Drug-drug interactions after oral and intramuscular/subcutaneous administration of cabotegravir, rilpivirine and lenacapavir

- Intramuscular (IM) or subcutaneous (SC) administration avoids drug-drug interactions at the gastrointestinal level.
- Drug-drug interactions can still occur with IM or SC administration.
- IM or SC administration does not necessarily mitigate the magnitude of interactions with inducers.

### Mechanisms of drug-drug interactions with cabotegravir, rilpivirine and lenacapavir

<table>
<thead>
<tr>
<th>Oral administration</th>
<th>IM/SC administration</th>
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</thead>
<tbody>
<tr>
<td><strong>Stomach/intestine</strong></td>
<td>• Change in gastric pH</td>
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<td></td>
<td>• Chelation with divalent cations</td>
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<td>• Inhibition/induction of CYP3A4 and transporters</td>
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<tr>
<td><strong>Liver</strong></td>
<td>• Inhibition/induction of CYP3A4, UGT1A1/9, transporters</td>
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</tbody>
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Examples of drugs interacting with oral but not IM/SC administration

**Cabotegravir**
- Antacids
- Calcium
- Colestyreimine
- Iron
- Magnesium
- Multivitamins containing divalent cations
- Orlistat
- Sevelamer
- Strontium ranelate

**Rilpivirine**
- Antacids
- Colestyreimine
- H2 receptor antagonists
- Liraglutide
- Orlistat
- Proton pump inhibitors
- Sevelamer
- Strontium ranelate

**Lenacapavir**
- Colestyreimine
- Orlistat
- Sevelamer
- Strontium ranelate