Regulatory Education for Industry (REdI):

PRESCRIPTION DRUG LABELING - CHALLENGES AND ISSUES

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Describing Clinically Significant Drug Interactions in WARNINGS AND PRECAUTIONS Section

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- The views and opinions expressed in this presentation represent those of the presenter, and do not necessarily represent an official FDA position.
- The labeling examples in this presentation are fictitious and are provided only to demonstrate current labeling development challenges.

W&P Section: Clinically Significant DI With Two Drug Classes – ENVARSUS XR

5.9 Risk of Rejection with Strong CYP3A Inducers and Risk of Serious Adverse Reactions with Strong CYP3A Inhibitors

The concomitant use of strong CYP3A inducers may increase the metabolism of tacrolimus, leading to lower whole blood trough concentrations and greater risk of rejection. In contrast, the concomitant use of strong CYP3A inhibitors may decrease the metabolism of tacrolimus, leading to higher whole blood trough concentrations and greater risk of serious adverse reactions (e.g., neurotoxicity, QT prolongation) *[see Warnings and Precautions (5.6, 5.10)]* Therefore, adjust ENVARSUS XR dose and monitor tacrolimus whole blood trough concentrations when coadministering ENVARSUS XR with strong CYP3A inhibitors (e.g., telaprevir, boceprevir, ritonavir, ketoconazole, itraconazole, voriconazole, clarithromycin) or strong CYP3A inducers (e.g., rifampin, rifabutin) *[see Dosage and Administration (2.3) and Drug Interactions (7.2)].*

W&P Section: Clinically Significant DI With Multiple Drugs - VITEKTA

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Adverse Reactions or Loss of Virologic Response Due to Drug Interactions

The concomitant use of VITEKTA and other drugs may result in known or potentially significant drug interactions, some of which may lead to *[see Drug Interactions (7)]:*

- Loss of therapeutic effect of VITEKTA and possible development of resistance.
- Possible clinically significant adverse reactions from greater exposures of concomitant drugs or elvitegravir.

See Table 4 for steps to prevent or manage these possible and known significant drug interactions, including dosing recommendations *[see Drug Interactions (7)]*. Consider the potential for drug interactions prior to and during VITEKTA therapy; review concomitant medications during VITEKTA therapy; and monitor for the adverse reactions associated with the concomitant drugs.