## Ordered Items
Cytochrome P450 2C9 Genotyping

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### CYP2C9 Genotype: *1/*1

The genotype listed above is associated with a normal CYP2C9 enzymatic activity. Individuals with this genotype are anticipated to have an expected response to a standard CYP2C9 target drug dose. All results must be interpreted in the context of other test results, co-administration of other drugs, and clinical findings. This does not rule out the possibility of other variant alleles in CYP2C9 or other drug metabolism pathways.

Cytochrome P450 2C9 is involved in the metabolism of clinically important drugs such as warfarin, phenytoin, celecoxib, ibuprofen, losartan, tolbutamide, glipizide, and diclofenac. The metabolism of drugs is also influenced by race, ethnicity, diet and other medications and all factors should be considered prior to initiating new therapy.

### Comment:
Warfarin metabolism:
Reduced by 30-50% by *2 and 90% by *3. This effect may be more pronounced in Asians as compared to Caucasians. Individuals with at least one copy of *2 or *3 have an increased risk of bleeding compared to individuals without *2 or *3. A lower maintenance dose may be required. Co-administration of inhibitors of CYP2C9 such as phenylbutazone, sulfipyrazone, amiodarone, miconazole, ticlopidine, tamoxifen and fluconazole will increase the anticoagulation effect. Theazole antifungal agent fluconazole (Diflucan) is a potent inhibitor of CYP2C9. Fluconazole, at conventional doses, abolishes CYP2C9 activity. Rifampin, barbituates, 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.

Phenytoin:
Decreased phenytoin clearance is noted in individuals with either *2 or *3, and individuals that are homozygous or compound heterozygotes for *2 and *3 may benefit from starting at a lower dose than standard. CYP2C9 inhibitors can increase serum levels of phenytoin.

Anti-diabetic drugs:
Glipizide, glyburide, glimepiride, tolbutamide
Clearance in *3 individuals is reduced by 50-80%. Studies in
normal volunteers suggest that *2 or *3 genotypes may not have
any impact on glucose regulation, but some data suggests that
PM individuals may be at higher risk for hypoglycemia. Inhibitors
of CYP2C9 may increase the risk of hypoglycemia. Preliminary data
of hospitalized patients with severe hypoglycemia found a higher
percentage of individuals with *3 than expected.
NSAIDS (non-steroidal anti-inflammatory drugs)
Aceclofenac, acetylsalicylic acid, apazone, celecoxib, diclofenac,
flubiprofen, ibuprofen, indomethacin, lornoxicam, mefenamic acid,
meloxicam, maprozin, phenylbutazone, piroxicam, suprofen, and
tenoxicam
A study in Caucasian individuals has shown that individuals with
*2 alleles (either heterozygous or homozygous) are at higher risk
for gastric bleeding complications after NSAID use. Further research
is ongoing.
Methodology:
DNA analysis is performed by allele-specific Real-time polymerase
chain reaction (PCR) to detect the *2 and *3 alleles in the CYP2C9
gene. No other variants in this gene are detected by this assay.
Molecular-based testing is highly accurate, but as in any laboratory
test, rare diagnostic errors may occur.
This test was developed and its performance characteristics
determined by LabCorp. It has not been cleared or approved by the
Food and Drug Administration.
References:
References available upon request.
Director Review: 
Hongli Zhan, PhD
Director, Molecular Genetics

For inquiries, the physician may contact Branch: 800-222-7566 Lab: 800-735-4087
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The genotype listed above is associated with significantly reduced CYP2C9 enzymatic activity. Individuals with this genotype are likely to metabolize target drugs slowly, resulting in an increased plasma concentration of the drug or reduced prodrug activation into a pharmacologically active agent. Individuals with CYP2C9 *3/*3 may experience a reduced therapeutic response and may be at increased risk for serious side effects. The exact effect of this particular genotype on individual drugs can vary (see below). About 20% of the Caucasian population have at least one *2 or *3 variant. These variants are rare in African and Asian populations.

Cytochrome P450 CYP2C9 is involved in the metabolism of several clinically important drugs. The metabolism of drugs is also influenced by race, ethnicity, diet and other medications and all factors should be considered prior to initiating new therapy. All results must be interpreted in the context of other test results and clinical findings. This does not rule out the possibility of variant alleles in other drug metabolism pathways.

**Comment:** 01

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01

LabCorp RTP
1912 TW Alexander Drive, RTP, NC 27709-0150

Dir: Arundhati Chatterjee, MD

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