P.O. Box 1000
North Wales, PA 19454-1099

March 2015

MERCK

SUBJECT: Merck Voluntarily Discontinuing All Doses of PEGINTRON® (peginterferon alfa-2b) REDIPEN® Single-Use Pre-Filled Pen

Dear Health Care Professional:

We would like to inform you that Merck has decided to voluntarily discontinue the manufacture of PEGINTRON REDIPEN Single-Use Pre-Filled Pen (PEGINTRON REDIPEN) for distribution in the United States. Based on current inventory levels and expected demand, Merck anticipates that inventory will be exhausted in or around July 2015, though inventory of certain images may be exhausted as early as the end of the first quarter of 2015. Please note that this is a business decision by Merck. This decision is not based on any safety or efficacy findings with this product. Due to scientific advancement, changes in treatment practices, and the consequent reduction in the demand for PEGINTRON, Merck plans to discontinue commercial supply of PEGINTRON REDIPEN in the United States in the following doses:

Deleted Product Name / Strength	Description	NDC
PEGINTRON (peginterferon alfa-2b) injection, 50 mcg per 0.5 mL	Box containing one 50 mcg per 0.5 mL PEGINTRON REDIPEN and 1 BD needle and 2 alcohol swabs	0085-1323-01
PEGINTRON (peginterferon alfa-2b) injection, 80 mcg per 0.5 mL	Box containing one 80 mcg per 0.5 mL PEGINTRON REDIPEN and 1 BD needle and 2 alcohol swabs	0085-1316-01
PEGINTRON (peginterferon alfa-2b) injection, 120 mcg per 0.5 mL	Box containing one 120 mcg per 0.5 mL PEGINTRON REDIPEN and 1 BD needle and 2 alcohol swabs	0085-1297-01
PEGINTRON (peginterferon alfa-2b) injection, 150 mcg per 0.5 mL	Box containing one 150 mcg per 0.5 mL PEGINTRON REDIPEN and 1 BD needle and 2 alcohol swabs	0085-1370-01

Merck remains committed to the treatment of chronic hepatitis C and will continue manufacturing and distributing PEGINTRON vials in all currently available doses. To facilitate patients currently undergoing therapy with PEGINTRON REDIPEN completing or switching their treatment to a doctor-directed, appropriate dose of PEGINTRON vial, Merck will continue to supply PEGINTRON REDIPEN to wholesalers until existing inventories have been exhausted. We recommend that no new patients be initiated on PEGINTRON REDIPEN moving forward. Appropriate patients should be switched to PEGINTRON vial as directed by their doctor. Patients transitioning from PEGINTRON REDIPEN to PEGINTRON vial should receive appropriate instruction from a healthcare provider, as well as the Medication Guide and Instructions for Use for PEGINTRON Powder for Injection, prior to first time use of PEGINTRON vial.

If you have any questions, please contact your Merck Account Executive.

Indications and Usage

PEGINTRON, as part of a combination regimen, is indicated for the treatment of chronic hepatitis C (CHC) in patients with compensated liver disease. PEGINTRON in combination with ribavirin and an approved hepatitis C virus (HCV) NS3/4A protease inhibitor is indicated in adult patients with HCV genotype 1 infection (see labeling of the specific HCV NS3/4A protease inhibitor for further information).

PEGINTRON in combination with ribavirin is indicated in patients with genotypes other than 1, pediatric patients (3–17 years of age), or in patients with genotype 1 infection where use of an HCV NS3/4A protease inhibitor is not warranted based on tolerability, contraindications, or other clinical factors.

PEGINTRON® (peginterferon alfa-2b) monotherapy should only be used in the treatment of CHC in patients with compensated liver disease if there are contraindications to or significant intolerance of ribavirin and is indicated for use only in previously untreated adult patients. Combination therapy provides substantially better response rates than monotherapy.

Selected Safety Information

WARNING: RISK OF SERIOUS DISORDERS AND RIBAVIRIN-ASSOCIATED EFFECTS

Alpha interferons, including PEGINTRON, may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Patients with persistently severe or worsening signs or symptoms of these conditions should be withdrawn from therapy. In many, but not all cases, these disorders resolve after stopping therapy with PEGINTRON.

Use with Ribavirin: Ribavirin may cause birth defects and death of the unborn child. Extreme care must be taken to avoid pregnancy in female patients and in female partners of male patients. Ribavirin causes hemolytic anemia. The anemia associated with ribavirin therapy may result in a worsening of cardiac disease.

Contraindications

PEGINTRON is contraindicated in patients with known hypersensitivity reactions, such as urticaria, angioedema, bronchoconstriction, anaphylaxis, Stevens-Johnson syndrome, and toxic epidermal necrolysis to interferon alpha or any other component of the product, autoimmune hepatitis, hepatic decompensation (Child-Pugh score >6 [Class B and C]) in cirrhotic CHC patients before or during treatment.

Combination therapy with PEGINTRON and ribavirin is additionally contraindicated in women who are pregnant or who may become pregnant, men whose female partners are pregnant, patients with hemoglobinopathies (eg, thalassemia major, sickle-cell anemia), and patients with creatinine clearance <50 mL/min. Ribavirin may cause fetal harm when administered to a pregnant woman. If ribavirin is used during pregnancy, or if the patient becomes pregnant while taking ribavirin, the patient should be apprised of the potential hazard to her fetus.

Pregnancy

Ribavirin may cause birth defects and death of the unborn child. Ribavirin therapy should not be started until a report of a negative pregnancy test has been obtained immediately prior to planned initiation of therapy. Patients should use at least 2 forms of contraception and have monthly pregnancy tests during treatment and during the 6-month period after treatment has been stopped.

Warnings

Patients should be monitored for the following serious conditions, some of which may become life threatening. Patients with persistently severe or worsening signs or symptoms should be withdrawn from therapy:

- Hemolytic anemia with ribavirin
- Neuropsychiatric events
- History of significant or unstable cardiac disease
- Hypothyroidism, hyperthyroidism, hyperglycemia, diabetes mellitus that cannot be effectively
- treated by medication
- New or worsening ophthalmologic disorders
- Ischemic and hemorrhagic cerebrovascular events
- Severe decreases in neutrophil or platelet counts
- History of autoimmune disorders
- Pancreatitis and ulcerative or hemorrhagic/ischemic colitis and pancreatitis
- Pulmonary infiltrates or pulmonary function impairment
- Child-Pugh score >6 (Class B and C)
- Increased creatinine levels in patients with renal insufficiency
- Serious, acute hypersensitivity reactions and cutaneous eruptions
- Dental/periodontal disorders reported with combination therapy
- Hypertriglyceridemia may result in pancreatitis (eg, triglycerides >1,000 mg/dL)
- Weight loss and growth inhibition reported during combination therapy in pediatric patients. Long-term growth inhibition (height) reported in some patients
- Peripheral neuropathy when used in combination with telbivudine

Selected Safety Information *(cont)*

Life-threatening or fatal neuropsychiatric events, including suicide, suicidal and homicidal ideation, depression, relapse of drug addiction/overdose, and aggressive behavior, sometimes directed towards others, have occurred in patients with and without a previous psychiatric disorder during treatment with PEGINTRON® (peginterferon alfa-2b) and follow-up. Psychoses, hallucinations, bipolar disorders, and mania have been observed in patients treated with interferon alpha. If patients develop psychiatric problems, including depression, it is recommended that the patients be carefully monitored during treatment and 6 months thereafter.

Blood Tests
Patients on therapy with peginterferon alfa/ribavirin (PR) should have complete blood count and blood chemistry testing before the start of treatment and then periodically thereafter. Patients who have preexisting cardiac abnormalities should have electrocardiograms done before PR therapy.

Adverse Events
Serious adverse reactions have occurred in approximately 12% of subjects in clinical trials. The most common serious events occurring in subjects treated with PEGINTRON and ribavirin were: depression and suicidal ideation, each occurring at a frequency of <1%. The most common fatal events occurring in subjects treated with PEGINTRON and ribavirin were: cardiac arrest, suicidal ideation, and suicide attempt, all occurring in <1% of subjects.

Greater than 96% of all subjects in clinical trials experienced 1 or more adverse events. The most commonly reported adverse reactions in adult subjects (<40%) were: injection-site inflammation/reaction, fatigue/asthenia, headache, rigors, fevers, nausea, myalgia, and anxiety/emotional lability/irritability. In general, the adverse reaction profile in the pediatric population was similar to that observed in adults. Most common adverse reactions (>25%) in pediatric patients were pyrexia (80%), headache (62%), neutropenia (33%), fatigue (30%), anorexia (29%), injection-site erythema (29%), and vomiting (27%). Important adverse reactions that occurred in <8% in pediatric patients were nervousness, aggression, anger, and depression. Weight and height gain of pediatric subjects treated with PEGINTRON plus ribavirin lagged behind that predicted by normative population data for the entire length of treatment. Severely inhibited growth velocity (less than 3rd percentile) was observed in 70% of the subjects while on treatment.

Drug Interactions
When administering PEGINTRON with medications metabolized by cytochrome P (CYP) 2C8/9 (eg, warfarin and phenytoin) or CYP2D6 (eg, flecainide), the therapeutic effect of these substrates may be decreased. PEGINTRON may increase methadone concentrations. Monitor patients for signs and symptoms of increased narcotic effects.

Patients receiving nucleoside analogues should be closely monitored for toxicities. Discontinue nucleoside reverse transcriptase inhibitors or reduce dose or discontinue interferon, ribavirin, or both with worsening toxicities. Concurrent use of didanosine with ribavirin is not recommended.

Before prescribing PEGINTRON, please read the accompanying Prescribing Information (1.25 mL diluent) and Prescribing Information (5 mL diluent), including the Boxed Warning about fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders and ribavirin-associated birth defects and fetal deaths. The Medication Guide, Instructions for Use (1.25 mL diluent) and Instructions for Use (5 mL diluent) for PEGINTRON Powder for Injection, and Instructions for Use for PEGINTRON REDIPEN also are available. For additional copies of the Prescribing Information, please call 800-672-6372, visit pegintron.com, or contact your Merck representative.

For more information about Merck products and services, please contact us at the Merck National Service Center at 800-444-2080.

Sincerely,

Bob McMahon
President, US Market
Merck Sharp & Dohme Corp.

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