Icahn School of Medicine at Mount Sinai | *Charles Bronfman Institute for Personalized Medicine*

Transitional Initiatives in Pharmacogenomics

Provider Summary for Clopidogrel and *CYP2C19*

Drug Name: Plavix® (clopidogrel bisulfate)

Indication:
Reduction of atherosclerotic events (myocardial infarction, stroke, and vascular death) in patients with atherosclerosis documented by recent stroke, recent myocardial infarction, or established peripheral arterial disease

Drug – Gene interaction:
Clopidogrel is a pro-drug that requires bioactivation into its active metabolite. The main enzyme responsible for its activation is CYP2C19. Loss-of-function polymorphisms in the CYP2C19 gene result in reduced plasma levels of the active metabolite; reduced platelet inhibition; increased residual platelet aggregation, and increased risks for adverse cardiovascular events.

Phenotypes Implicated	**Genotypes**	**Associated Risks**	**Recommendations**
Intermediate metabolizers (~18 – 45% of patients)	Carrier of one loss-of-function allele (*2 - *8) and one functional or increased activity allele (*1, *17) Example: *1/*2, *1/*3, *2/*17	Reduced platelet inhibition; increased residual platelet aggregation; increased risk for adverse cardiovascular events	If patient has undergone or will be undergoing PCI, choose an alternative antiplatelet agent (if no contraindication) e.g., prasugrel or ticagrelor
Poor metabolizers (~2 – 15% of patients)	Carrier of two loss-of-function alleles (*2 - *8). Example: *2/*2, *2/*3, *3/*3.	Significantly reduced platelet inhibition; increased residual platelet aggregation; increased risk for adverse cardiovascular events	If patient has undergone or will be undergoing PCI, choose an alternative antiplatelet agent (if no contraindication) e.g., prasugrel or ticagrelor

References:
CPIC peer-reviewed guideline for Clopidogrel (PMID: 23698643)
Clopidogrel - https://www.pharmgkb.org/chemical/PA449053

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