Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	Unknown
Gender:	Male
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Warfarin Sensitivity (CYP2C9, CYP2C cluster, CYP4F2, VKORC1) Genotyping

ARUP test code 3001541

WARF PAN Specimen	Whole Blood	
CYP2C9 Genotype	*1/*3	
CYP2C9 Phenotype	Intermediate	*
CYP2C Cluster Geno	Heterozygous	*
CYP2C Cluster Pheno	See Note	*
CYP4F2 Genotype	*1/*3	*
CYP4F2 Phenotype	See Note	
VKORC1 Genotype	*1/*2	*
VKORC1 Phenotype	See Note	*
WARF PAN Interpretation	See Note	

H=High, L=Low, *=Abnormal, C=Critical

The following CYP2C9 allele(s) were detected: *1/*3. This result predicts the intermediate metabolizer phenotype, with an activity score of 1 of 2.

One copy of the 2C cluster rs12777823 was detected. This variant is associated with reduced warfarin dose requirement in some individuals of African ancestry.

CYP4F2 is associated with vitamin K recycling. Presence of the *3 allele could be associated with a modest increased warfarin dose requirement in some populations, such as Whites and Asians, but not in other populations such as African Americans or Egyptians.

VKORC1 is the therapeutic target for warfarin. The *2 allele is associated with decreased gene expression and increased warfarin sensitivity (reduced dose requirement). The effect on warfarin sensitivity and dose requirement is more significant for homozygotes than for heterozygotes.

Gene-based dosing calculators such as www.WarfarinDosing.org are available. Guidelines for genotype-based dosing are published by the Clinical Pharmacogenetics Implementation Consortium (CPIC) and can be found at: https://cpicpgx.org/ and https://www.pharmgkb.org/.

This result has been reviewed and approved by [redacted]

BACKGROUND INFORMATION: 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 non-standard 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 approximately 25 percent, is found to be associated with warfarin dose in this population. Genetic information and non-genetic 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:
(Variants are numbered according to the following transcripts: CYP2C9 NM_000771, 2C cluster rs12777823, CYP4F2 NM_001082 and VKORC1 NM_024006).

*1: Indicative of no detected targeted variants and an assumption of functional allele.

CYP2C9*2: rs1799853, c.430C>T
CYP2C9*3: rs1057910, c.1075A>C
CYP2C9*4: rs56165452, c.1076T>C
CYP2C9*5: rs28371686, c.1080C>G
CYP2C9*6: rs9332131, c.818del
CYP2C9*8: rs7900194, c.449G>A
CYP2C9*11: rs28371685, c.1003C>T
CYP2C9*12: rs9332239, c.1465C>T

CYP2C rs12777823, g.96405502 G>A

CYP4F2*3: rs2108622, c.1297g>a

VKORC1*2: rs9923231, c.-1639G>A

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 non-genetic 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.

EER Warfarin Sensitivity Genotyping

See Note

Authorized individuals can access the ARUP Enhanced Report using the following link:

[redacted]

H=High, L=Low, *=Abnormal, C=Critical

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
WARF PAN Specimen	23-316-101143	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
CYP2C9 Genotype	23-316-101143	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
CYP2C9 Phenotype	23-316-101143	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
CYP2C Cluster Geno	23-316-101143	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
CYP2C Cluster Pheno	23-316-101143	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
CYP4F2 Genotype	23-316-101143	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
CYP4F2 Phenotype	23-316-101143	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
VKORC1 Genotype	23-316-101143	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
VKORC1 Phenotype	23-316-101143	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
WARF PAN Interpretation	23-316-101143	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
EER Warfarin Sensitivity Genotyping	23-316-101143	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

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