CYP2C9 metabolizes warfarin in the body. VKORC1 also affects the warfarin level in the body.

Some CYP2C9 and VKORC1 forms caused by changes in the genes may affect the way your body responds to warfarin.

Genetic testing results help your doctor in choosing the initial warfarin dose. However, careful monitoring of INR is still required.

Other medications may also affect your response to warfarin. Therefore, it is important to let your physician know all the medications that you are taking so that any potential interactions may be avoided.

**Glossary**

- **Active drug**: the form of drug which produces an effect after it enters the body
- **Enzyme**: a protein that breaks down a drug
- **General population**: a group of people made up of different races/ethnicities
- **INR (International Normalized Ratio)**: a test used in patients taking warfarin to see if the blood is too thin or too thick
- **Metabolism**: the breakdown of a drug

**Things To Remember:**

- At least one change in **CYP2C9** gene
  - 17 in 100 people
  - 4 in 100 people
  - 2 in 100 people
  - Whites, Blacks, Asians

- At least one change in **VKORC1** gene
  - 89 in 100 people
  - 37 in 100 people
  - 14 in 100 people
  - Whites, Blacks, Asians

**“One size does not fit all.”**
Pharmacogenetics is the study of how your genes affect the medications you take.

Genes are the instruction manuals contained in each person’s body.

The instructions the body receives from the genes is what controls how we look, how to grow, and how we function.

They also contain instructions for how to make enzymes, which are proteins the body use to break down or “metabolize” what we take in, including medications.

Changes in some genes may result in different instructions for how to make the enzymes. This could result in the body having a different form of the enzyme that may metabolize medications differently.

*CYP2C9* is an enzyme that is responsible for the metabolism of many commonly prescribed drugs, such as warfarin.

*VKORC1* is a protein that regulates Vitamin K level in the body, which affects the warfarin level, making blood too thin or too thick.

Changes in the *CYP2C19* and *VKORC1* genes lead to different forms of *CYP2C19* enzyme and *VKORC1* protein; which affect the way your body responds to warfarin.

### Warfarin (Coumadin®)

- Warfarin is a medication used to thin blood to prevent various conditions such as stroke or blood clots.
- Changes in *CYP2C19* and *VKORC1* can lead to increased amount of active warfarin in the body and reduced clotting activity. This can lead to side effects such as bleeding.

<table>
<thead>
<tr>
<th>General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extensive Metabolizer/Normal Function</td>
</tr>
<tr>
<td>Intermediate Metabolizer/Function</td>
</tr>
<tr>
<td>Poor Metabolizer/Function</td>
</tr>
</tbody>
</table>

Table: *CYP2C9* and *VKORC1* forms and their effects on the breakdown of warfarin

<table>
<thead>
<tr>
<th><em>alleles for CYP2C9</em></th>
<th>*1/*1</th>
<th>*1/*2</th>
<th>*1/*3</th>
<th>*2/*2</th>
<th>*2/*3</th>
<th>*3/*3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Function</td>
<td>Green</td>
<td>Green</td>
<td>Green</td>
<td>Orange</td>
<td>Orange</td>
<td>Red</td>
</tr>
<tr>
<td>Intermediate Function</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Yellow</td>
<td>Red</td>
</tr>
<tr>
<td>Poor Function</td>
<td>Red</td>
<td>Red</td>
<td>Red</td>
<td>Red</td>
<td>Red</td>
<td>Red</td>
</tr>
</tbody>
</table>

**Classification**  | **Protein activity** | **Clinical Relevance**
--- | --- | ---
Normal activity of the enzyme and normal clotting activity | Expected blood thinning effect
Low activity of the enzyme (increased amounts of active warfarin) and less clotting activity | May have higher risk of bleeding
Lowest activity of the enzyme (very high amounts of active warfarin) and very little clotting activity | May have highest risk of bleeding

The *CYP2C9* and *VKORC1* genetic tests provide information that helps to estimate the dose of warfarin needed to reach the desired blood thinning effect.

In Mount Sinai’s pharmacogenetics program, your genetic test results including your *CYP2C9* and *VKORC1* results are added to the electronic medical records.

Depending on your genetic test results, your doctor will receive an alert when prescribing warfarin for you.

This alert will tell the doctor to doses that you will need, based on your genetic test results, to prevent clotting and avoid bleeding. (see tables below)