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.

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

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

Contact IPM PGx Team:
Email us at clipmergeteam@mssm.edu
Call us at 212 241 7371