**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 1 of 17)

This table provides information on the known or predicted interactions between INSTIs (BIC, DTG, EVG, or RAL) and non-ARV drugs. EVG is always coadministered with COBI. For information regarding interactions between INSTIs and other ARV drugs, including dosing recommendations, refer to Tables 21c, 22a, and 22b.

Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Acid Reducers** | | | |
| **Al, Mg, +/- Ca-Containing Antacids**<br><br>Please refer to the Miscellaneous Drugs section of this table for recommendations on use with other polyvalent cation products (e.g., Fe and Ca supplements, multivitamins). | BIC | **Al/Mg Hydroxide Antacid:**<br>• ↔ BIC AUC if antacid is administered 2 hours after BIC and under fasting conditions<br>• BIC AUC ↓ 52% if antacid is administered 2 hours before BIC<br>• BIC AUC ↓ 47% to 79% if administered simultaneously with antacid<br><br>**$CaCO_3$ Antacid:**<br>• ↔ BIC AUC if administered with food<br>• BIC AUC ↓ 33% if administered under fasting conditions | **With Antacids That Contain Al/Mg:**<br>• Administer antacids that contain Al/Mg at least 2 hours after or 6 hours before BIC.<br><br>**With Antacids That Contain Ca:**<br>• Administer BIC and antacids that contain Ca together with food.<br>• **Do not coadminister BIC simultaneously with antacids that contain Ca on an empty stomach.** |
| | DTG | DTG AUC ↓ 74% if administered simultaneously with antacid<br><br>DTG AUC ↓ 26% if administered 2 hours before antacid | Administer DTG at least 2 hours before or at least 6 hours after antacids that contain polyvalent cations. |
| | EVG/c | EVG AUC ↓ 40% to 50% if administered simultaneously with antacid<br><br>EVG AUC ↓ 15% to 20% if administered 2 hours before or after antacid; ↔ with 4-hour interval | Separate EVG/c and antacid administration by more than 2 hours. |
| | RAL | **Al/Mg Hydroxide Antacid:**<br>• RAL $C_{min}$ ↓ 49% to 63%<br><br>**$CaCO_3$ Antacid:**<br>• RAL 400 mg twice daily: $C_{min}$ ↓ 32%<br>• RAL 1,200 mg once daily: $C_{min}$ ↓ 48% to 57% | **Do not coadminister RAL and Al/Mg hydroxide antacids.** Use alternative acid-reducing agent.<br><br>**With $CaCO_3$ Antacids:**<br>• RAL 1,200 mg once daily: **Do not coadminister.**<br>• RAL 400 mg twice daily: No dose adjustment or separation needed. |
| **H2-Receptor Antagonists** | BIC, DTG, EVG/c | ↔ INSTI | No dose adjustment needed. |
| | RAL | RAL AUC ↑ 44% and $C_{max}$ ↑ 60% | No dose adjustment needed. |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 2 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Acid Reducers**, continued | | | |
| **Proton Pump Inhibitors** | BIC, DTG, EVG/c | ↔ INSTI | No dose adjustment needed. |
| | RAL | RAL AUC ↑ 37% and $C_{min}$ ↑ 24% | No dose adjustment needed. |
| **Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia** | | | |
| **Alfuzosin** | BIC, DTG, RAL | ↔ alfuzosin expected | No dose adjustment needed. |
| | EVG/c | ↑ alfuzosin expected | **Contraindicated.** |
| **Doxazosin** | BIC, DTG, RAL | ↔ doxazosin expected | No dose adjustment needed. |
| | EVG/c | ↑ doxazosin possible | Initiate doxazosin at lowest dose and titrate based on doxazosin efficacy and adverse events. Doxazosin dose reduction may be needed. |
| **Tamsulosin** | BIC, DTG, RAL | ↔ tamsulosin expected | No dose adjustment needed. |
| | EVG/c | ↑ tamsulosin expected | **Do not coadminister, unless benefits outweigh risks.** If coadministered, monitor for tamsulosin-related adverse events. |
| **Terazosin** | BIC, DTG, RAL | ↔ terazosin expected | No dose adjustment needed. |
| | EVG/c | ↑ terazosin possible | Initiate terazosin at lowest dose and titrate based on terazosin efficacy and adverse events. Terazosin dose reduction may be necessary. |
| **Silodosin** | BIC, DTG, RAL | ↔ silodosin expected | No dose adjustment needed. |
| | EVG/c | ↑ silodosin expected | **Contraindicated.** |
| **Antibacterials** | | | |
| ***Antimycobacterials*** | | | |
| **Rifabutin** | BIC | **Rifabutin 300 mg Once Daily:**<br>• BIC AUC ↓ 38% and $C_{min}$ ↓ 56% | **Do not coadminister.** |
| | DTG | **Rifabutin 300 mg Once Daily:**<br>• ↔ DTG AUC and $C_{min}$ ↓ 30% | No dose adjustment needed. |
| | EVG/c | **Rifabutin 150 mg Every Other Day with EVG/c Once Daily Compared to Rifabutin 300 mg Once Daily Alone:**<br>• ↔ rifabutin AUC<br>• 25-O-desacetyl-rifabutin AUC ↑ 625%<br>• EVG AUC ↓ 21% and $C_{min}$ ↓ 67% | **Do not coadminister.** |
| | RAL | RAL AUC ↑ 19% and $C_{min}$ ↓ 20% | No dose adjustment needed. |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 3 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| ***Antimycobacterials***, continued | | | |
| **Rifampin** | BIC | BIC AUC ↓ 75% | **Contraindicated.** |
| | DTG | **Rifampin with DTG 50 mg Twice Daily Compared to DTG 50 mg Twice Daily Alone:**<br>• DTG AUC ↓ 54% and $C_{min}$ ↓ 72%<br>**Rifampin with DTG 50 mg Twice Daily Compared to DTG 50 mg Once Daily Alone:**<br>• DTG AUC ↑ 33% and $C_{min}$ ↑ 22% | Use DTG 50 mg twice daily (instead of DTG 50 mg once daily) in patients without suspected or documented INSTI-associated resistance mutations.<br>Consider an alternative to rifampin, such as rifabutin, in patients with certain suspected or documented INSTI-associated resistance mutations. |
| | EVG/c | Significant ↓ EVG and COBI expected | **Contraindicated.** |
| | RAL | **RAL 400 mg:**<br>• RAL AUC ↓ 40% and $C_{min}$ ↓ 61%<br>**Rifampin with RAL 800 mg Twice Daily Compared to RAL 400 mg Twice Daily Alone:**<br>• RAL AUC ↑ 27% and $C_{min}$ ↓ 53% | Use RAL 800 mg twice daily instead of 400 mg twice daily.<br>**Do not coadminister RAL 1,200 mg once daily with rifampin.**<br>Monitor closely for virologic response, or consider using rifabutin as an alternative rifamycin. |
| **Rifapentine** | BIC, DTG, EVG/c | Significant ↓ BIC, DTG, EVG, and COBI expected | **Do not coadminister.** |
| | RAL | **Rifapentine 900 mg Once Weekly:**<br>• RAL AUC ↑ 71% and $C_{min}$ ↓ 12%<br>**Rifapentine 600 mg Once Daily:**<br>• RAL $C_{min}$ ↓ 41% | For once-weekly rifapentine and RAL 400 mg twice daily, no dose adjustment needed.<br>**Do not coadminister with once-daily rifapentine.** |
| ***Macrolides*** | | | |
| **Azithromycin** | All INSTIs | ↔ azithromycin expected | No dose adjustment needed. |
| **Clarithromycin** | BIC | ↑ BIC possible | No dose adjustment needed. |
| | DTG, RAL | ↔ clarithromycin expected | No dose adjustment needed. |
| | EVG/c | ↑ clarithromycin expected<br>↑ COBI possible | Reduce clarithromycin dose by 50% in patients with CrCl 50 to 60 mL/min.<br>**Do not coadminister in patients with CrCl <50 mL/min.** Consider alternative ARV or use azithromycin. |
| **Erythromycin** | BIC | ↑ BIC possible | No dose adjustment needed. |
| | DTG, RAL | ↔ INSTI expected<br>↔ erythromycin expected | No dose adjustment needed. |
| | EVG/c | ↑ erythromycin expected<br>↑ COBI possible | No data available for dose recommendation. Consider alternative ARV or use azithromycin. |
| **Anticoagulants** | | | |
| **Apixaban** | BIC, DTG, RAL | ↔ apixaban expected | No dose adjustment needed. |
| | EVG/c | ↑ apixaban expected | **Do not coadminister** in patients who require apixaban 2.5 mg twice daily.<br>Reduce apixaban dose by 50% in patients who require apixaban 5 mg or 10 mg twice daily. |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 4 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Anticoagulants**, continued | | | |
| **Betrixaban** | BIC, DTG, RAL | ↔ betrixaban expected | No dose adjustment needed. |
| | EVG/c | ↑ betrixaban expected | Administer initial single dose of betrixaban 80 mg, followed by betrixaban 40 mg once daily. |
| **Dabigatran** | BIC, DTG, RAL | ↔ dabigatran expected | No dose adjustment needed. |
| | EVG/c | ↑ dabigatran expected<br>**With COBI 150 mg Alone:**<br>• Dabigatran AUC ↑ 110% to 127% | Dabigatran dosing recommendation depends on indication and renal function. Refer to dabigatran prescribing information for dosing instructions when using dabigatran concomitantly with P-glycoprotein inhibitors. |
| **Edoxaban** | BIC, DTG, RAL | ↔ edoxaban expected | No dose adjustment needed. |
| | EVG/c | ↔ or ↑ edoxaban expected | **Stroke Prevention in Nonvalvular Atrial Fibrillation:**<br>• No dose adjustment needed.<br>**Deep Venous Thrombosis and Pulmonary Embolism:**<br>• Administer edoxaban 30 mg once daily. |
| **Rivaroxaban** | BIC, DTG, RAL | ↔ rivaroxaban expected | No dose adjustment needed. |
| | EVG/c | ↑ rivaroxaban expected | **Do not coadminister.** |
| **Warfarin** | BIC, DTG, RAL | ↔ warfarin expected | No dose adjustment needed. |
| | EVG/c | ↑ or ↓ warfarin possible | Monitor INR and adjust warfarin dose accordingly. |
| **Anticonvulsants** | | | |
| **Carbamazepine** | BIC | ↓ BIC possible | **Do not coadminister.** |
| | DTG | DTG AUC ↓ 49% | Increase DTG dose to 50 mg twice daily in ART-naive or ART-experienced, INSTI-naive patients.<br>**Do not coadminister in INSTI-experienced patients with known or suspected INSTI resistance.** |
| | EVG/c | Carbamazepine AUC ↑ 43%<br>EVG AUC ↓ 69% and $C_{min}$ ↓ >99%<br>↓ COBI expected | **Contraindicated.** |
| | RAL | ↓ or ↔ RAL possible | **Do not coadminister.** |
| **Eslicarbazepine** | All INSTIs | ↓ INSTI possible<br>↓ COBI possible | Consider alternative ARV or anticonvulsant. |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 5 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Anticonvulsants**, continued | | | |
| **Ethosuximide** | BIC, DTG, RAL | ↔ ethosuximide expected | No dose adjustment needed. |
| | EVG/c | ↑ ethosuximide possible | Monitor for ethosuximide-related adverse events. |
| **Lamotrigine** | BIC, DTG, RAL | ↔ lamotrigine expected | No dose adjustment needed. |
| | EVG/c | No data | Monitor anticonvulsant concentrations and adjust dose accordingly. |
| **Oxcarbazepine** | BIC, DTG | ↓ BIC and DTG possible | **Do not coadminister.** |
| | EVG/c, RAL | ↓ EVG/c and RAL possible | Consider alternative ARV or anticonvulsant. |
| **Phenobarbital Phenytoin** | BIC | ↓ BIC possible | **Do not coadminister.** |
| | DTG | ↓ DTG possible | **Do not coadminister.** |
| | EVG/c | ↓ EVG/c expected | **Contraindicated.** |
| | RAL | ↓ or ↔ RAL possible | **Do not coadminister.** |
| **Valproic Acid** | All INSTIs | No data | Monitor valproic acid concentration and virologic response. |
| **Antidepressants, Anxiolytics, Antipsychotics**<br>Also see Sedative/Hypnotics section below | | | |
| **Aripiprazole** | BIC, DTG, RAL | ↔ aripiprazole expected | No dose adjustment needed. |
| | EVG/c | ↑ aripiprazole expected | Administer 25% of the usual aripiprazole dose. Titrate based on aripiprazole efficacy and adverse events. Refer to aripiprazole label for dosing recommendations in patients who are known to be CYP2D6 poor metabolizers or who have major depressive disorder. |
| **Brexpiprazole** | BIC, DTG, RAL | ↔ brexpiprazole expected | No dose adjustment needed. |
| | EVG/c | ↑ brexpiprazole expected | Administer 25% of the usual brexpiprazole dose. Titrate based on brexpiprazole efficacy and adverse events. Refer to brexpiprazole label for dosing recommendations in patients who are known to be CYP2D6 poor metabolizers or who have major depressive disorder. |
| **Bupropion** | BIC, DTG, RAL | ↔ bupropion expected | No dose adjustment needed. |
| | EVG/c | ↑ bupropion possible | Titrate bupropion dose based on clinical response. |
| **Buspirone** | BIC, DTG, RAL | ↔ buspirone expected | No dose adjustment needed. |
| | EVG/c | ↑ buspirone possible | Initiate buspirone at a low dose. Buspirone dose reduction may be needed. |

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Antidepressants, Anxiolytics, Antipsychotics**, continued<br>Also see Sedative/Hypnotics section below | | | |
| **Cariprazine** | BIC, DTG, RAL | ↔ cariprazine expected | No dose adjustment needed. |
| | EVG/c | ↑ cariprazine expected | **Starting Cariprazine in a Patient Who Is Already Receiving EVG/c:**<br>• Administer cariprazine 1.5 mg on Day 1 and Day 3, with no dose given on Day 2. From Day 4 onward, administer cariprazine 1.5 mg daily. Dose can be increased to a maximum dose of 3 mg daily. If EVG/c is withdrawn, cariprazine dose may need to be increased.<br>**Starting EVG/c in a Patient Who is Already Receiving Cariprazine:**<br>• For patients receiving cariprazine 3 mg or 6 mg daily, reduce cariprazine dose by half. For patients taking cariprazine 4.5 mg daily, the dose should be reduced to 1.5 mg or 3 mg daily. For patients taking cariprazine 1.5 mg daily, change to 1.5 mg every other day. If EVG/c is withdrawn, cariprazine dose may need to be increased. |
| **Iloperidone** | BIC, DTG, RAL | ↔ iloperidone expected | No dose adjustment needed. |
| | EVG/c | ↑ iloperidone expected | Decrease iloperidone dose by 50%. |
| **Lurasidone** | BIC, DTG, RAL | ↔ lurasidone expected | No dose adjustment needed. |
| | EVG/c | ↑ lurasidone expected | **Contraindicated.** |
| **Nefazodone** | BIC, DTG, RAL | ↔ nefazodone expected | No dose adjustment needed. |
| | EVG/c | ↑ nefazodone expected | Consider alternative ARV or antidepressant. |
| **Pimavanserin** | BIC, DTG, RAL | ↔ pimavanserin expected | No dose adjustment needed. |
| | EVG/c | ↑ pimavanserin expected | Reduce pimavanserin dose to 10 mg. |
| **Pimozide** | BIC, DTG, RAL | ↔ pimozide expected | No dose adjustment needed. |
| | EVG/c | ↑ pimozide expected | **Contraindicated.** |
| **Quetiapine** | BIC, DTG, RAL | ↔ quetiapine expected | No dose adjustment needed. |
| | EVG/c | ↑ quetiapine AUC expected | **Starting Quetiapine in a Patient Receiving EVG/c:**<br>• Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine efficacy and adverse events.<br>**Starting EVG/c in a Patient Receiving a Stable Dose of Quetiapine:**<br>• Reduce quetiapine dose to 1/6 of the current dose, and closely monitor for quetiapine efficacy and adverse events. |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 7 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Antidepressants, Anxiolytics, Antipsychotics**, continued<br>Also see Sedative/Hypnotics section below | | | |
| **Selective Serotonin Reuptake Inhibitors**<br>Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline | EVG/c | ↔ EVG<br>↔ sertraline | No dose adjustment needed. |
| | | ↑ other SSRIs possible | Initiate with lowest dose of SSRI and titrate dose carefully based on antidepressant response. |
| | BIC, DTG, RAL | ↔ BIC, DTG and RAL expected<br>↔ SSRI expected | No dose adjustment needed. |
| **Tricyclic Antidepressants**<br>Amitriptyline, desipramine, doxepin, imipramine, nortriptyline | BIC, DTG, RAL | ↔ TCA expected | No dose adjustment needed. |
| | EVG/c | Desipramine AUC ↑ 65% | Initiate with lowest dose of TCA and titrate dose carefully. |
| | | ↑ TCA expected | Initiate with lowest dose of TCA and titrate dose carefully based on antidepressant response and/or drug concentrations. |
| **Trazodone** | BIC, DTG, RAL | ↔ trazodone expected | No dose adjustment needed. |
| | EVG/c | ↑ trazodone possible | Initiate with lowest dose of trazodone and titrate dose carefully. |
| **Ziprasidone** | BIC, DTG, RAL | ↔ ziprasidone expected | No dose adjustment needed. |
| | EVG/c | ↑ ziprasidone possible | Monitor for ziprasidone-related adverse events. |
| **Other Antipsychotics**<br>CYP3A4 and/or CYP2D6 substrates (e.g., perphenazine, risperidone, thioridazine) | EVG/c | ↑ antipsychotic possible | Initiate antipsychotic at a low dose. Antipsychotic dose reduction may be needed. |
| **Antifungals** | | | |
| **Isavuconazole** | BIC | ↑ BIC possible | No dose adjustment needed. |
| | EVG/c | ↑ isavuconazole expected<br>↑ or ↓ EVG and COBI possible | If coadministered, consider monitoring isavuconazole concentrations and assessing virologic response. |
| **Itraconazole** | BIC | ↑ BIC expected | No dose adjustment needed. |
| | DTG, RAL | ↔ INSTI expected<br>↔ itraconazole expected | No dose adjustment needed. |
| | EVG/c | ↑ itraconazole expected<br>↑ EVG and COBI possible | Consider monitoring itraconazole concentrations to guide dose adjustments. **Do not coadminister with high itraconazole doses (>200 mg/day) unless guided by itraconazole concentrations.** |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 8 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Antifungals**, continued | | | |
| **Posaconazole** | BIC | ↑ BIC expected | No dose adjustment needed. |
| | DTG, RAL | ↔ INSTI expected<br>↔ posaconazole expected | No dose adjustment needed. |
| | EVG/c | ↑ EVG and COBI possible<br>↑ posaconazole possible | If coadministered, monitor posaconazole concentrations. |
| **Voriconazole** | BIC | ↑ BIC possible | No dose adjustment needed. |
| | DTG, RAL | ↔ INSTI expected<br>↔ voriconazole expected | No dose adjustment needed. |
| | EVG/c | ↑ voriconazole expected<br>↑ EVG and COBI possible | **Do not coadminister voriconazole and COBI unless benefit outweighs risk.** If coadministered, consider monitoring voriconazole concentrations and adjust dose accordingly. |
| **Antihyperglycemics** | | | |
| **Metformin** | BIC | Metformin AUC ↑ 39% | Monitor for adverse events of metformin. |
| | DTG | **DTG 50 mg Once Daily plus Metformin 500 mg Twice Daily:**<br>• Metformin AUC ↑ 79% and $C_{max}$ ↑ 66%<br>**DTG 50 mg Twice Daily plus Metformin 500 mg Twice Daily:**<br>• Metformin AUC ↑ 2.4-fold and $C_{max}$ ↑ 2-fold | Start metformin at lowest dose and titrate based on glycemic control. Monitor for adverse events of metformin.<br>When starting/stopping DTG in patients on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control and/or minimize adverse events of metformin. |
| | RAL | ↔ metformin expected | No dose adjustment needed. |
| **Saxagliptin** | BIC, DTG, RAL | ↔ saxagliptin expected | No dose adjustment needed. |
| | EVG/c | ↑ saxagliptin expected | Limit saxagliptin dose to 2.5 mg once daily. |
| **Dapagliflozin/Saxagliptin** | BIC, DTG, RAL | ↔ dapagliflozin or saxagliptin expected | No dose adjustment needed. |
| | EVG/c | ↑ saxagliptin expected | **Do not coadminister.** Dapagliflozin is only available as a coformulated drug that contains 5 mg of saxagliptin. When coadministered with EVG/c, the dose of saxagliptin should not exceed 2.5 mg once daily; thus, this combination **is not recommended**. |
| **Antiplatelets** | | | |
| **Clopidogrel** | BIC, DTG, RAL | ↔ clopidogrel expected | No dose adjustment needed. |
| | EVG/c | ↓ clopidogrel active metabolite, with impaired platelet inhibition expected | **Do not coadminister.** |
| **Prasugrel** | BIC, DTG, RAL | ↔ prasugrel expected | No dose adjustment needed. |
| | EVG/c | ↓ prasugrel active metabolite, with no impairment of platelet inhibition expected | Insufficient data to make a dose recommendation. |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 9 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Antiplatelets**, continued | | | |
| **Ticagrelor** | BIC, DTG, RAL | ↔ ticagrelor expected | No dose adjustment needed. |
| | EVG/c | ↑ ticagrelor expected | **Do not coadminister.** |
| **Vorapaxar** | BIC, DTG, RAL | ↔ vorapaxar expected | No dose adjustment needed. |
| | EVG/c | ↑ vorapaxar expected | **Do not coadminister.** |
| **Beta-Agonists, Long-Acting Inhaled** | | | |
| **Arformoterol, Formoterol** | All INSTIs | ↔ arformoterol or formoterol expected | No dose adjustment needed. |
| **Indacaterol** | BIC, DTG, RAL | ↔ indacaterol expected | No dose adjustment needed. |
| | EVG/c | ↑ indacaterol expected | |
| **Olodaterol** | BIC, DTG, RAL | ↔ olodaterol expected | No dose adjustment needed. |
| | EVG/c | ↑ olodaterol expected | |
| **Salmeterol** | BIC, DTG, RAL | ↔ salmeterol expected | No dose adjustment needed. |
| | EVG/c | ↑ salmeterol possible | **Do not coadminister** because of potential increased risk of salmeterol-associated cardiovascular events. |
| **Cardiac Medications** | | | |
| **Amiodarone** | BIC, DTG, RAL | ↔ INSTI expected<br>↔ amiodarone expected | No dose adjustment needed. |
| | EVG/c | ↑ INSTI possible<br>↑ amiodarone possible | **Do not coadminister, unless benefits outweigh risks.** If coadministration is necessary, monitor for amiodarone-related adverse events and consider monitoring ECG and amiodarone concentrations. |
| **Bepridil, Digoxin, Disopyramide, Dronedarone, Flecainide, Systemic Lidocaine, Mexilitine, Propafenone, Quinidine** | BIC, DTG | ↔ expected for the listed antiarrhythmics, except for disopyramide<br>↑ disopyramide possible | No dose adjustment needed.<br>Monitor for disopyramide-related adverse events. |
| | RAL | ↔ expected for the listed antiarrhythmics | No dose adjustment needed. |
| | EVG/c | ↑ antiarrhythmics possible<br>Digoxin $C_{max}$ ↑ 41% and ↔ AUC | Therapeutic drug monitoring for antiarrhythmics, if available, is recommended. |
| **Beta-Blockers** (e.g., metoprolol, timolol) | BIC, DTG, RAL | ↔ beta-blocker expected | No dose adjustment needed. |
| | EVG/c | ↑ beta-blocker possible | Beta-blocker dose may need to be decreased; adjust dose based on clinical response.<br>Consider using an alternative ARV, or a beta-blocker that is not metabolized by CYP450 enzymes (e.g., atenolol, labetalol, nadolol, sotalol). |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 10 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Cardiac Medications**, continued | | | |
| **Bosentan** | BIC, DTG | ↓ BIC and DTG possible | No dose adjustment needed. |
| | RAL | ↔ bosentan expected | No dose adjustment needed. |
| | EVG/c | ↑ bosentan possible | **In Patients on EVG/c ≥10 Days:**<br>• Start bosentan at 62.5 mg once daily or every other day based on individual tolerability.<br>**In Patients on Bosentan Who Require EVG/c:**<br>• Stop bosentan ≥36 hours before EVG/c initiation. At least 10 days after initiation of EVG/c, resume bosentan at 62.5 mg once daily or every other day based on individual tolerability. |
| **Calcium Channel Blockers** | BIC | ↑ BIC possible with diltiazem<br>↔ expected for all other CCBs | No dose adjustment needed. |
| | DTG, RAL | ↔ INSTI expected<br>↔ CCB expected | No dose adjustment needed. |
| | EVG/c | ↑ CCB possible | Titrate CCB dose and monitor for CCB efficacy and adverse events. |
| **Dofetilide** | BIC, DTG | ↑ dofetilide expected | **Contraindicated.** |
| | RAL | ↔ dofetilide expected | No dose adjustment needed. |
| | EVG/c | ↑ dofetilide possible | **Do not coadminister.** |
| **Eplerenone** | BIC, DTG, RAL | ↔ eplerenone expected | No dose adjustment needed. |
| | EVG/c | ↑ eplerenone expected | **Contraindicated.** |
| **Ivabradine** | BIC, DTG, RAL | ↔ ivabradine expected | No dose adjustment needed. |
| | EVG/c | ↑ ivabradine expected | **Contraindicated.** |
| **Ranolazine** | BIC, DTG, RAL | ↔ ranolazine expected | No dose adjustment needed. |
| | EVG/c | ↑ ranolazine expected | **Contraindicated.** |
| **Corticosteroids** | | | |
| **Beclomethasone**<br>Inhaled or intranasal | BIC, DTG, EVG/c, RAL | ↔ glucocorticoid expected | No dose adjustment needed. |
| **Budesonide, Ciclesonide, Fluticasone, Mometasone**<br>Inhaled or intranasal | BIC, DTG, RAL | ↔ glucocorticoid expected | No dose adjustment needed. |
| | EVG/c | ↑ glucocorticoid possible | **Do not coadminister unless potential benefits of inhaled or intranasal corticosteroid outweigh the risks of systemic corticosteroid adverse effects.** Coadministration can result in adrenal insufficiency and Cushing's syndrome. Consider using an alternative corticosteroid (e.g., beclomethasone). |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 11 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Corticosteroids**, continued | | | |
| **Betamethasone, Budesonide**<br>Systemic | BIC, DTG, RAL | ↔ INSTI expected<br>↔ glucocorticoid expected | No dose adjustment needed. |
| | EVG/c | ↑ glucocorticoids possible<br>↓ EVG possible | **Do not coadminister unless potential benefits of systemic budesonide outweigh the risks of systemic corticosteroid adverse effects.** Coadministration can result in adrenal insufficiency and Cushing's syndrome. |
| **Dexamethasone**<br>Systemic | BIC | ↓ BIC possible | Consider alternative corticosteroid for long-term use or alternative ARV. If coadministration is necessary, monitor virologic response to ART. |
| | DTG, RAL | ↔ INSTI expected | No dose adjustment needed. |
| | EVG/c | ↓ EVG and COBI possible | Consider alternative corticosteroid for long-term use or alternative ARV. If coadministration is necessary, monitor virologic response to ART. |
| **Prednisone, Prednisolone**<br>Systemic | BIC, DTG, RAL | ↔ glucocorticoid expected | No dose adjustment needed. |
| | EVG/c | ↑ prednisolone possible | Coadministration may be considered if the potential benefits outweigh the risks of systemic corticosteroid adverse effects. If coadministration is necessary, monitor for adrenal insufficiency and Cushing's syndrome. |
| **Betamethasone, Methylprednisolone, Prednisolone, Triamcinolone**<br>Local injections, including intra-articular, epidural, or intra-orbital | BIC, DTG, RAL | ↔ glucocorticoid expected | No dose adjustment needed. |
| | EVG/c | ↑ glucocorticoid expected | **Do not coadminister.** Coadministration may result in adrenal insufficiency and Cushing's syndrome. |
| **Hepatitis C Direct-Acting Antiviral Agents** | | | |
| **Daclatasvir** | BIC, RAL | No data | No dose adjustment needed. |
| | DTG | ↔ daclatasvir | No dose adjustment needed. |
| | EVG/c | ↑ daclatasvir | Decrease daclatasvir dose to 30 mg once daily. |
| **Dasabuvir plus Ombitasvir/Paritaprevir/RTV** | BIC, DTG | No data | No dose adjustment needed. |
| | EVG/c | No data | **Do not coadminister.** |
| | RAL | RAL AUC ↑ 134% | No dose adjustment needed. |
| **Elbasvir/Grazoprevir** | BIC | ↔ BIC expected | No dose adjustment needed. |
| | DTG | ↔ elbasvir<br>↔ grazoprevir<br>↔ DTG | No dose adjustment needed. |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 12 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Hepatitis C Direct-Acting Antiviral Agents**, continued | | | |
| **Elbasvir/Grazoprevir** | EVG/c | ↑ elbasvir expected<br>↑ grazoprevir expected | **Do not coadminister.** |
| | RAL | ↔ elbasvir<br>↔ grazoprevir<br>↔ RAL with elbasvir<br>RAL AUC ↑ 43% with grazoprevir | No dose adjustment needed. |
| **Glecaprevir/Pibrentasvir** | BIC | ↔ BIC expected | No dose adjustment needed. |
| | DTG, RAL | No significant effect | No dose adjustment needed. |
| | EVG/c | Glecaprevir AUC ↑ 3-fold<br>Pibrentasvir AUC ↑ 57%<br>EVG AUC ↑ 47% | No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events. Consider monitoring for hepatotoxicity if coadministered with TDF or TAF. |
| **Ledipasvir/Sofosbuvir** | BIC, DTG, RAL | ↔ DTG and RAL | No dose adjustment needed. |
| | EVG/c/ TDF/FTC | ↑ TDF expected<br>↑ ledipasvir expected | **Do not coadminister.** |
| | EVG/c/ TAF/FTC | ↔ EVG/c/TAF/FTC expected | No dose adjustment needed. |
| **Sofosbuvir** | All INSTIs | ↔ INSTI expected<br>↔ sofosbuvir expected | No dose adjustment needed. |
| **Sofosbuvir/Velpatasvir** | All INSTIs | ↔ INSTI expected<br>↔ sofosbuvir and velpatasvir expected | No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events. |
| **Sofosbuvir/Velpatasvir/ Voxilaprevir** | EVG/c | **When Administered with Sofosbuvir/ Velpatasvir/Voxilaprevir (400 mg/100 mg/100 mg) plus Voxilaprevir 100 mg:**<br>• Sofosbuvir AUC ↑ 22%<br>• ↔ velpatasvir<br>• Voxilaprevir AUC ↑ 2-fold | No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events. Consider monitoring for hepatotoxicity if coadministered with TDF or TAF. |
| | BIC, DTG, RAL | ↔ INSTI expected<br>↔ sofosbuvir, velpatasvir, and voxilaprevir expected | No dose adjustment needed. |
| **Herbal Products** | | | |
| **St. John's Wort** | BIC, DTG | ↓ BIC and DTG possible | **Do not coadminister.** |
| | EVG/c | ↓ EVG and COBI expected | **Contraindicated.** |
| **Hormonal Therapies** | | | |
| **Contraceptives: Non-Oral** | All INSTIs | No data | No drug-drug interaction studies have been conducted with INSTIs and non-oral routes of hormone administration. It is unclear whether drug-drug interaction data for oral drugs can be used to predict interactions for non-oral drugs. |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 13 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Hormonal Therapies**, continued | | | |
| **Contraceptives – Oral** | BIC, DTG, RAL | ↔ ethinyl estradiol and norgestimate<br>↔ INSTI | No dose adjustment needed. |
| | EVG/c | Norgestimate AUC, $C_{max}$, and $C_{min}$ ↑ >2-fold<br>Ethinyl estradiol AUC ↓ 25% and $C_{min}$ ↓ 44% | The effects of increases in progestin (norgestimate) are not fully known and may include insulin resistance, dyslipidemia, acne, and venous thrombosis. Weigh the risks and benefits of using the drug and consider using an alternative ARV or contraceptive method. |
| | | ↑ drospirenone possible | Clinical monitoring is recommended, due to the potential for hyperkalemia. Consider using alternative ARV or contraceptive method. |
| **Gender-Affirming Therapy** | BIC, DTG, EVG/c, RAL | ↔ goserelin, leuprolide acetate, and spironolactone expected | No dose adjustment needed. |
| | BIC, DTG, RAL | ↔ estrogen expected | No dose adjustment needed. |
| | | ↔ testosterone expected | No dose adjustment needed. |
| | EVG/c | ↓ or ↑ estradiol possible<br>↑ dutasteride and finasteride possible | Adjust dutasteride dose as needed based on clinical effects and endogenous hormone concentrations. |
| | | ↑ testosterone possible | Monitor masculinizing effects of testosterone and monitor for adverse effects. Adjust testosterone dose as necessary. |
| **Menopausal Replacement Therapy** | BIC, DTG, RAL | ↔ estrogen expected with estradiol or conjugated estrogen (equine and synthetic)<br>↔ drospirenone, medroxyprogesterone, and micronized progesterone expected | No dose adjustment needed. |
| | EVG/c | ↓ or ↑ estrogen possible<br>↑ drospirenone possible<br>↑ oral medroxyprogesterone possible<br>↑ oral micronized progesterone possible | Adjust estrogen and progestin dose as needed based on clinical effects. |
| **Immunosuppressants** | | | |
| **Cyclosporine, Everolimus, Sirolimus, Tacrolimus** | BIC, DTG, RAL | ↔ immunosuppressant expected | No dose adjustment needed. |
| | EVG/c | ↑ immunosuppressant possible | Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary. |
| **Lipid-Modifying Agents** | | | |
| **Atorvastatin** | BIC, DTG, RAL | ↔ atorvastatin expected | No dose adjustment needed. |
| | EVG/c | Atorvastatin AUC ↑ 2.6-fold and $C_{max}$ ↑ 2.3-fold | Titrate statin dose carefully and administer the lowest effective dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily. |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 14 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Lipid-Modifying Agents**, continued | | | |
| **Lomitapide** | BIC, DTG, RAL | ↔ lomitapide expected | No dose adjustment needed. |
| | EVG/c | ↑ lomitapide expected | **Contraindicated.** |
| **Lovastatin** | BIC, DTG, RAL | ↔ lovastatin expected | No dose adjustment needed. |
| | EVG/c | Significant ↑ lovastatin expected | **Contraindicated.** |
| **Pitavastatin, Pravastatin** | BIC, DTG, RAL | ↔ statin expected | No dose adjustment needed. |
| | EVG/c | No data | No data available for dose recommendation. |
| **Rosuvastatin** | BIC, DTG, RAL | ↔ rosuvastatin expected | No dose adjustment needed. |
| | EVG/c | Rosuvastatin AUC ↑ 38% and $C_{max}$ ↑ 89% | Titrate statin dose carefully and use the lowest effective dose while monitoring for adverse events. |
| **Simvastatin** | BIC, DTG, RAL | ↔ simvastatin expected | No dose adjustment needed. |
| | EVG/c | Significant ↑ simvastatin expected | **Contraindicated.** |
| **Narcotics and Treatment for Opioid Dependence** | | | |
| **Buprenorphine**<br>Sublingual, buccal, or implant | BIC, DTG | ↔ buprenorphine and norbuprenorphine (active metabolite) expected | No dose adjustment needed. |
| | EVG/c | Buprenorphine AUC ↑ 35% and $C_{min}$ ↑ 66%<br>Norbuprenorphine (active metabolite) AUC ↑ 42% and $C_{min}$ ↑ 57% | No dose adjustment needed. Monitor for adverse events of buprenorphine. When transferring buprenorphine from transmucosal administration to implantation, monitor to ensure buprenorphine effect is adequate and not excessive. |
| | RAL | ↔ buprenorphine and norbuprenorphine (active metabolite) (sublingual)<br>↔ buprenorphine or norbuprenorphine (active metabolite) expected (implant) | No dose adjustment needed. |
| **Fentanyl** | BIC, DTG, RAL | ↔ fentanyl expected | No dose adjustment needed. |
| | EVG/c | ↑ fentanyl | Monitor for fentanyl efficacy and adverse events, including potentially fatal respiratory depression. |
| **Lofexidine** | BIC, DTG, RAL | ↔ lofexidine expected | No dose adjustment needed. |
| | EVG/c | ↑ lofexidine possible | Monitor for lofexidine-related adverse events, including symptoms of orthostasis and bradycardia. |
| **Methadone** | All INSTIs | ↔ methadone | No dose adjustment needed. |
| **Tramadol** | BIC, DTG, RAL | ↔ tramadol and M1 (active metabolite) expected | No dose adjustment needed. |
| | EVG/c | ↑ tramadol expected<br>↓ M1 (active metabolite) possible | Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events. |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 15 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **PDE5 Inhibitors** | | | |
| **Avanafil** | BIC, DTG, RAL | ↔ avanafil expected | No dose adjustment needed. |
| | EVG/c | No data | **Do not coadminister.** |
| **Sildenafil** | BIC, DTG, RAL | ↔ sildenafil expected | No dose adjustment needed. |
| | EVG/c | ↑ sildenafil expected | **For Treatment of Erectile Dysfunction:**<br>• Start with sildenafil 25 mg every 48 hours and monitor for adverse effects of sildenafil.<br>**Contraindicated** for treatment of PAH. |
| **Tadalafil** | BIC, DTG, RAL | ↔ tadalafil expected | No dose adjustment needed. |
| | EVG/c | ↑ tadalafil expected | **For Treatment of Erectile Dysfunction:**<br>• Start with tadalafil 5 mg and do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for adverse effects of tadalafil.<br>**For Treatment of PAH**<br>*In Patients on EVG/c >7 Days:*<br>• Start with tadalafil 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability.<br>*In Patients on Tadalafil who Require EVG/c:*<br>• Stop tadalafil ≥24 hours before EVG/c initiation. Seven days after EVG/c initiation, restart tadalafil at 20 mg once daily, and increase to tadalafil 40 mg once daily based on tolerability. |
| **Vardenafil** | BIC, DTG, RAL | ↔ vardenafil expected | No dose adjustment needed. |
| | EVG/c | ↑ vardenafil expected | Start with vardenafil 2.5 mg every 72 hours and monitor for adverse effects of vardenafil. |
| **Sedative/Hypnotics** | | | |
| **Buspirone** | BIC, DTG, RAL | ↔ buspirone expected | No dose adjustment needed. |
| | EVG/c | ↑ buspirone expected | Initiate buspirone at a low dose. Dose reduction may be needed. |
| **Clonazepam, Clorazepate, Diazepam, Estazolam, Flurazepam** | BIC, DTG, RAL | ↔ benzodiazepine expected | No dose adjustment needed. |
| | EVG/c | ↑ benzodiazepine possible | Dose reduction of benzodiazepine may be necessary. Initiate with a low dose and monitor for benzodiazepine-related adverse events.<br>Consider using an alternative benzodiazepine, such as lorazepam, oxazepam, or temazepam. |
| **Midazolam, Triazolam** | BIC, RAL | ↔ benzodiazepine expected | No dose adjustment needed. |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 16 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Sedative/Hypnotics**, continued | | | |
| **Midazolam, Triazolam**, continued | DTG | **With DTG 25 mg:**<br>• ↔ midazolam AUC | No dose adjustment needed. |
| | EVG/c | ↑ midazolam expected<br>↑ triazolam expected | **Contraindicated. Do not coadminister triazolam or oral midazolam and EVG/c.**<br>Parenteral midazolam can be administered in a closely monitored setting. Consider dose reduction, especially if >1 dose is administered. |
| **Suvorexant** | BIC, DTG, RAL | ↔ suvorexant expected | No dose adjustment needed. |
| | EVG/c | ↑ suvorexant expected | **Do not coadminister.** |
| **Zolpidem** | BIC, DTG, RAL | ↔ zolpidem expected | No dose adjustment needed. |
| | EVG/c | ↑ zolpidem expected | Initiate zolpidem at a low dose. Dose reduction of zolpidem may be necessary. |
| **Miscellaneous Drugs** | | | |
| **Calcifediol** | BIC, DTG, RAL | ↔ calcifediol expected | No dose adjustment needed. |
| | EVG/c | ↑ calcifediol possible | Dose adjustment of calcifediol may be required. Monitor serum 25-hydroxyvitamin D, intact PTH, and serum Ca concentrations. |
| **Cisapride** | BIC, DTG, RAL | ↔ cisapride expected | No dose adjustment needed. |
| | EVG/c | ↑ cisapride expected | **Contraindicated.** |
| **Colchicine** | BIC, DTG, RAL | ↔ colchicine expected | No dose adjustment needed. |
| | EVG/c | ↑ colchicine expected | **Do not coadminister in patients with hepatic or renal impairment.**<br>**For Treatment of Gout Flares:**<br>• Administer a single dose of colchicine 0.6 mg, followed by colchicine 0.3 mg 1 hour later. Do not repeat dose for at least 3 days.<br>**For Prophylaxis of Gout Flares:**<br>• If original dose was colchicine 0.6 mg twice daily, decrease to colchicine 0.3 mg once daily. If dose was 0.6 mg once daily, decrease to 0.3 mg every other day.<br>**For Treatment of Familial Mediterranean Fever:**<br>• Do not exceed colchicine 0.6 mg once daily or 0.3 mg twice daily. |
| **Dronabinol** | BIC, DTG, RAL | ↔ dronabinol expected | No dose adjustment needed. |
| | EVG/c | ↑ dronabinol possible | Monitor for dronabinol-related adverse events. |

**Table 21d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 17 of 17)

| Concomitant Drug | INSTI | Effect on INSTI or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Miscellaneous Drugs**, continued | | | |
| **Eluxadoline** | BIC, DTG, RAL | ↔ eluxadoline expected | No dose adjustment needed. |
| | EVG/c | ↑ eluxadoline possible | Monitor for eluxadoline-related adverse events. |
| **Ergot Derivatives** | BIC, DTG, RAL | ↔ dihydroergotamine, ergotamine, and methylergonovine expected | No dose adjustment needed. |
| | EVG/c | ↑ dihydroergotamine, ergotamine, and methylergonovine expected | **Contraindicated.** |
| **Flibanserin** | BIC, DTG, RAL | ↔ flibanserin expected | No dose adjustment needed. |
| | EVG/c | ↑ flibanserin expected | **Contraindicated.** |
| **Polyvalent Cation Supplements**<br>Mg, Al, Fe, Ca, Zn, including multivitamins with minerals<br>**Note:** Please refer to the Acid Reducers section in this table for recommendations on use with Al-, Mg-, and Ca-containing antacids. | BIC | ↔ BIC AUC if administered simultaneously with Fe or Ca and food<br>BIC AUC ↓ 33% if administered simultaneously with $CaCO_3$ under fasting conditions<br>BIC AUC ↓ 63% if administered simultaneously with Fe under fasting conditions | **With Supplements That Contain Ca or Fe:**<br>• Administer BIC and supplements that contain Ca or Fe together with food.<br>**Do not coadminister BIC under fasting conditions simultaneously with, or 2 hours after, supplements that contain Ca or Fe.** |
| | DTG | DTG AUC ↓ 39% if administered simultaneously with $CaCO_3$ under fasting conditions<br>DTG AUC ↓ 54% if administered simultaneously with Fe under fasting conditions<br>↔ DTG when administered with Ca or Fe supplement simultaneously with food | **With Supplements That Contain Ca or Fe:**<br>• Administer DTG and supplements that contain Ca or Fe together with food, or administer DTG at least 2 hours before or at least 6 hours after supplement.<br>**Do not coadminister DTG under fasting conditions simultaneously with, or 2 hours after, supplements that contain Ca or Fe.** |
| | EVG/c, RAL | ↓ INSTI possible | If coadministration is necessary, administer INSTI at least 2 hours before or at least 6 hours after supplements that contain polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic response.<br>Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown. |

**Key to Symbols:**

↑ = increase

↓ = decrease

↔ = no change

**Key:** Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; AUC = area under the curve; BIC = bictegravir; Ca = calcium; $CaCO_3$ = calcium carbonate; CCB = calcium channel blocker; $C_{max}$ = maximum plasma concentration; $C_{min}$ = minimum plasma concentration; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DAA = direct-acting antiviral; DTG = dolutegravir; ECG = electrocardiogram; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; Fe = iron; FTC = emtricitabine; HCV = hepatitis C virus; INR= international normalized ratio; INSTI = integrase strand transfer inhibitor; Mg = magnesium; PAH = pulmonary arterial hypertension; PDE5 = Phosphodiesterase Type 5; PTH = parathyroid hormone; RAL = raltegravir; RTV = ritonavir; SSRI = selective serotonin reuptake inhibitors; TAF = tenofovir alafenamide; TCA = tricyclic antidepressants; TDF = tenofovir disoproxil fumarate; Zn = zinc