HOTLINE: Effective February 22, 2022

3001541 Warfarin Sensitivity (*CYP2C9, CYP2C* cluster, *CYP4F2, VKORC1*) Genotyping WARF PAN

Interpretive Data:

Background Information for Warfarin Sensitivity (*CYP2C9, CYP2C* cluster, *CYP4F2, VKORC1*) Genotyping:
Characteristics: Warfarin sensitivity can lead to a life-threatening overdose event such as excessive bleeding. Genetic variation is recognized to explain a large proportion of variability in warfarin dose requirements. This test may predict individual warfarin sensitivity and non-standard dose requirements. The cytochrome P450 (CYP) isozyme 2C9 is involved in the metabolism of many drugs. Variants in the gene that codes CYP2C9 may influence pharmacokinetics of substrates such as warfarin, and may predict or explain nonstandard dose requirements, therapeutic failure, or adverse reactions. Variants in the *VKORC1* and *CYP4F2* genes may predict sensitivity to warfarin. The *CYP2C* cluster variant, rs12777823, common in people of African descent, with a minor allele frequency of approximately25 percent, is found to be associated with warfarin dose in this population. Genetic information and nongenetic factors can be used in combination with warfarin dose calculators, such as through www.WarfarinDosing.org.
Inheritance: Autosomal codominant.
Cause: *CYP2C9* and *CYP2C* cluster variants are associated with reduced dose requirements. The *VKORC1*2* allele is associated with reduced expression of the warfarin target, vitamin K epoxide reductase (VKOR), and a reduced dose requirement. The *CYP4F2* variant is associated with an increased dose requirement.
Variants Tested: See the "Additional Technical Information" document.
Clinical Sensitivity: Genetic factors and known non-genetic factors account for approximately 50 percent of the variability in warfarin dose.
Methodology: Polymerase chain reaction (PCR) and fluorescence monitoring.
Analytical Sensitivity and Specificity: Greater than 99 percent.
Limitations: Only the targeted *CYP2C9, CYP2C* cluster, *CYP4F2*, and *VKORC1* variants will be detected by this panel, and assumptions about phase and content are made to assign alleles. Publicly available sources such as the www.pharmvar.org or www.pharmgkb.org provide guidance on phenotype predictions and allele frequencies. 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 nongenetic factors that are not detected by this test. This result does not replace the need for therapeutic drug or clinical monitoring.

Please note the information contained in this report does not contain medication recommendations, and should not be interpreted as recommending any specific medications. Any dosage adjustments or other changes to medications should be evaluated in consultation with a medical provider.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.

HOTLINE NOTE: There is a component change associated with this test.
Add component 2008931, CYP2C9 Phenotype
Add component 3004499, CYP2C Cluster Geno
Add component 3004500, CYP2C Cluster Pheno
Add component 3004506, CYP4F2 Phenotype
Add component 3004507, VKORC1 Phenotype
Remove component 3001503, CYP2C8 Genotype