HOTLINE: Effective May 20, 2019

New Test **3001541** **Warfarin Sensitivity (*CYP2C8, CYP2C9, CYP4F2, VKORC1*) Genotyping** **WARF PAN**

Additional Technical Information

Out of Pocket Estimator

Supplemental Resources

Methodology: Polymerase Chain Reaction/Fluorescence Monitoring
Performed: Varies
Reported: 5-10 days

Specimen Required: Collect: **Whole Blood:** Lavender (EDTA), Pink (K_2EDTA), or Yellow (ACD Solution A or B).
Saliva: Collection Device by DNA Genotek (OCD-100, ARUP Supply #49295) available online through eSupply using ARUP Connect™ or by contacting ARUP Client Services at (800) 522-2787.
Specimen Preparation: Transport 3 mL whole blood. (Min: 1 mL) OR Transport the Saliva Collection Device.
Storage/Transport Temperature: **Whole Blood:** Refrigerated.
Saliva: Room temperature.
Unacceptable Conditions: Plasma or serum. Specimens collected in sodium heparin or lithium heparin.
Stability (collection to initiation of testing): **Whole Blood:** Ambient: 72 hours; Refrigerated: 1 week; Frozen: 1 month
Saliva: Ambient: 2 weeks; Refrigerated: Unacceptable; Frozen: Unacceptable

Reference Interval: By report

Interpretive Data:
Background Information for Warfarin Sensitivity (CYP2C8, CYP2C9, 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) isozymes 2C8 and 2C9 are involved in the metabolism of many drugs. Variants in the genes that code for CYP2C8 and CYP2C9 may influence pharmacokinetics of substrates such as warfarin, and may predict or explain non-standard dose requirements, therapeutic failure or adverse reactions. Variants in the *VKORC1* and *CYP4F2* genes may predict sensitivity to warfarin. Genetic information and non-genetic factors can be used in combination with warfarin dose calculators, such as through www.WarfarinDosing.org.
Inheritance: Autosomal co-dominant**.**
Cause: *CYP2C8*, *CYP2C9* and *CYP4F2* gene variants affect enzyme expression or activity. The *VKORC1*2* allele is associated with reduced expression of the warfarin target, vitamin K epoxide reductase (VKOR), and a reduced dose requirement.
Variants Tested: See the "Additional Technical Information" document.
Clinical Sensitivity: Genetic factors and known non-genetic factors account for ~50% 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 *CYP2C8, CYP2C9, CYP4F2* and *VKORC1* variants will be detected by this panel, and assumptions about phase and content are made to assign alleles. Publically 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 CYP2C8 or 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 monitoring.

See Compliance Statement C: www.aruplab.com/CS

Note: Whole blood is the preferred specimen. Saliva samples that yield inadequate DNA quality and/or quantity will be reported as inconclusive if test performance does not meet laboratory-determined criteria for reporting.

CPT Code(s): 81227; 81355

New York DOH approval pending. Call for status update.

HOTLINE NOTE: Refer to the Test Mix Addendum for interface build information.