Rivaroxaban Drug Interaction Potential

Tags: Rivaroxaban
drug interactions

**Pharmacodynamic Interactions**
The concurrent use of rivaroxaban with other anticoagulants, antiplatelet agents, and nonsteroidal anti-inflammatory agents is expected to increase the risk of bleeding in comparison to use of rivaroxaban alone.

**Pharmacokinetic Interactions**
1. The absorption of rivaroxaban is mediated by P-glycoprotein (P-gp). P-gp inhibitors can increase the absorption of rivaroxaban, increasing both AUC and Cmax. Conversely, P-gp inducers can reduce the absorption of rivaroxaban, decreasing AUC and Cmax.

2. The metabolism of rivaroxaban is mediated by CYP3A4. CYP3A4 inhibitors can decrease the metabolism of rivaroxaban, increasing both AUC and Cmax. Conversely, CYP3A4 inducers can increase the metabolism of rivaroxaban, decreasing AUC and Cmax.

3. Agents that interfere with both P-gp and CYP3A4 are likely to cause more significant interactions with rivaroxaban than agents that interfere with P-gp or CYP3A4 alone.

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Examples (based on human <em>in vivo</em> data*)</th>
<th>Known or Probable Effect</th>
<th>US PI Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined P-gp inhibitor and strong CYP3A4 inhibitor</td>
<td>cobicistat, conivaptan, indinavir, itraconazole, ketoconazole*, posaconazole, ritonavir*, saquinavir, telaprevir, telithromycin</td>
<td>Significant increase in rivaroxaban concentration</td>
<td>Avoid use</td>
</tr>
<tr>
<td>Combined P-gp inhibitor and moderate CYP3A4 inhibitor OR strong CYP3A4 inhibitor alone</td>
<td>amiodarone, azithromycin, clarithromycin*, cyclosporine, diltiazem, dronedarone, erythromycin*, fluconazole*, grapefruit, lapatinib, mifepristone, nefazodone, nicardipine, ranolazine, tamoxifen, ticagrelor, verapamil, voriconazole</td>
<td>Moderate increase in rivaroxaban concentration in patients with normal renal function. Significant increase in rivaroxaban concentrations in patients with renal impairment</td>
<td>Combined P-gp and moderate 3A4 inhibitors (e.g. diltiazem, verapamil, dronedarone and erythromycin): Avoid use if CrCl &lt; 80 ml/min unless potential benefits outweigh the risks</td>
</tr>
<tr>
<td>Combined P-gp inducer and strong CYP3A4 inhibitor</td>
<td>carbamazepine*, dexamethsone, rifampin**, St John's wort*</td>
<td>Significant reduction in rivaroxaban</td>
<td>Avoid use</td>
</tr>
</tbody>
</table>

* cited as example in US PI, with pharmacokinetic data cited.
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#### Published on Anticoagulation Services

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<table>
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<tr>
<th>Inducer</th>
<th>Concentration Effect may persist for several weeks following discontinuation of strong inducers of P-gp and/or CYP3A4.</th>
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<tr>
<td><strong>Inducers of P-gp</strong></td>
<td>tipranavir</td>
</tr>
</tbody>
</table>

**Strong inducers of CYP3A4**

- bosentan, efavirenz, etravirine, fosphenytoin, nafcillin, nevirapine, oxarbazepine, phenobarbital phenytoin*, primidone, rifabutin, rifapentine
- * cited as example of combined P-gp inducer and strong CYP3A4 inducer in US PI

Avoid use of phenytoin

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(2) based on probable effects on rivaroxaban, taking into consideration known characteristics of the precipitant drug according to human *in vivo* data

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