Warfarin

Class: Anticoagulant, Coumarin Derivative

Pharmacokinetics

Absorption

i.)	Non-genetic
	a. Manufacturer: possible variability in bioavailability
	b. Concomitant medication: cholestyramine, colestipol, aluminum hydroxide decrease
	absorption
ii.)	Genetic
	a. No clear genetic factors affecting absorption
Distribution	
i.)	Non-genetic
	a. Altered serum protein (99% bound to albumin and alpha-1 acid glycoprotein)
1	b. Concomitant medication: highly protein-bound drugs can displace warfarin from plasma
	protein binding sites; warfarin can displace other drugs from protein binding sites
ii.)	Genetic
	a. No clear genetic factors affecting distribution
<u>Metabolism</u>	
i.)	Non-genetic
	a. Concomitant medications/substances: Cytochromes P450 (CYPs) 2C9 , 1A2, 2C19, 3A4 inducers or inhibitors
	b. Ethanol: acute ingestion decreases metabolism; chronic daily use increases metabolism
	c. Thyroid disease: may alter metabolism (increased effect in hyperthyroidism)
ii.)	Genetic
	a. Genetic variation in drug metabolizing enzyme gene: CYP2C9 , CYP1A2, CYP2C19, CYP3A4
Excretion	
i.)	Non-genetic
,	a. Hemodialysis: significantly decreased half-life
	b. Age: slight decrease in clearance in elderly
ii.)	Genetic
	a. No clear genetic factors affecting excretion
Pharmacodynan	nics
Receptors	
- i.)	Non-genetic
	a. No clear non-genetic factors affecting receptors

- ii.) Genetic
 - a. No clear genetic factors affecting receptors

Transporters

- i.) Non-genetic
 - a. No clear non-genetic factors affecting transporters
- ii.) Genetic
 - a. No clear genetic factors affecting transporters

Other proteins involved in drug action

- i.) Non-genetic
 - a. A diet high in vitamin K may decrease anticoagulant effect
- ii.) Genetic
 - a. Genetic variation vitamin K epoxide reductase complex subunit-1 gene: VKORC1
 - b. Genetic variation in gamma-glutamyl carboxylase gene: GGCX