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Gene test information

PHARMACOGENETICS OF COUMARINS (VKORC1 AND CYP2C9 GENE TESTS)

- **Background**

  Coumarins, such as warfarin and phenprocoumon, are vitamin K agonists that have been widely used as orally administered anticoagulants for therapy and prophylaxis of thromboembolic conditions. Due to its narrow effective therapeutic concentration ranges and broad variation in required individual dosage, clinical management of coumarin therapy may be demanding.

  Vitamin K epoxide reductase (VKORC1), the main target of coumarins, carries a common G/A polymorphism which plays an important role in coumarin dose. Additionally, cytochrome CYP2C9 is essential for the metabolism of coumarins. Defective CYP2C9 gene variants (*2, *3) lead to reduced enzymatic degradation of coumarins, resulting in lower coumarin dosages and an increased tendency to severe overanticoagulation and retarded stabilization.

- **VKORC1 genotypes**

Genotype	Frequency	Commentary
VKORC1 -1639 GG	38%	Lower coumarin sensitivity (higher dosage of coumarin may be required)
VKORC1 -1639 GA	43%	Normal coumarin sensitivity
VKORC1 -1639 AA	19%	Higher coumarin sensitivity (lower dosage of coumarins may be required)

- **CYP2C9 genotypes**

Genotype	Frequency	Commentary
CYP2C9 *1*1	67%	Wild-type genotype
CYP2C9 *1*2 or *1*3 (heterozygous deficiency)	29%	Heterozygous CYP2C9 deficiency (Lower dosage of coumarins may be required, increased risk for over-anticoagulation)
CYP2C9 *2*2, *2*3, *3*3 (homozygous deficiency)	4%	Homozygous CYP2C9 deficiency (Lower dosage of coumarins may be required, increased risk for over-anticoagulation)

- **Indications for testing**

  - Individuals starting coumarin therapy
  - Individuals receiving coumarin therapy, without achieving an acceptable stable international normalized ratio (INR).

References:

Oldenburg J et al. Current pharmacogenetic developments in oral anticoagulation therapy: The influence of variant VKORC1 and CYP2C9 alleles. Thromb Haemost. 2007;98:570-578.

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