



## Pharmacogenomic Testing to Aid Warfarin Dosing

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WARFARIN THERAPY CAN BE DIFFICULT TO MANAGE BECAUSE OF THE DRUG'S NARROW THERAPEUTIC INDEX AND THE WIDE INTERINDIVIDUAL VARIABILITY IN PATIENT RESPONSE.

It is now clear that much of this variability is largely genetically determined.

Two common single nucleotide polymorphisms (SNPs) in the cytochrome P450 (CYP) 2C9 system (CYP2C9\*2 and CYP2C9\*3) are associated with impaired metabolism of Warfarin, while SNPs in the gene for Vitamin K Epoxide Reductase Complex 1 (VKORC1) correlate with Warfarin sensitivity and resistance.

By combining patient clinical characteristics with knowledge of CYP2C9 and VKORC1 genotypes, as much as 60% of the variability in Warfarin dose requirements can be explained.

Genotyping patients prior to, or shortly after, starting Warfarin could improve achievement of a stable INR and potentially reduce the rate of early bleeding.

### ADVANTAGES OF GENOTYPING IN PREDICTING WARFARIN MAINTENANCE DOSES

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- By establishing the genotype of CYP2C9 and VKORC1, a clinician can now more accurately determine the Warfarin induction and maintenance dosage, thereby minimising possible adverse reactions such as excessive bleeding or harmful clot formation.
- By using genotyping information a patient's Warfarin therapeutic steady state level is reached more quickly thereby reducing the period of trial and error.
- Adjustment of induction and maintenance Warfarin doses based on CYP2C9 and VKORC1 genotype can be determined by genetic pre-induction and up to four days post induction (as S-Warfarin plasma concentrations are subtherapeutic for at least three days). As such, standard induction regimes do not need to be postponed until the genetic test results are available. Simply send a sample for gene testing at, or prior to, commencement of treatment. Test results can then be applied to select maintenance dose on or shortly after days four or five.

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## SPECIMEN REQUIREMENTS

**Test Name:** Warfarin PredictAR

**Sample Required:** 4mL EDTA whole blood (Two buccal swabs are also accepted)

**Frequency:** Daily (Mon-Fri)

Please note that these tests are not Medicare rebated.

## [www.warfarindosing.org](http://www.warfarindosing.org)

This is a free website to help clinicians begin Warfarin therapy by estimating the therapeutic dose in patients new to Warfarin. Estimates are based on clinical factors and genotypes of CYP2C9 and VKORC1.

Recommendations on the website are based on data from over 1000 patients. Ultimately, this website allows clinicians to incorporate pharmacogenetics into their dosing plans.<sup>2</sup>

## REFERENCES

1. Wadelius M, Chen LY, Downes K, et al. Pharmacogenomics J. 2005; 5: 262-270
2. Millican E, Lenzini P.A., Milligan P.E. et al. Blood. 2007; 110(5): 1511-1515
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6. Peyvandi et al. Clin Pharm Ther. 2004; 75: 198 - 203
7. Aquilante et al. Clin Pharm Ther. 2006; 79: 291 - 302

All pharmacogenetic test results are interpreted and reported by clinical geneticists at GenesFX Health. The GenesFX Health scientific advisory board comprises clinicians, geneticists, pharmacists and clinical pharmacologists.

More information can be found at [www.genesfx.com.au](http://www.genesfx.com.au)

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