HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use AVONEX safely and effectively. See full prescribing information for AVONEX.

AVONEX (interferon beta-1a) injection, for intramuscular injection
Initial U.S. Approval: 1996

----------INDICATIONS AND USAGE ----------

AVONEX is an interferon beta indicated for the treatment of patients with relapsing forms of multiple sclerosis to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations. Patients with multiple sclerosis in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis. (1)

----------DOSAGE AND ADMINISTRATION ----------

- For intramuscular use only (2.1)
- Recommended dose: 30 micrograms once a week (2.1)
- AVONEX may be titrated, starting with 7.5 micrograms for first week, to reduce flu-like symptoms (2.1)
- Increase dose by 7.5 micrograms each week for next 3 weeks until recommended dose of 30 micrograms (2.1)
- See patient instructions for use for complete administration instructions (2.2)
- Perform first injection under the supervision of an appropriately qualified health care professional (2.2)
- Analgesics and/or antipyretics on treatment days may help ameliorate flu-like symptoms (2.3)

----------DOSAGE FORMS AND STRENGTH ----------

- For Injection: 30 micrograms lyophilized powder in a single-use vial (3)
- Injection: 30 micrograms per 0.5 mL solution in single-use prefilled syringe (3)
- Injection: Single-use prefilled autoinjector containing 0.5 mL solution with 30 mcg (3)

----------CONTRAINDICATIONS ----------

- History of hypersensitivity to natural or recombinant interferon beta, albumin or any other component of the formulation (4)

----------WARNINGS AND PRECAUTIONS----------

- Depression, Suicide, and Psychotic Disorders: advise patients to immediately report any symptoms of depression, suicidal ideation, and/or psychosis; consider discontinuation of AVONEX if depression occurs (5.1)
- Hepatic Injury: monitor liver function tests; monitor patients for signs and symptoms of hepatic injury; consider discontinuation of AVONEX if hepatic injury occurs (5.2, 5.8)
- Anaphylaxis and Other Allergic-Reactions: Discontinue if occurs (5.3)
- Congestive Heart Failure: monitor patients with pre-existing significant cardiac disease for worsening of cardiac symptoms (5.4)
- Decreased Peripheral Blood Counts: monitor complete blood count (5.5, 5.8)
- Autoimmune Disorders: consider discontinuation of AVONEX if new autoimmune disorder occurs (5.7, 5.8)

----------ADVERSE REACTIONS ----------

The most common adverse reactions (at least 5% more frequent on AVONEX than on placebo) were flu-like symptoms including chills, fever, myalgia, and asthenia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Biogen Idec at 1-800-456-2255 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

----------USE IN SPECIFIC POPULATIONS---------- ----------

- Pregnancy: Based on animal data, may cause fetal harm (8.1)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 2/2012

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AVONEX® (interferon beta-1a) Intramuscular Injection

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

AVONEX (interferon beta-1a) is indicated for the treatment of patients with relapsing forms of multiple sclerosis to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations. Patients with multiple sclerosis in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

AVONEX is administered intramuscularly.

The recommended dose is 30 micrograms once a week. To reduce the incidence and severity of flu-like symptoms that may occur when initiating AVONEX therapy at a dose of 30 micrograms, AVONEX may be started at a dose of 7.5 micrograms and the dose may be increased by 7.5 micrograms each week for the next three weeks until the recommended dose of 30 micrograms is achieved (see Table 1). An AVOSTARTGRIP™ kit containing 3 titration devices can be used for titration and is to be used only with AVONEX Prefilled Syringes.

Table 1: Schedule for Dose Titration

	AVONEX Dose[1]	Recommended Dose
Week 1	7.5 micrograms	1/4 dose
Week 2	15 micrograms	1/2 dose
Week 3	22.5 micrograms	3/4 dose
Week 4+	30 micrograms	full dose

[1] Dosed once a week, intramuscularly

2.2 Important Administration Instructions (All Dosage Forms)

All AVONEX dosage forms are single-use (injection of reconstituted solution, prefilled syringe, and prefilled autoinjector). See Patient's Instructions for Use for complete administration instructions.

The first AVONEX injection should be performed under the supervision of an appropriately qualified health care professional. If patients or caregivers are to administer AVONEX, train them in the proper intramuscular injection technique and assess their ability to inject intramuscularly to ensure the proper administration of AVONEX.

Advise patients and caregivers to:

- rotate sites for intramuscular injections with each injection to minimize the likelihood of injection site reactions
- NOT inject into an area of the body where the skin is irritated, reddened, bruised,

infected or scarred in any way
- Check the injection site after 2 hours for redness, swelling, or tenderness
- Contact their doctor or nurse if they have a skin reaction and it does not clear up in a few days

A 25 gauge, 1" needle for intramuscular injection with AVONEX prefilled syringe or injection of reconstituted solution may be substituted for the 23 gauge, 1 ¼" needle by the healthcare provider, if deemed appropriate. A 25 gauge, 5/8" needle specific to the prefilled autoinjector is supplied with the AVONEX PEN Administration Dose Pack. **DO NOT** use any other needle with the autoinjector.

Use safe disposal procedures for needles and syringes. Do not re-use needles, syringes, prefilled syringes, or autoinjectors. Following the administration of each titrated dose, discard any remaining product.

2.3 Premedication for Flu-like Symptoms

Concurrent use of analgesics and/or antipyretics on treatment days may help ameliorate flu-like symptoms associated with AVONEX use.

3 DOSAGE FORMS AND STRENGTHS

- For injection: 30 micrograms lyophilized powder in a single-use vial
- Injection: 30 micrograms per 0.5 mL solution in a single-use prefilled syringe
- Injection: 30 micrograms per 0.5 mL solution in a single-use prefilled autoinjector

4 CONTRAINDICATIONS

AVONEX is contraindicated in patients with a history of hypersensitivity to natural or recombinant interferon beta, or any other component of the formulation [see *Warnings and Precautions (5.3)*].

The lyophilized vial formulation of AVONEX is contraindicated in patients with a history of hypersensitivity to albumin (human).

5 WARNINGS AND PRECAUTIONS

5.1 Depression, Suicide, and Psychotic Disorders

Patients treated with AVONEX and their caregivers should be advised to report immediately any symptoms of depression, suicidal ideation, and/or psychosis to their prescribing physicians. If a patient develops depression or other severe psychiatric symptoms, cessation of AVONEX therapy should be considered.

Depression and suicide have been reported to occur with increased frequency in patients receiving AVONEX. In Study 1, the incidence of depression was similar in placebo-treated and in AVONEX-treated patients, but suicidal tendency was seen more frequently in AVONEX-treated patients (4% in AVONEX group vs. 1% in placebo group). In Study 2, there was a greater incidence of depression in AVONEX-treated patients than in placebo-treated patients (20% in AVONEX group vs. 13% in placebo group) [see *Clinical Studies (14)*].

Additionally, there have been post-marketing reports of depression, suicidal ideation, and/or development of new or worsening of other pre-existing psychiatric disorders, including psychosis. For some of these patients, symptoms of depression improved upon cessation of AVONEX.

5.2 Hepatic Injury

Severe hepatic injury, including cases of hepatic failure, has been reported rarely in patients taking AVONEX. Asymptomatic elevation of hepatic transaminases has also been reported, and in some patients has recurred upon rechallenge with AVONEX. In some cases, these events have occurred in the presence of other drugs that have been associated with hepatic injury. The potential risk of AVONEX used in combination with known hepatotoxic drugs or other products (e.g., alcohol) should be considered prior to starting AVONEX, or before starting hepatotoxic drugs. Patients should be monitored for signs of hepatic injury [see *Warnings and Precautions (5.8)*].

5.3 Anaphylaxis and Other Allergic-Reactions

Anaphylaxis has been reported as a rare complication of AVONEX use. Other allergic reactions have included dyspnea, orolingual edema, skin rash and urticaria. Discontinue AVONEX if anaphylaxis or other allergic reactions occur.

5.4 Congestive Heart Failure

Patients with pre-existing congestive heart failure should be monitored for worsening of their cardiac condition during initiation of and continued treatment with AVONEX. While beta interferons do not have any known direct cardiac toxicity, during the post-marketing period cases of congestive heart failure, cardiomyopathy, and cardiomyopathy with congestive heart failure have been reported in patients without known predisposition to these events, and without other etiologies being established. In some cases, these events have been temporally related to the administration of AVONEX. In some of these instances recurrence upon rechallenge was observed.

5.5 Decreased Peripheral Blood Counts

Decreased peripheral blood counts in all cell lines, including rare pancytopenia and thrombocytopenia, have been reported from postmarketing experience in AVONEX-treated patients [see *Adverse Reactions (6.2)*]. In some cases, platelet counts were below 10,000/microliter. Some cases recurred with rechallenge [see *Adverse Reactions (6.2)*]. Patients should be monitored for symptoms or signs of decreased blood counts.

5.6 Seizures

Seizures have been temporally associated with the use of beta interferons in clinical trials and postmarketing safety surveillance. In the two placebo-controlled studies in multiple sclerosis (Studies 1 and 2), 4 patients receiving AVONEX experienced seizures, while no seizures occurred in the placebo group [see *Clinical Studies (14)*]. Three of these 4 patients had no prior history of seizure [see *Adverse Reactions (6.1)*]. It is not known whether these events were related to the effects of multiple sclerosis alone, to AVONEX, or to a combination of both.

5.7 Autoimmune Disorders

Post-marketing reports of autoimmune disorders of multiple target organs in AVONEX-treated patients included idiopathic thrombocytopenia, hyper- and hypothyroidism, and rare cases of autoimmune hepatitis. If AVONEX-treated patients develop a new autoimmune disorder, consider stopping the therapy.

5.8 Laboratory Tests

In addition to those laboratory tests normally required for monitoring patients with multiple sclerosis, complete blood and differential white blood cell counts, platelet counts, and blood chemistries, including liver function tests, are recommended during AVONEX therapy [see *Warnings and Precautions (5.2, 5.5, 5.7)*]. Patients with myelosuppression may require more intensive monitoring of complete blood cell counts, with differential and platelet counts. Thyroid function should be monitored periodically. If patients have or develop symptoms of thyroid dysfunction (hypo- or hyperthyroidism), thyroid function tests should be performed according to standard medical practice.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed in more detail in other sections of labeling:

- Depression, Suicide, and Psychotic Disorders [see *Warnings and Precautions (5.1)*]
- Hepatic Injury [see *Warnings and Precautions (5.2)*]
- Anaphylaxis and Other Allergic-Reactions [see *Warnings and Precautions (5.3)*]
- Congestive Heart Failure [see *Warnings and Precautions (5.4)*]
- Decreased Peripheral Blood Counts [see *Warnings and Precautions (5.5)]*
- Seizures [see *Warnings and Precautions (5.6)*]
- Autoimmune Disorders [see *Warnings and Precautions (5.7)*]
- Laboratory Tests [*see Warnings and Precautions* (5.8)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of AVONEX cannot be directly compared to rates in clinical trials of other drugs and may not reflect the rates observed in practice.

Among 351 patients with relapsing forms of MS treated with AVONEX 30 micrograms (including 319 patients treated for 6 months and 288 patients treated for greater than one year) the most commonly reported adverse reactions (at least 5% more frequent on AVONEX than on placebo) were flu-like symptoms. Symptoms can include chills, fever, myalgia and asthenia occurring within hours to days following an injection. Most people who take AVONEX have flu-like symptoms early during the course of therapy. Usually, these symptoms last for a day after the injection. For many people, these symptoms lessen or go away over time. The most frequently reported adverse reactions resulting in clinical intervention (for example, discontinuation of AVONEX or the need for concomitant medication to treat an adverse reaction symptom) were flu-like symptoms and depression.

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