Overview of 04/2016 and 08/2018 Betaseron (interferon beta-1b) Prescribing Information and Medication Guides

Section Updated	Text From Previous Betaseron PI (April 2016)	Text From Current Betaseron PI (August 2018)
Recent Major Changes	**----------RECENT MAJOR CHANGES----------** Dosage and Administration (2.3) 9/2015 Warnings and Precautions, Thrombotic Microangiopathy (5.7) 12/2015 Warnings and Precautions, Drug-induced Lupus Erythematosus (5.10) 4/2016	*[Recent Major Changes section removed]*
8.1 Pregnancy	**8.1 Pregnancy** Pregnancy Category C: There are no adequate and well-controlled studies in pregnant women; however, spontaneous abortions while on treatment were reported in four patients participating in the BETASERON RRMS clinical trial. BETASERON should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. When BETASERON (doses ranging from 0.028 to 0.42 mg/kg/day) was administered to pregnant rhesus monkeys throughout the period of organogenesis (gestation days 20 to 70), a dose-related abortifacient effect was observed. The low-effect dose is approximately 3 times the recommended human dose of 0.25 mg on a body surface area (mg/m2) basis. A no-effect dose for embryo-fetal developmental toxicity in rhesus monkeys was not established.	**8.1 Pregnancy** *Risk Summary* Although there have been no well-controlled studies in pregnant women, available data, which includes prospective observational studies, have not generally indicated a drug-associated risk of major birth defects with interferon beta-1b during pregnancy. Administration of BETASERON to monkeys during gestation resulted in increased embryo-fetal death at or above exposures greater than 3 times the human therapeutic dose (see Animal Data). In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively. The background risk of major birth defects and miscarriage for the indicated population is unknown. *Data* Human Data The majority of the observational studies reporting on pregnancies exposed to interferon beta-1b did not identify an association between the use of interferon beta-1b during pregnancy and an increased risk of major birth defects. Animal Data When BETASERON (doses ranging from 0.028 to 0.42 mg/kg/day) was administered to pregnant rhesus monkeys throughout the period of organogenesis (gestation days 20 to 70), a dose-related abortifacient effect was observed. The low-effect dose is approximately 3 times the recommended human dose of 0.25 mg on a body surface area (mg/m2) basis. A no-effect dose for embryo-fetal developmental toxicity in rhesus monkeys was not established.

Section Updated	Text From Previous Betaseron PI (April 2016)	Text From Current Betaseron PI (August 2018)
8.2 Lactation	[Section 8.2 not present in previous USPI]	**8.2 Lactation** *Risk Summary* There are no data on the presence of BETASERON in human milk, the effects on the breastfed infant, or the effects of the drug on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for BETASERON and any potential adverse effects on the breastfed child from BETASERON or from the underlying maternal condition.
8.3. Nursing Mothers	**8.3 Nursing Mothers** It is not known whether BETASERON is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from BETASERON, a decision should be made to either discontinue nursing or discontinue the drug, taking into account the importance of drug to the mother.	[Section 8.3 removed]
17 Patient Counseling Information - Pregnancy	*Pregnancy* Advise patients that BETASERON should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus [see Use in Special Population (8.1)]. Therefore, inform patients that if a pregnancy is considered, or does occur, the risks and benefits of continuing BETASERON should be discussed with their healthcare provider.	*Pregnancy* Advise patients to notify their healthcare provider if they are pregnant or plan to become pregnant [see Use in Specific Populations (8.1)].

Section Updated	Text From Previous Betaseron PI (April 2016)	Text From Current Betaseron PI (August 2018)
What should I tell my health care provider before taking Betaseron?	**Before you take BETASERON, tell your healthcare provider if you:** • have or have had depression (sinking feeling or sadness), anxiety (feeling uneasy, nervous, or fearful for no reason) or trouble sleeping • have or have had liver problems • have or have had blood problems such as bleeding or bruising easily, low red blood cells (anemia) or low white blood cells • have or have had seizures • have or have had heart problems • are pregnant or plan to become pregnant. BETASERON can harm your unborn baby. BETASERON may cause you to lose your baby (miscarry). If you become pregnant while taking BETASERON call your healthcare provider right away. You and your healthcare provider should decide if you should continue to take BETASERON. • are breastfeeding or plan to breastfeed. It is not known if BETASERON passes into your breast milk. You and your healthcare provider should decide if you will take BETASERON or breastfeed. You should not do both. **Tell your healthcare provider about all the medicines you take,** including prescription and nonprescription medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.	**Before you take BETASERON, tell your healthcare provider if you:** • have or have had depression (sinking feeling or sadness), anxiety (feeling uneasy, nervous, or fearful for no reason) or trouble sleeping • have or have had liver problems • have or have had blood problems such as bleeding or bruising easily, low red blood cells (anemia) or low white blood cells • have or have had seizures • have or have had heart problems • are pregnant or plan to become pregnant. • are breastfeeding or plan to breastfeed. It is not known if BETASERON passes into your breast milk. **Tell your healthcare provider about all the medicines you take,** including prescription and nonprescription medicines, vitamins, and herbal supplements. Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.