis

NY State Available
Yes

Specimen

Specimen Type
Varies

Advisory Information
This test does not detect or report variants other than the *2A, *7, *8, *9B, *10, *11, *13, rs67376798, rs75017182, and rs115232898 alleles. Sequencing of the full gene is also available for detection of additional variants as well as the alleles listed: order DPYDG / Dihydropyrimidine Dehydrogenase, *DPYD* Full Gene Sequencing, Varies.

Specimen Required
Multiple genotype tests can be performed on a single specimen after a single extraction. See Multiple Genotype Test List in Special Instructions for a list of tests that can be ordered together.

Submit only 1 of the following specimens:

Specimen Type: Whole blood

Container/Tube: Lavender top (EDTA)

Specimen Volume: 3 mL

Collection Instructions:
1. Invert several times to mix blood.
2. Send specimen in original tube.

**Specimen Stability Information:** Ambient (preferred) 9 days/Refrigerated 30 days

**Specimen Type:** Saliva

**Patient Preparation:** Patient should not eat, drink, smoke, or chew gum 30 minutes prior to collection.

**Supplies:** DNA Saliva Collection Kit (T786)

**Container/Tube:** Saliva Swab Collection Kit

**Specimen Volume:** 1 swab

**Collection Instructions:** Collect and send specimen per kit instructions.

**Specimen Stability Information:** Ambient 30 days

**Specimen Type:** DNA

**Container/Tube:** 2 mL screw top tube

**Specimen Volume:** 100 mcL (microliters)

**Collection Instructions:**
1. The preferred volume is 100 mcL at a concentration of 50 ng/mcL.
2. Include concentration and volume on tube.

**Specimen Stability Information:** Frozen (preferred)/Ambient/Refrigerated

**Forms**
1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:
   - Informed Consent for Genetic Testing (T576)
   - Informed Consent for Genetic Testing (Spanish) (T826)

2. If not ordering electronically, complete, print, and send a [Therapeutics Test Request](#) (T831) form with the specimen.

**Specimen Minimum Volume**

Blood: 0.4 mL
Saliva: 1 swab

**Reject Due To**

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.
5-Fluorouracil (5-FU) and its orally administered prodrug, capecitabine, are fluoropyrimidine-based chemotherapeutic agents that are widely used for the treatment of colorectal cancer and other solid tumors.

The dihydropyrimidine dehydrogenase (DPYD) gene encodes the rate-limiting enzyme for fluoropyrimidine catabolism and eliminates over 80% of administered 5-FU. Dihydropyrimidine dehydrogenase (DPYD) activity is subject to wide variability, mainly due to genetic variation. This results in a broad range of enzymatic deficiency from partial (3%-5% of population) to complete loss (0.2% of population) of enzyme activity. Patients who are deficient in DPYD are at an increased risk for side effects and toxicity when undergoing 5-FU treatment. In addition, pathogenic homozygous or compound heterozygous variants within DPYD are associated with dihydropyrimidine dehydrogenase (DPD) deficiency. DPD deficiency shows large phenotypic variability, ranging from no symptoms to a convulsive disorder with motor and mental retardation.

The following table displays the DPYD variants detected by this assay, the corresponding star allele, and the effect on DPYD enzyme activity. Other or novel variations, besides those listed here, may also impact fluoropyrimidine-related side effects and tumor response.

<table>
<thead>
<tr>
<th>DPYD Allele</th>
<th>cDNA Nucleotide Change</th>
<th>Effect on Enzyme Activity</th>
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<tbody>
<tr>
<td>*1</td>
<td>None (wild type)</td>
<td>Normal activity</td>
</tr>
<tr>
<td>*2A</td>
<td>1905+1G-&gt;A</td>
<td>No activity</td>
</tr>
<tr>
<td>*7</td>
<td>299_302delTCAT</td>
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</tr>
<tr>
<td>*8</td>
<td>703C-&gt;T</td>
<td>Probable reduced activity</td>
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<tr>
<td>*9B</td>
<td>2657G-&gt;A</td>
<td>Variant of unknown significance</td>
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<tr>
<td>*10</td>
<td>2983G-&gt;T</td>
<td>Probable reduced activity</td>
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<tr>
<td>*11</td>
<td>1003G-&gt;T</td>
<td>Probable reduced activity</td>
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<tr>
<td>*13</td>
<td>1679T-&gt;G</td>
<td>No activity</td>
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<tr>
<td>rs67376798</td>
<td>2846A-&gt;T</td>
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<tr>
<td>rs75017182</td>
<td>1129-5923C-&gt;G</td>
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<tr>
<td>rs115232898</td>
<td>557A-&gt;G</td>
<td>Probable reduced activity</td>
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</tbody>
</table>

Reference Values
An interpretive report will be provided.

Interpretation
Test Definition: DPYDV
DPYD Genotype

An interpretive report will be provided.

For additional information regarding pharmacogenomic genes and their associated drugs, see Pharmacogenomic Associations Tables in Special Instructions. This resource also includes information regarding enzyme inhibitors and inducers, as well as potential alternate drug choices.

Cautions

Rare genetic variants may be present that could lead to false-negative or false-positive results. Other variants in the primer binding regions can affect the testing, and ultimately, the genotype assessment made.

Samples may contain donor DNA if obtained from patients who received heterologous blood transfusions or allogeneic blood or marrow transplantation. Results from samples obtained under these circumstances may not accurately reflect the recipient's genotype. For individuals who have received blood transfusions, the genotype usually reverts to that of the recipient within 6 weeks. For individuals who have received allogeneic blood or marrow transplantation, a pretransplant DNA specimen is recommended for testing.

Dihydropyrimidine dehydrogenase (DPYD) genetic test results in patients who have undergone liver transplantation may not accurately reflect the patient's DPYD status.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Large deletions or rearrangements are not detected by this assay, and these may affect DPYD protein expression and their impact on fluoropyrimidine related side effects and tumor response.

This test is not designed to provide specific dosing or drug selection recommendations and is to be used as an aid to clinical decision making only. Drug-label guidance should be used when dosing patients with medications regardless of the predicted phenotype.

Clinical Reference


Performance

Method Description

Genomic DNA is extracted from whole blood or saliva. Genotyping for DPYD alleles is performed using a PCR-based 5'-nuclease assay. Fluorescently labeled detection probes anneal to the target DNA. PCR is used to amplify the section of DNA that contains the variant. If the detection probe is an exact match to the target DNA, the 5'-nuclease polymerase degrades the probe, the reporter dye is released from the effects of the quencher dye, and a fluorescent signal is detected. Genotypes are assigned based on the allele-specific fluorescent signals that are detected.

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday; 8 a.m.

Analytic Time
3 days (Not reported on Saturday or Sunday)

Maximum Laboratory Time
10 days

Specimen Retention Time
Whole blood/Saliva swab: 2 weeks; Extracted DNA: 2 months

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
81232

LOINC® Information

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Test Definition: DPYDV

DPYD Genotype