**Telaprevir (Incivek)**

**Discontinued.** This treatment has been discontinued.

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**Drug Summary**

Although telaprevir was a promising direct-acting antiviral agent that had impact in the hepatitis C treatment field during 2011 to 2013, it was subsequently replaced by newer direct-acting antiviral agents that were more effective, better tolerated, and more convenient. Based on the dwindling role of telaprevir after newer direct-acting antiviral agents were approved, Vertex pharmaceuticals discontinued the sales and distribution of telaprevir in the United States in October 2014. Telaprevir does have some current importance since persons who previously failed a telaprevir-based regimen may have developed resistant associated variants, which could potentially impact subsequent therapy.

**Adverse Effects**

The most significant adverse effects reported in the main registration trials and in post-marketing experience were rash, anorectal complaints, and anemia. When comparing triple therapy of telaprevir, peginterferon, and ribavirin with dual therapy of peginterferon and ribavirin alone significant differences were noted with rash (56% versus 34%), anemia (36% versus 17%), and anorectal complaints that include anorectal discomfort, anal pruritus, and hemorrhoids (29% versus 7%). In most cases, the rash that develops is eczematous or maculopapular in character and mild to moderate in severity; the rash is typically manageable with good skin care and topical emollients or corticosteroids. In some instances, however, telaprevir has caused serious skin rashes, including Steven's Johnson Syndrome (SJS), Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), and Toxic Epidermal Necrolysis (TEN). Teleprevir has a black box warning for fatal and non-fatal serious skin reactions.

**Resistance**
Treatment-emergent resistance mutations (NS3 amino acid substitutions conferring reduced susceptibility to telaprevir) were common among subjects in phase 3 trials who did not achieve SVR. In pooled analysis of the 525 subjects who did not achieve an SVR, 62% developed treatment-emergent variants – this occurred more frequently in genotype 1A patients (69%) than 1B patients (45%), and was observed in nearly all patients who failed telaprevir-based therapy during the first 12 weeks. The most common mutations to develop were V36M/A/L, T54A/S, R155K/T, and A156S/T; these mutations may develop alone or as combinations of mutations.

**Key Drug Interactions**

Telaprevir is a strong inhibitor of cytochrome p450 3A4 (CYP3A) and can also inhibit p-glycoprotein (P-gp), OATP1B1, and OATP2B1. Accordingly, when used concomitantly, telaprevir can have a significant impact on plasma concentrations of drugs that are metabolized by CYP3A, P-gp, OATP1B1, or OATP2B1. In addition, telaprevir is primarily metabolized by CYP3A. The coadministration of telaprevir with drugs that induce or inhibit CYP3A4/5 could decrease or increase telaprevir levels. See the [Telaprevir (Incivek) Full Prescribing Information](https://www.hepatitisc.uw.edu/page/treatment/drugs/telaprevir-drug) for a detailed description of important drug interactions with telaprevir. For complete information on telaprevir-related drug interactions, see the [Drug Interactions section in the Telaprevir (Incivek) Prescribing Information](https://www.hepatitisc.uw.edu/page/treatment/drugs/telaprevir-drug).