# TEST DEFINITION

6/23/2010

<table>
<thead>
<tr>
<th>Code</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>60439</td>
<td>CYP2C19 Sequence Genotype</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ORDER</th>
<th>EFF</th>
<th>CODE</th>
<th>DATE</th>
<th>TC</th>
<th>TITLE</th>
<th>Checking Normals</th>
<th>Print normals (# coded)</th>
<th>Perform</th>
</tr>
</thead>
<tbody>
<tr>
<td>------</td>
<td>-----</td>
<td>------</td>
<td>----------</td>
<td>----</td>
<td>----------------------------</td>
<td>------------------</td>
<td>-------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>60439</td>
<td></td>
<td></td>
<td>6/10/2010</td>
<td></td>
<td>CYP2C19 Sequence Genotype</td>
<td></td>
<td></td>
<td>MCR</td>
</tr>
<tr>
<td>83639</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Transport temp : Ambient\Refrig OK\Frozen NO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>83639</td>
<td></td>
<td></td>
<td></td>
<td>2C19 Interpretation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24065</td>
<td></td>
<td></td>
<td></td>
<td>2C19 Genotype Star Alleles</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>31969</td>
<td></td>
<td></td>
<td></td>
<td>2C19 -806C&gt;T (*17)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>31987</td>
<td></td>
<td></td>
<td></td>
<td>2C19 1A&gt;G (*4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24058</td>
<td></td>
<td></td>
<td></td>
<td>2C19 358T&gt;C (*8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24059</td>
<td></td>
<td></td>
<td></td>
<td>2C19 395G&gt;A (*6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24060</td>
<td></td>
<td></td>
<td></td>
<td>2C19 636G&gt;A (*3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24061</td>
<td></td>
<td></td>
<td></td>
<td>2C19 681G&gt;A (*2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24062</td>
<td></td>
<td></td>
<td></td>
<td>2C19 IVS5+2T&gt;A (*7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>24063</td>
<td></td>
<td></td>
<td></td>
<td>2C19 Reviewed by</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**TEST CODE ALWAYS MESSAGE** – [Z83639S,ASR]

Z83639S: A combination of bidirectional and dual monodirectional DNA sequence analysis was used to test for the presence of variants in the promoter as well as exons 1, 3, 4, and 5 of the CYP2C19 gene. These sequencing reactions detect the presence of -806C>T (*17), 1A>G (*4), 358T>C (*8), 395G>A (*6), 636G>A (*3), 681G>A (*2), and IVS5+2T>A (*7). This sequencing assay will not detect all the known mutations that
result in decreased or inactive CYP2C19. Absence of a
detectable gene mutation or polymorphism does not rule out
the possibility that a patient has an intermediate or poor
metabolizer phenotype.

Individuals receiving clopidogrel who have one copy
(heterozygous) of the null or deficient CYP2C19
polymorphisms detected by this test will likely require a
dose increase to achieve effective inhibition of platelet
aggregation. Individuals who have two defective copies of
these CYP2C19 deficient alleles (poor metabolizers) may not
achieve effective inhibition of platelet aggregation using
the standard doses of clopidogrel. An increased dose of
clopidogrel, or switching to other antiplatelet drugs such
as prasugrel, should be considered for CYP2C19 poor metabolizers.

The presence of the *17 promoter polymorphism will increase the
expression of the CYP2C19 enzyme encoded by the allele on which it
is found. When found in combination with other polymorphisms,
we are unable to ascertain the mode of inheritance to predict
which allele includes the *17 promoter polymorphism but will make
our best prediction of the impact of the findings.

Patients with an extensive (normal) or intermediate
metabolizer genotype may have CYP2C19 enzyme activity
inhibited by a variety of medications or their metabolites.

The following is a partial listing of drugs known to affect
CYP2C19 activity as of the date of this report.

Drugs that undergo metabolism by CYP2C19:
  Anticoagulants: clopidogrel
  Anticonvulsants: mephenytoin, phenytoin, primidone
  Antidepressants: amitriptyline, citalopram, S-citalopram,
                  clomipramine
  Antineoplastic drugs: cyclophosphamide
  Antiretroviral: nelfinavir
  Proton pump inhibitors: lansoprazole, omeprazole, pantoprazole
  Miscellaneous drugs: diazepam, progesterone, propranolol,
                      R-warfarin (less active isomer), proguanil

Coadministration may decrease the rate of elimination of other drugs
metabolized by CYP2C19.

Drugs known to increase CYP2C19 activity:
  carbamazepine
  prednisone
  rifampin

Coadministration of these drugs increases synthesis of CYP2C19 and
increases the rate of elimination of drugs metabolized by CYP2C19.

Drugs known to decrease CYP2C19 activity:
  chloramphenicol
  cimetidine
  felbamate
  fluoxetine
  fluvoxamine
  indomethacin
  ketoconazole
lansoprazole
modafinil
omeprazole
probenecid
ticlopidine
topiramate

Coadministration will decrease the rate of metabolism of CYP2C19 metabolized drugs, increasing the possibility of toxicity, particularly in heterozygous individuals.

ASR

This test was developed and its performance characteristics determined by Laboratory Medicine and Pathology, Mayo Clinic, Rochester MN. It has not been cleared or approved by the U.S. Food and Drug Administration.

---

ORDER EFF CODE DATE TC TITLE Checking Normals Print normals (# coded) Perform Site *
----- ---- ---- ------ ----------- -------------- ------------------
60439 (continued)

60416 6/9/2010 CYP2C19 Sequencing MCR

Transport temp: Ambient\Refrig OK\Frozen NO

60416 Sequencing

*Performing Site Legend

MCR Mayo Clinic Dpt of Lab Med & Pathology LAB DIRECTOR: Franklin R. Cockerill, III, M.D.

200 First Street SW
Rochester, MN 55905

Total of 0 normals codes

*** End of Report ***