

## Warfarin Sensitivity Test (P450 2C9 and VKORC1)

### DESCRIPTION:

- Warfarin, the coumarin derivative, is the most widely prescribed anticoagulant for thromboembolic disorders. This test detects variants within two genes, CYP2C9 and VKORC1, that impact the rate of warfarin metabolism. VKORC1 (vitamin K epoxide reductase complex sub unit 1) and cytochrome P450 CYP2C9 account for up to 50% of the interindividual variability of the warfarin response. These genetic markers may serve as clinically-relevant predictors of warfarin dosing.
- The presence of the heterozygous missense mutation (-1639 G>A) in the VKORC1 gene can result in warfarin resistance. The homozygous or compound heterozygous missense mutations in the VKORC1 gene leads to combined deficiency of vitamin K-dependent coagulation factor type 2 (VKCFD2). The risk of bleeding complication during oral anticoagulation is high. Low dosage warfarin treatment should be considered.
- The presence of the \*2 and/or \*3 alleles in the CYP2C9 gene can result in poor metabolizer (PM) phenotypes. The PM phenotype is associated with lack of enzyme activity and the drug may be metabolized slowly or not at all. This results in increased concentrations of the drug with a reduced or absent therapeutic response and the potential for serious side effects. A lower maintenance dose may be required. Co-administration of inhibitors of CYP2C9, such as phenylbutazone, sulfinpyrazone, amiodarone, miconazole, isoniazid, ticlopidine, tamoxifen, and fluconazole will increase the anticoagulation effect. The azole antifungal agent fluconazole (Diflucan®) is a potent inhibitor of CYP2C9. Rifampin, barbiturates, carbamazepine, and St. John's wort will increase warfarin metabolism and increase the chance of reduced efficacy, and the warfarin dose may need to be increased.

### REASONS FOR REFERRAL:

- Warfarin Sensitivity Genotyping; Drug Metabolizing Enzyme (DME) Genotyping

### METHOD OF ANALYSIS:

- Luminex Molecular Diagnostics Tag-It Mutation Detection Kit for CYP2C9+VKORC1 analyzed on Luminex microbead detection platform.
- The metabolism of drugs is also influenced by ethnicity, diet, and other medications. All factors should be considered prior to initiating new therapy. Diagnostic testing is limited to the number of CYP2C9 and VKORC1 genetic variations that can be identified using this methodology.

### SAMPLE REQUIREMENTS:

- 5-7 mL whole blood collected in a lavender-top (EDTA) or gold-top (ACD) Vacutainer
- Maintain specimens at room temperature or refrigerate.

### TEST CPT CODES:

- CPT 83891 Isolation
- CPT 83892 Enzymatic digestion
- CPT83900 Amplification of patient nucleic acid, multiplex, first two nucleic acid sequences, each
- CPT83901 Amplification of patient nucleic acid, multiplex, each additional
- CPT 83914 Mutation ID enzymatic ligation or primer extension single segment, each segment
- CPT 83909 Separation and identification by high resolution technique
- CPT83912 Interpretation and report

*Discounts from list price are available for institutional billing under contractual arrangement with the laboratory. Contact Ellen Livers at 800-447-6614 ext 7523.*