Paritaprevir may have its concentration decreased by Valproic Acid.

Concurrent administration of valproic acid with dasabuvir; ombitasvir; paritaprevir; ritonavir may result in altered valproic acid plasma concentrations and decreased concentrations of dasabuvir, ombitasvir, paritaprevir, and ritonavir. Valproic acid is an inducer of the drug transporter P-glycoprotein (P-gp) and an inhibitor/inducer of CYP3A4. Dasabuvir, ombitasvir, paritaprevir, and ritonavir are all substrates of P-gp, while ritonavir, paritaprevir, and dasabuvir (minor) are partially metabolized by CYP3A4. In addition, in a case report, possible ritonavir-mediated induction of valproic acid glucuronidation resulted in a decrease in valproic acid concentrations and efficacy. Caution and close monitoring are advised if these drugs are administered together.

Ribavirin and **Protease inhibitors**

Ribavirin causes synergistic or additive toxicity with Protease inhibitors.

The concomitant use of ribavirin and anti-retroviral protease inhibitors should be done with caution as both can cause hepatic damage. Most protease inhibitors have been associated with episodes of liver toxicity, with lopinavir/low-dose ritonavir, fosamprenavir/low-dose ritonavir, and nelfinavir being less hepatotoxic and tipranavir/low-dose ritonavir being the most hepatotoxic. Hyperbilirubinemia is often associated with atazanavir and/or indinavir therapy but does not reflect liver damage and is related to the inhibition of UDP glucuronosyltransferase. Overall, the HCV-HIV International Panel recommends the management of hepatotoxicity should be based on the knowledge of the mechanisms involved for each drug. Furthermore, they state that there are lower rates of liver-related mortality in coinfected patients taking HAART, even in those with end-stage liver disease, compared with patients not receiving HAART. Closely monitor patients for treatment-associated toxicities, especially hepatic decompensation.

Ritonavir and **Valproic Acid**

Ritonavir reduces effect of Valproic Acid.

In a single case report, possible ritonavir-mediated induction of valproic acid glucuronidation resulted in a decrease in valproic acid concentrations and efficacy. A man with bipolar disorder and HIV was stabilized on valproic acid 250 mg PO three times daily. Treatment was started with lopinavir; ritonavir and lamivudine, 3TC; zidovudine, ZDV in addition to the valproic acid. Three weeks after starting the antiretroviral medication, his manic symptoms worsened. Upon hospital admission due to the mania, his valproic acid concentration had decreased 48% (from 495 to 238 micromol/l). His valproic acid dose was increased to 1500 mg and olanzapine was introduced. The valproic acid concentration following this dose escalation was 392 micromol/l, and the patient improved clinically. Of note, the patient had also received paroxetine for treatment of comorbid depression when the antiretrovirals were initiated, but the SSRI was discontinued by the patient after 5 days. The SSRI may have