Peginterferon alfa-2b (*PegIntron*)

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### Drug Summary

Peginterferon alfa-2b has played a central role in the treatment for chronic hepatitis C for more than a decade when it replaced standard interferon alfa as a treatment for hepatitis C. In 2014, peginterferon alfa-2b remains an important component of hepatitis C therapy. The combination of peginterferon alfa plus ribavirin plus sofosbuvir is currently the preferred regimen for patients with genotypes 1 and 4, with peginterferon alfa plus ribavirin plus simeprevir an alternative. Peginterferon alfa-containing regimens that were previously considered preferred, but are no longer recommended as first-line regimens (a) peginterferon alfa plus ribavirin plus either boceprevir or telaprevir for genotype 1, and (b) peginterferon alfa plus ribavirin for genotype 2 or 3. Although peginterferon alfa-2b is expensive, it is significantly less expensive than direct acting antiviral agents, particularly sofosbuvir and simeprevir. In addition, enthusiasm for peginterferon alfa-2b has been hindered by its extensive adverse effects, necessity for weekly injections, and limited efficacy in certain patient populations, including those patients who are cirrhotic, HIV-coinfected, or who carry the *IL28B* TT genotype. With the anticipation that numerous direct acting agents will be approved in the next several years, it is likely that peginterferon alfa will become obsolete as the interferon-free combination regimens become available and become recommended for all hepatitis C genotypes.

### Class and Mechanism

Peginterferon alfa-2b consists of interferon alfa-2b covalently linked to a 12-kd linear polyethylene glycol (PEG). The biologic activity of peginterferon-alfa-2b derives from its interferon alfa-2b moiety, which impacts both adaptive and innate immune responses against hepatitis C virus. This alpha interferon binds to and activates human type 1 interferon receptors on hepatocytes which activates multiple intracellular signal transduction pathways, culminating in the expression of interferon-stimulated genes that produce an array of antiviral effects, such as blocking viral protein synthesis and inducing viral RNA mutagenesis. Compared with the native interferon alfa-2b, the peginterferon alfa-2b has sustained absorption, delayed clearance, and a prolonged half life.
Manufacturer for United States

Peginterferon alfa-2b (PegIntron) (Figure 1) is manufactured in the United States by Schering Corporation, a subsidiary of Merck & Co., Inc.

Cost and Medication Access

The wholesale acquisition cost (WAC) for peginterferon alfa-2b is approximately $8,400 for a 12-week supply, $16,800 for a 24-week supply, and $33,600 for a 48-week supply.

Adverse Effects

In most patients, peginterferon alfa-2b causes numerous problematic side effects. In clinical studies, the most common adverse reactions (reported in greater than 40%) were injection site inflammation/reaction, fatigue, headache, rigors, fevers, nausea, myalgia, and anxiety or emotional lability/irritability. In addition, significant hematologic toxicity can occur due to peginterferon alfa-2a, including neutropenia and thrombocytopenia. Patients can develop ophthalmologic disorders and all patients should receive a baseline eye examination and should have a prompt eye examination if they develop ocular symptoms while on therapy. Neuropsychiatric effects such as insomnia, depression, and irritability can also occur. Peginterferon alfa-2b may cause or aggravate life-threatening neuropsychiatric, autoimmune, ischemic, or infectious disorders. Further, the use of peginterferon alfa-2b in patients with cirrhosis can cause life-threatening hepatic decompensation. To report suspected adverse reactions, contact (1) Schering Corporation, a subsidiary of Merck & Co., at 1-800-526-4099 or (2) the FDA at 1-800-FDA-1088.

Key Drug Interactions

Caution is advised when administering peginterferon alfa-2b with drugs metabolized by cytochrome CYP2C8/9 (e.g., warfarin and phenytoin) or CYP2D6 (e.g. flecainide, dextromethorphan). Co-administration of peginterferon alfa-2b with methadone may result in increased drug levels of methadone and thus patients should undergo monitoring for any signs or symptoms of increased narcotic effect.

For complete information on peginterferon alfa-2b-related drug interactions, see the Drug Interactions section in the Peginterferon alfa-2b (PegIntron) Prescribing Information.
Figures

Figure 1 Packaging - Peginterferon alfa-2b *(PegIntron)*

Photo: Andrew Karpenko, University of Washington
Figure 2 RediPen® - Peginterferon alfa-2b (*PegIntron*)

Photo: Andrew Karpenko, University of Washington
Figure 3 RediPen® Dose Selector - Peginterferon alfa-2b (PegIntron)

Photo: Andrew Karpenko, University of Washington