Pharmacogenomics Testing for Warfarin Metabolism

Disease Overview

The *CYP2C9* gene encodes an enzyme involved in the metabolism of warfarin. Genetic variations in *CYP2C9* alleles are associated with reduced enzyme activity that results in reduced clearance of warfarin. The *VKORC1* gene encodes vitamin K epoxide reductase, which is the target of warfarin. A common variant, -1639G>A, is associated with an increased sensitivity to warfarin. Patients who carry the -1639G>A polymorphism are more sensitive to warfarin and thus may require lower initiation doses. *CYP4F2* acts as an important counterpart to *VKORC1* to decrease accumulation of Vitamin K. *CYP2C cluster* (rs12777823) has a clinical relevant effect on warfarin dosing due to alterations in warfarin clearance. Patient specific maintenance doses will be determined based on PT/INR.

Uses for Test

- To estimate the genetic risk for abnormal sensitivity to warfarin.
- Identify genotypes shown to have a drug-gene variant relationship.
- Pharmacogenomic orders may be reviewed by a pharmacist for clinical appropriateness prior to test completion if clinical data is available.

Therapeutic Implications

CYP2C9, VKORC1, CYP2C cluster, and *CYP4F2* genotypes are the important genetic determinants of warfarin dosing. A patient's *CYP2C9, VKORC1, CYP2C cluster*, and *CYP4F2* genotype can be used to help determine a starting dose of warfarin.

Refer to the warfarin product insert approved by the United States Food and Drug Administration for recommended daily warfarin doses (mg/day) to achieve therapeutic INR based on *CYP2C9* and *VKORC1* genotyping.

Treatment Guidelines

The Clinical Pharmacogenetics Implementation Consortium (CPIC) has published dosing guidelines for warfarin and *CYP2C9, VKORC1, CYP2C cluster*, and *CYP4F2* genotypes: https://cpicpgx.org/

Results

A detailed report is provided. This report is reviewed and signed out by the Laboratory Director.
No mutations detected is predictive for *1 functional alleles.

Test Limitations

- Only the targeted *CYP2C9, CYP2C cluster, CYP4F2,* and *VKORC1* variants will be detected.
- Diagnostic errors can occur due to rare sequence variations.
- Risk of therapeutic failure or adverse reactions with *CYP2C9* substrates may be affected by genetic and non-genetic factors that are not detected by this test.
- This result does not replace the need for therapeutic drug or clinical evaluation and monitoring.

Related Tests

- Multiple genes can be involved in drug metabolism, drug activation and drug action on the target tissue. Additional genotyping tests are available for *CYP2D6, CYP2C19, SLCO1B1, TPMT, CYP3A5, IFNL3,* and *DPYD* as individual tests or as a PGx Panel.
- The panel includes a comprehensive medication report based on the genotypes detected.
- Therapeutic drug monitoring and/or metabolic ratios may be useful for evaluating the pharmacokinetics of a particular drug, for a particular patient.

Sample Requirements

Collection

- Lavender-top tube (EDTA)
- All specimens should be sent in the original container and should not be aliquoted to another tube
- The specimen submitted should only be used for this testing and should not be shared with any other testing that would also utilize this specimen type

Specimen

- Whole Blood, preferred Volume: 2 mL to 4 mL (1mL minimum)

Stability

- Room temp – 72 hours
- Refrigerated – 7 days
- Frozen – 7 days
- Not affected by hemolysis
- Not affected by lipemia

Tests Involved

- CPT code: 81227, 81479, and 81355
- Lab Test ID: LBOR0204

Test Schedule

- Set up Monday to Friday
- Turn Around Time: 5-7 days

Additional information

- These tests are available through the Sanford Imagenetics program. Contact Sanford Laboratories at (605) 328-5464 or (800) 522-2561 for questions regarding this testing.

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References

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