



CIGNA HEALTHCARE COVERAGE POSITION

Subject: Multiple Sclerosis Interferon Therapy

Coverage Position Number: 4011

Effective Date: 4/15/2004

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Related Coverage Positions:

INSTRUCTIONS FOR USE

Coverage Positions are intended to supplement certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Positions are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Position. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Positions. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Positions and; 4) the specific facts of the particular situation. ©2004 CIGNA Health Corporation

Coverage Position

Multiple Sclerosis Interferon Therapy includes the following drugs:

- Interferon beta-1a (Avonex®.)
- Interferon beta-1a (Rebif®)
- Interferon beta-1b (Betaseron®)

CIGNA HealthCare covers Multiple Sclerosis Interferon Therapy when the following medical necessity criteria are met:

- diagnosis of clinically definite Multiple Sclerosis **OR**
- diagnosis of Relapsing Remitting Multiple Sclerosis (RRMS) **OR**
- diagnosis of Secondary Progressive Multiple Sclerosis (SPMS) with relapses

General Background

The following information is abstracted from a larger drug review monograph.

Multiple sclerosis (MS) is an inflammatory disease of the central nervous system. It affects 250,000-350,000 people in the US. MS usually occurs in women (2:1 ratio versus men) at ages 20-45 years. The prevalence is higher above the 37th parallel in the US. In MS, demyelination occurs with inflammatory responses, causing plaques in the brain, spinal cord, and optic nerves. This causes disruption of the transmission of nerve impulses, resulting in the following classic symptoms: gait problems, paresthesias, pain, spasticity, speech difficulty, bowel/bladder dysfunction, tremor, etc. Multiple sclerosis can be classified into 3 clinical types: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), and primary progressive MS (PPMS). The neurological dysfunction seen with RRMS is

characterized by acute, self-limited attacks that may evolve over days to week and last weeks to months. The patients are neurologically and symptomatically stable between attacks. In SPMS, patients begin a clinical course similar to RRMS but the number of attacks decreases over time. The patient's neurological function steadily deteriorates unrelated to the acute attacks. Patients with PPMS do not present with acute attacks at the onset of disease; their function steadily declines.¹

Summary

Guidelines from the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines recommend that interferon beta is appropriate therapy for any patient with clinically definite MS, or anyone who already has RRMS or SPMS and is experiencing relapses. This committee cannot recommend interferon beta therapy for patients with SPMS without relapses because of inadequate or conflicting data. The committee could not recommend a specific route of administration of the interferon beta (intramuscular versus subcutaneous) to obtain the greatest efficacy. The Austrian-German-Swiss Multiple Sclerosis Therapy Consensus Group (MSTCG) feels that interferon beta significantly reduces the relapse rates and is appropriate therapy for this indication. This group does not recommend one agent over another. However, the MSTCG states that patients who are experiencing sustained and intolerable side effects (other than persistent flu-like symptoms) to subcutaneous interferon beta may benefit by switching to the intramuscular interferon beta product. The MSTCG does consider Betaseron (interferon beta-1b) as an effective immunomodulatory agent for delaying disease progression in patients with SPMS.

The interferon beta products have the same mechanism of action. The amino acid sequence, specific activity, source, molecular weight and pharmacokinetic parameters differ slightly, although these differences have not correlated into known differences in clinical efficacy or safety.

Overall in non-comparative trials, the interferon beta products have been effective in reducing relapses, reducing disease progression and improving MRI outcomes in RRMS. Comparative trials in RRMS have detected some differences between products. Rebif and Betaseron decreased relapse rates more than Avonex in RRMS. Betaseron significantly reduced disease progression in RRMS versus Avonex, while no difference was seen with Rebif and Avonex. Betaseron and Rebif were more effective than Avonex in improving MRI outcomes in RRMS. In SPMS, all interferon beta products decreased relapse rates. In non-comparative trials in SPMS, Betaseron decreased disease progression while Avonex and Rebif did not. Avonex, Betaseron, and Rebif all showed benefit in MRI outcomes in patients with SPMS. Interferon beta products were not effective in treating patients with PPMS and these patients may see increased spasticity. All interferon beta products were effective in reducing the onset to CDMS in patients with a first demyelinating event.

Overall side effects may be more common with Betaseron or Rebif versus Avonex (i.e., rigors, white blood cell adverse events, liver enzyme elevations, injection site disorders, neutralizing antibodies). This may be explained by the more frequent administration with Rebif and Betaseron (thrice weekly and every other day) versus the weekly administration of Avonex. The most common adverse effects seen with interferon beta-1a during clinical trials include anemia, asthenia, diarrhea, infection, flu-like illness (arthralgias, chills, fever, headache and myalgia), nausea and pain. The most common adverse effects seen with interferon beta-1b during clinical trials include abdominal pain, headache/migraine, hypertension, injection site reactions (hypersensitivity, inflammation, necrosis and pain), flu-like illness (chills, fever, sweating, malaise and myalgia), palpitations and sinusitis.

Avonex is administered by a once-weekly intramuscular injection. Betaseron and Rebif are administered by the subcutaneous route, given either every other day or thrice weekly, respectively. Avonex and Betaseron require reconstitution prior to injection. A starter kit is available for Rebif to allow for dose titration in the first four weeks of therapy.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

CPT [®] * Codes	Description

HCPCS Codes	Description

ICD-9-CM Diagnosis Codes	Description

Experimental/Investigational/Unproven/Not Covered:

CPT* Codes	Description

HCPCS Codes	Description

ICD-9-CM Diagnosis Codes	Description

*Current Procedural Terminology (CPT[®]) ©2003 American Medical Association: Chicago, IL.

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The following lists the complete references used within a larger drug review monograph. To obtain a copy of the full drug review monograph, please contact the Pharmacy Services Center at 800-832-3211.

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