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Clopidogrel Therapy and *CYP2C19* Genotype

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Introduction

Clopidogrel (brand name Plavix) is an antiplatelet agent. Clopidogrel reduces the risk of myocardial infarction (MI) and stroke in patients with acute coronary syndrome (ACS), and in patients with atherosclerotic vascular disease (indicated by a recent MI or stroke, or established peripheral arterial disease) (1). Clopidogrel is also indicated in combination with aspirin in patients undergoing percutaneous coronary interventions (PCI), e.g., the placement of a stent.

The effectiveness of clopidogrel depends on its conversion to an active metabolite by CY2C19. Individuals who carry 2 non-functional copies of the *CYP2C19* gene are classified as CYP2C19 poor metabolizers. They have no enzyme activity and cannot activate clopidogrel via the CYP2C19 pathway, which means the drug will have no effect. Approximately 2% of Caucasians, 4% of African Americans, and 14% of Chinese are CYP2C19 poor metabolizers.

The 2017 FDA-approved drug label for clopidogrel includes a boxed warning concerning the diminished antiplatelet effect of clopidogrel in CYP2C19 poor metabolizers (Table 1). The warning states that tests are available to identify patients who are CYP2C19 poor metabolizers, and to consider the use of another platelet P2Y12 inhibitor in patients identified as CYP2C19 poor metabolizers.

The effectiveness of clopidogrel is also reduced in individuals who are CYP2C19 intermediate metabolizers. These individuals carry one non-functional copy of *CYP2C19*, with either one normal function copy or one increased function copy. For patients with ACS who are undergoing PCI, the 2013 Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for clopidogrel recommends an alternative antiplatelet therapy (e.g., prasugrel, ticagrelor) for CYP2C19 poor or intermediate metabolizers, if there is no contraindication (Table 2) (2).

The Dutch Pharmacogenetics Working Group (DPWG) of the Royal Dutch Association for the Advancement of Pharmacy (KNMP) have also made antiplatelet therapy recommendations based on *CYP2C19* genotype. For patients with ACS who receive PCI, they recommend an alternative drug to clopidogrel in poor metabolizers, and for intermediate metabolizers, they recommend choosing an alternative drug, or doubling the dose of clopidogrel to 150 mg daily dose, 600 mg loading dose (Table 3) (3).

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Table 1. FDA (2017) Drug Label for Clopidogrel. Warning: Diminished Antiplatelet Effect in Patients with 2 Loss-of-Function Alleles of the *CYP2C19* Gene.

Phenotype	Recommendations
CYP2C19 poor metabolizer	Consider use of another platelet P2Y12 inhibitor in patients identified as CYP2C19 poor metabolizers

Please see Therapeutic Recommendations based on Genotype for more information from the FDA. This table is adapted from (1).

Table 2. CPIC (2013) Antiplatelet Therapy Recommendations based on *CYP2C19* Status when considering Clopidogrel for ACS/PCI Patients.

Phenotype	Examples of diplotypes	Implications for clopidogrel	Therapeutic recommendations for clopidogrel in ACS/PCI[a]
Ultrarapid metabolizer	**17/*17*	Increased platelet inhibition; decreased residual platelet aggregation[b]	Dose recommended by drugs label
Rapid metabolizer	**1/*17*		
Normal metabolizer	**1/*1*	Normal platelet inhibition; normal residual platelet aggregation	Dose recommended by drug label
Intermediate metabolizer	**1/*2* **1/*3* **2/*17*	Reduced platelet inhibition; increased residual platelet aggregation; increased risk for adverse cardiovascular events	Alternative antiplatelet therapy recommended if no contraindication, e.g., prasugrel, ticagrelor
Poor metabolizer	**2/*2* **2/*3* **3/*3*	Significantly reduced platelet inhibition; increased residual platelet aggregation; increased risk for adverse cardiovascular events	Alternative antiplatelet therapy recommended if no contraindication, e.g., prasugrel, ticagrelor

[a] The strength of therapeutic recommendations is "moderate" for intermediate metabolizers and "strong" for all other metabolizers. See Supplementary Materials and Methods (Strength of Therapeutic Recommendations) online.
[b] The *CYP2C19*17* allele may be associated with increased bleeding risks, see (4).
ACS, acute coronary syndrome
PCI, percutaneous coronary intervention
Please see Therapeutic Recommendations based on Genotype for more information from CPIC. This table is adapted from (2).
The nomenclature used in this table reflects the standardized nomenclature for pharmacogenetic terms proposed by CPIC in a 2017 paper, "Standardizing terms for clinical pharmacogenetic test results: consensus terms from the Clinical Pharmacogenetics Implementation Consortium (CPIC)" (5). Note: the 2013 CPIC guideline for clopidogrel therapy includes *1/*17 as an example diplotype for the ultrarapid metabolizer phenotype and does not include the rapid metabolizer phenotype. However, in more recent guidelines using updated nomenclature, *1/*17 is included as an example diplotype for the rapid metabolizer phenotype (Table 4).

Table 3. DPWG (2017) Recommendations for Clopidogrel and *CYP2C19* Phenotype.

Phenotype	Recommendation
Ultrarapid metabolizer	NO action is required for this gene-drug interaction
Intermediate metabolizer	Percutaneous coronary intervention: 1 choose an alternative or double the dose to 150 mg/day (600 mg loading dose) Prasugrel and ticagrelor are not metabolised by CYP2C19 (or to a lesser extent) Other indications: 1 no action required

Table 3. continued from previous page.

Phenotype	Recommendation
Poor metabolizer	Percutaneous coronary intervention: 1 choose an alternative Prasugrel and ticagrelor are not metabolised by CYP2C19 (or to a lesser extent) Other indications: 1. determine the level of inhibition of platelet aggregation by clopidogrel 2. consider an alternative in poor responders Prasugrel and ticagrelor are not metabolised by CYP2C19 (or to a lesser extent)

Please see Therapeutic Recommendations based on Genotype for more information from DPWG. This table is adapted from (3).

Drug: Clopidogrel

Clopidogrel is an antiplatelet drug used in the treatment of patients with ACS, managed medically or with PCI. Clopidogrel is also used in the treatment of patients with atherosclerotic vascular disease, as indicated by a recent MI, a recent ischemic stroke, or symptomatic peripheral arterial disease. Clopidogrel has been shown to reduce the rate of subsequent MI and stroke in these patients (1, 6).

Clopidogrel is a P2RY12 inhibitor (purinergic receptor P2Y, G-protein coupled 12). Clopidogrel acts by irreversibly binding to the platelet P2RY12 receptor, and blocking adenosine diphosphate (ADP)-mediated platelet activation and aggregation. Clopidogrel belongs to the second generation of thienopyridine antiplatelet agents.

Clopidogrel is given to treat or to prevent further occurrences of arterial thrombosis, which occurs when a blood clot (thrombus) forms inside an artery. Often, arterial thrombosis is triggered in response to the rupturing of the atherosclerotic plaque lining the arterial wall. If the thrombus occludes the arterial lumen, the blood flow is reduced or stopped, resulting in ischemia. In the brain, thrombosis in the cerebral arteries can cause a transient ischemic attack (TIA) or ischemic stroke. In the peripheral vessels, thrombosis can cause peripheral artery disease, and in the heart, a thrombosis in the coronary arteries is a common cause of ACS. Platelet inhibitors such as clopidogrel interrupt the formation of the thrombus, which involves the rapid recruitment and activation of platelets.

ACS reflects a decreased blood flow in the coronary arteries and comprises unstable angina and MI. Unstable angina occurs suddenly, often at rest or with minimal exertion, and may be new in onset or may occur with less exertion than previously. An MI may be classified as “STEMI” or “NSTEMI” based on EKG findings. EKG findings that include ST segment elevation are termed “ST segment elevation MI” (STEMI). If no ST segment elevation is present but myocardial biomarkers such as troponin I or T are increased, the term “non-ST segment elevation MI” (NSTEMI) is applied.

In patients with ACS (unstable angina, NSTEMI, or STEMI), the addition of 75 mg daily clopidogrel to aspirin and other standard treatments reduces the risk of MI, stroke, and death, compared with the addition of placebo (7, 8).

However, despite the general efficacy of clopidogrel, resistance is common. Resistance to an antiplatelet drug occurs when there is no significant reduction in platelet function after therapy, compared with baseline platelet function. Clopidogrel treatment failure occurs when there is a thrombotic or ischemic event (e.g., stent thrombosis or recurrent ACS) during clopidogrel therapy in patients with “High on-Treatment Platelet Reactivity” (HTPR).

HTPR occurs when the platelet P2Y12 receptors are still responsive despite clopidogrel therapy. It is tested for by adding an ADP agonist to a plasma sample and measuring aggregation or intracellular markers of platelet activation. It has been estimated that between 16–50% of patients treated with clopidogrel have HTPR (9).

Platelet function assays are used to assess platelet response; they measure "Platelet Reactivity Units" (PRU). The PRU cut-off values vary, but generally, the therapeutic window for clopidogrel is around 95-208 PRU. A PRU value higher than 208 indicates clopidogrel resistance, and a value below 95 is associated with a higher risk for major bleeding (10, 11). Most (but not all) studies report an association between clopidogrel resistance (HTPR or high PRU) and an increased risk of thrombotic/ischemic event following PCI, such as stent thrombosis (12).

A poor response to clopidogrel is due to, in part, genetic variations in the *CYP2C19* gene. Other genes that may influence clopidogrel response include *ABCB1* (13-15), *P2Y12*, and *GPIIIA* (16-18). Clopidogrel is a prodrug, and CYP2C19 is the major enzyme involved in the conversion of clopidogrel into an active metabolite.

Several studies have reported an increase in adverse cardiovascular events in patients who carry one or 2 non-functional copies of the *CYP2C19* gene ("intermediate metabolizers" and "poor metabolizers", respectively), compared with patients with 2 normal copies of the *CYP2C19* gene ("normal metabolizers"). These studies focus on patients with ACS undergoing PCI, with carriers of non-functional alleles also being at a higher risk of stent thrombosis (19-21). These patients may require much higher doses of clopidogrel (e.g., 4-fold higher) or an alternative drug (22, 23).

The studies that did not find a significant association between *CYP2C19* and clinical outcome in patients with ACS, often included some data from non-PCI patients (12, 24, 25).

Several studies of patients with TIA have reported that *CYP2C19* status influences the risk of having an ischemic stroke or adverse clinical outcomes following a stroke (26-28). A recent trial (CHANCE - (Clopidogrel in High-risk Patients with Acute Nondisabling Cerebrovascular Events) found that the use of clopidogrel plus aspirin compared with aspirin alone reduced the risk of a new stroke only in the subgroup of patients who were not carriers of the *CYP2C19* non-functional alleles (29).

Alternative antiplatelet drugs to clopidogrel, such as prasugrel (a third generation thienopyridine) and ticagrelor (a cyclopentyl triazolopyrimidine), are not dependent upon CYP2C19 for activation. Although both clopidogrel and prasugrel form active metabolites with similar potency, in the population overall, prasugrel is a more potent antiplatelet agent than clopidogrel due to the more efficient formation of the active metabolite from the prodrug (30).

A large trial, TRITON-TIMI 38, compared prasugrel with clopidogrel in 13,608 patients with ACS who were undergoing PCI. Prasugrel was found to provide more potent platelet inhibition than clopidogrel: and after 15 months, the patients treated with prasugrel had a lower incidence of the combined endpoint of cardiovascular death, nonfatal MI, or nonfatal stroke as compared with patients treated with clopidogrel (9.9% vs. 12.1%) (31, 32). However, prasugrel was associated with a higher risk of bleeding, leading to the FDA warning that the use of prasugrel is contraindicated in patients with active pathological bleeding, or a history of stroke or TIA (33, 34). In addition, prasugrel has also an FDA box warning for patients with a high probability of undergoing coronary artery bypass grafting (prasugrel should not be started, or when possible, discontinue prasugrel at least 7 days prior to any surgery) (35).

In an analysis from the recent PLATO trial, ticagrelor was found to be superior to clopidogrel in a subgroup of patients with STEMI who were treated with PCI. Consistent with the overall results of the trial, ticagrelor was found to have superior efficacy and similar safety compared with clopidogrel (36).

In addition, the latest guideline from the American College of Cardiology/American Heart Association includes a preference for alternative therapy over clopidogrel in patients with ACS/PCI. This is a class IIa recommendation based on moderate quality, from the 2016 focused update on dual antiplatelet therapy (37). In

full, this recommendation states "In patients with ACS (NSTE-ACS or STEMI) treated with dual antiplatelet therapy after coronary stent implantation who are not at high risk for bleeding complications and who do not have a history of stroke or TIA, it is reasonable to choose prasugrel over clopidogrel for maintenance P2Y12 inhibitor therapy" (37).

Although prasugrel is more effective than standard-dose clopidogrel, dual antiplatelet therapy with clopidogrel and aspirin remains the standard of care at many institutions for patients with ACS undergoing PCI (38-40). This may be because clopidogrel has a lower bleeding risk and is less expensive (41). However, the availability of *CYP2C19* genetic testing can facilitate personalized antiplatelet therapy, with individuals with impaired CYP2C19 activity being identified early, and offered an alternative antiplatelet agent, such as prasugrel (39, 42-45).

Recent studies have found that *CYP2C19*-genotype guided antiplatelet therapy results in a higher likelihood of achieving a therapeutic level of on-treatment platelet reactivity (10, 46-48), which may also be cost effective among ACS patients undergoing PCI (39, 49-51). However, more data are needed to determine whether routine genotyping and platelet function tests could help reduce future cardiovascular events in ACS patients (52-54).

Gene: CYP2C19

The cytochrome P450 superfamily (CYP) is a large and diverse group of enzymes that form the major system for metabolizing lipids, hormones, toxins, and drugs. The CYP genes are very polymorphic and can result in reduced, absent, or increased drug metabolism.

The CYP2C19 enzyme contributes to the metabolism of a range of clinically important drugs, such as antidepressants, benzodiazepines, voriconazole (55), some proton pump inhibitors, and the antiplatelet agent, clopidogrel.

The variability of clopidogrel metabolism and treatment outcomes between individuals is partly determined by variant alleles of the *CYP2C19* gene.

The *CYP2C19* gene is highly polymorphic—35 variant star (*) alleles are catalogued at the Pharmacogene Variation (PharmVar) Consortium. The *CYP2C19*1* is considered the wild type allele when no variants are detected, and is categorized as normal enzyme activity and the "normal metabolizer" phenotype.

The *CYP2C19*17* allele is associated with increased enzyme activity and, depending on the number of alleles present, is associated with the "rapid" (one **17* allele) and "ultrarapid" (2 **17* alleles) metabolizer phenotypes. Non-functional alleles include *CYP2C19*2* and **3*. *CYP2C19* intermediate metabolizers carry one copy of an allele that encodes a non-functional allele (e.g. **1/*2*), whereas "poor metabolizers" carry 2 non-functional alleles (e.g., **2/*2*, **2/*3*) (Table 4).

Table 4. *CYP2C19* Functional Status and Phenotypes, CPIC 2016.

Phenotype	Genotype	Examples of diplotypes
CYP2C19 ultrarapid metabolizer (~2–5% of patients)[a]	An individual carrying 2 increased function alleles	**17/*17*
CYP2C19 rapid metabolizer (~2–30% of patients)	An individual carrying one normal function allele and one increased function allele	**1/*17*
CYP2C19 normal metabolizer (~35–50% of patients)	An individual carrying 2 normal function alleles	**1/*1*
CYP2C19 intermediate metabolizer (~18–45% of patients)	An individual carrying one normal function allele and one no function allele or one no function allele and one increased function allele	**1/*2* **1/*3* **2/*17*[b]

Table 4. continued from previous page.

Phenotype	Genotype	Examples of diplotypes
CYP2C19 poor metabolizer (~2–15% of patients)	An individual carrying 2 no function alleles	**2/*2* **2/*3* **3/*3*

[a] CYP2C19 metabolizer status frequencies are based on average multi-ethnic frequencies. See the *CYP2C19* Frequency Tables for population-specific allele and phenotype frequencies (56).
[b] The predicted metabolizer phenotype for the**2/*17* genotype is a provisional classification. The currently available evidence indicates that the *CYP2C19*17* increased function allele is unable to completely compensate for the *CYP2C19*2* non-functional allele.
This table is adapted from (56).

Approximately 2% of Caucasians, 4% of African Americans, and 14% of Chinese are CYP2C19 poor metabolizers (57); and up to 45% of patients are CYP2C19 intermediate metabolizers. As noted above, ACS/PCI patients that are CYP2C19 intermediate or poor metabolizers and who are treated with clopidogrel have increased risks for major cardiovascular events including stent thrombosis, compared with similarly treated patients without a non-functional allele (57) (19, 21).

The most common non-functional variant is *CYP2C19*2*, which contains the NM_000769.1:c.681G>A variant in exon 5 that results in an aberrant splice site that produces a truncated and non-functioning protein. The *CYP2C19*2* allele frequencies are ~15% in Caucasians and Africans, and ~29–35% in Asians (2). Approximately 6–12% of the observed variability in antiplatelet effect of clopidogrel is thought to be attributed to *CYP2C19*2* allele(s) (58).

For *CYP2C19*, another commonly tested non-functional variant is *CYP2C19*3*, which contains a c.636G>A variant in exon 4 that causes a premature stop codon. The *CYP2C19*3* allele frequencies are ~2–9% in Asian populations, but rare in other racial groups. Other non-functional variants occur in less than 1% of the general population and include *CYP2C19*4–*8* (2).

Genetic Testing

Clinical genotyping tests are available for several *CYP2C19* alleles. The NIH's Genetic Testing Registry (GTR) provides examples of the genetic tests that are currently available for clopidogrel response, CYP2C19-related poor drug metabolism, and the *CYP2C19* gene.

Usually a patient's result is reported as a diplotype, such as *CYP2C19 *1/*1*, and may also include an interpretation of the patient's predicted metabolizer phenotype (ultrarapid, rapid, normal, intermediate, or poor). Table 2 and Table 3 summarize the common *CYP2C19* phenotypes with antiplatelet therapy recommendations developed by CPIC and DPWG, respectively.

The association between *CYP2C19*2* and **3* and clopidogrel response has been extensively studied; however, the less common non-functional alleles (e.g., *CYP2C19*4–*8*) also likely influence clopidogrel response similar to **2* and **3*, but the body of evidence is not as extensive. Therefore, when other non-functional alleles are identified in patients undergoing PCI, these alleles should be considered to reduce the effectiveness of clopidogrel therapy in a similar manner to the more common *CYP2C19**2 allele (2, 59).

Therapeutic Recommendations based on Genotype

This section contains excerpted[1] information on gene-based dosing recommendations. Neither this section nor other parts of this review contain the complete recommendations from the sources.

[1] The FDA labels specific drug formulations. We have substituted the generic names for any drug labels in this excerpt. The FDA may not have labeled all formulations containing the generic drug. Certain terms, genes and genetic variants

2017 Statement from the US Food and Drug Administration (FDA)

WARNING: DIMINISHED ANTIPLATELET EFFECT IN PATIENTS WITH TWO LOSS-OF-FUNCTION ALLELES OF THE CYP2C19 GENE

The effectiveness of clopidogrel tablets results from its antiplatelet activity, which is dependent on its conversion to an active metabolite by the cytochrome P450 (CYP) system, principally CYP2C19. Clopidogrel tablets at recommended doses form less of the active metabolite and so has a reduced effect on platelet activity in patients who are homozygous for nonfunctional alleles of the CYP2C19 gene, (termed "CYP2C19 poor metabolizers"). Tests are available to identify patients who are CYP2C19 poor metabolizers. Consider use of another platelet P2Y12 inhibitor in patients identified as CYP2C19 poor metabolizers.

[...]

CYP2C19 is involved in the formation of both the active metabolite and the 2-oxo-clopidogrel intermediate metabolite. Clopidogrel active metabolite pharmacokinetics and antiplatelet effects, as measured by ex vivo platelet aggregation assays, differ according to CYP2C19 genotype.

Patients who are homozygous for nonfunctional alleles of the CYP2C19 gene are termed "CYP2C19 poor metabolizers". Approximately 2% of White and 4% of Black patients are poor metabolizers; the prevalence of poor metabolism is higher in Asian patients (e.g., 14% of Chinese). Tests are available to identify patients who are CYP2C19 poor metabolizers.

A crossover study in 40 healthy subjects, 10 each in the four CYP2C19 metabolizer groups, evaluated pharmacokinetic and antiplatelet responses using 300 mg followed by 75 mg per day and 600 mg followed by 150 mg per day, each for a total of 5 days. Decreased active metabolite exposure and diminished inhibition of platelet aggregation were observed in the poor metabolizers as compared to the other groups.
Please review the complete therapeutic recommendations that are located here: (1).

2017 Summary of Recommendations from the Dutch Pharmacogenetics Working Group (DPWG) of the Royal Dutch Association for the Advancement of Pharmacy (KNMP)

CYP2C19 PM: CLOPIDOGREL

Genetic variation reduces activation of clopidogrel. This increases the risk of serious cardiovascular events in patients undergoing balloon angioplasty or stent placement (percutaneous coronary intervention). No negative clinical consequences have been proved in other patients.

Recommendation:

- PERCUTANEOUS CORONARY INTERVENTION:
  1 choose an alternative

Prasugrel and ticagrelor are not metabolised by CYP2C19 (or to a lesser extent).

- OTHER INDICATIONS:
  1. determine the level of inhibition of platelet aggregation by clopidogrel
  2. consider an alternative in poor responders

Prasugrel and ticagrelor are not metabolised by CYP2C19 (or to a lesser extent).

CYP2C19 IM: CLOPIDOGREL

Genetic variation reduces activation of clopidogrel. This increases the risk of serious cardiovascular events in patients undergoing balloon angioplasty or stent placement (percutaneous coronary intervention). No negative clinical consequences have been observed in other patients.

Recommendation:

- PERCUTANEOUS CORONARY INTERVENTION:
  1 choose an alternative or double the dose to 150 mg/day (600 mg loading dose)

Prasugrel and ticagrelor are not metabolised by CYP2C19 (or to a lesser extent).

- OTHER INDICATIONS:
  1 no action required

CYP2C19 UM: CLOPIDOGREL

NO action is required for this gene-drug interaction.

The genetic variation results in increased conversion of clopidogrel to the active metabolite. However, this can result in both positive effects (reduction in the risk of serious cardiovascular events) and negative effects (increase in the risk of bleeding).

Please review the complete therapeutic recommendations that are located here: (3).

2013 Statement from the Clinical Pharmacogenetics Implementation Consortium (CPIC)

Standard dosing of clopidogrel, as recommended in the product insert, is warranted among ACS/PCI patients with a predicted *CYP2C19* extensive metabolizer or ultrarapid metabolizer phenotype (i.e., **1/*1*, **1/*17*, and **17/*17*). If genotyping from a Clinical Laboratory Improvement Amendments–certified laboratory identifies a patient as a *CYP2C19* PM (i.e., **2/*2*), current literature supports the use of an alternative antiplatelet agent (e.g., prasugrel or ticagrelor) when not contraindicated clinically.

The most challenging patient population to address is the *CYP2C19* IM [intermediate metabolizer] phenotype (e.g., **1/*2*, **1/*3*, and **2/*17*). IMs have higher on-treatment residual platelet activity on average as compared with extensive metabolizers, and ACS/PCI *CYP2C19*2* heterozygotes treated with clopidogrel have increased risks for serious adverse CV [cardiovascular] outcomes, including stent thrombosis. Consequently, these data support switching to an alternative antiplatelet agent for IMs when not contraindicated. However, given the wide interindividual variability in residual platelet activity observed among clopidogrel-treated IMs, clinical judgment also taking into account other factors that may place an IM at increased risk of a CV event (or adverse bleeding event) must be considered to most effectively individualize therapy.
Please review the complete therapeutic recommendations that are located here: (2).

Nomenclature of Selected *CYP2C19* Alleles

Common allele name	Alternative names	HGVS reference sequence		dbSNP reference identifier for allele location
		Coding	Protein	
*CYP2C19*2*	681G>A Pro227Pro	NM_000769.1:c.681G>A	NP_000760.1:p.Pro227=	rs4244285
*CYP2C19*3*	636G>A Trp212Ter	NM_000769.1:c.636G>A	NP_000760.1:p.Trp212Ter	rs4986893

Table continued from previous page.

Common allele name	Alternative names	HGVS reference sequence		dbSNP reference identifier for allele location
		Coding	Protein	
*CYP2C19*17*	-806C>T	NM_000769.1:c.-806C>T	Not applicable - variant occurs in a non-coding region	rs12248560

Note: the normal "wild type" allele is *CYP2C19*1* and is reported when no variant is detected.
Pharmacogenetic Allele Nomenclature: International Workgroup Recommendations for Test Result Reporting (60).
Guidelines for the description and nomenclature of gene variations are available from the Human Genome Variation Society (HGVS).
Nomenclature for cytochrome P450 enzymes is available from Pharmacogene Variation (PharmVar) Consortium.

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Version History

To view the 2015 version of this summary (Created: November 19, 2015) please click here.

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