



Medication Policy Manual

Policy No: dru108

Topic: Betaseron[®], interferon beta-1b

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Revised/Effective Date: January 15, 2010

Next Review Date: September 2010

IMPORTANT REMINDER

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Betaseron (interferon beta-1b) is an interferon used in the treatment of multiple sclerosis (MS). It helps to reduce the number of clinical exacerbations associated with this condition.

Policy/Criteria

I. Most contracts require prior authorization approval of Betaseron (interferon beta-1b) prior to coverage. Betaseron (interferon beta-1b) may be considered medically necessary in patients with multiple sclerosis when criteria A and B below are met.

A. Treatment with Avonex[®] (interferon beta-1a), Rebif[®] (interferon beta-1a), or Copaxone[®] (glatiramer acetate) is ineffective or not tolerated.

AND

B. Treatment with Extavia (interferon beta-1b) is ineffective or not tolerated.

II. Administration, Quantity Limitations and Authorization Period

A. Regence considers Betaseron (interferon beta-1b) to be a self-administered medication.

B. When prior authorization is approved, Betaseron (interferon beta-1b) may be authorized in quantities of 15 vials (one 0.3 mg vial injected subcutaneously every other day) per month.

C. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

Position Statement

Summary

- All interferon formulations (interferon beta-1a and interferon beta-1b) and glatiramer acetate decrease the number of attacks in patients with relapsing remitting multiple sclerosis. ^[2, 7-8]
- There is no reliable evidence of increased efficacy or safety of one interferon beta product over another in reducing the signs and symptoms of multiple sclerosis or slowing the progression of disease. ^[1, 9-11]
- Betaseron and Extavia both contain the same formulation of interferon beta-1b. The only difference between the products is their packaging.

Clinical efficacy

- There are several randomized, controlled trials comparing the efficacy of the different interferon products. The studies contain sufficient flaws (e.g., open-label design, large proportion of patients not included in the efficacy analysis) so as to render conclusions regarding the comparative efficacy unreliable. ^[9-11]
- Extavia and Betaseron are identical formulations of interferon beta-1b. In fact, the FDA approved Extavia based on clinical studies that were conducted with Betaseron.

Guidelines and Dosing Considerations

- The American Academy of Neurology Clinical Practice Guidelines on the treatment of Multiple Sclerosis and a Cochrane analysis do not clearly indicate that one interferon beta product is superior to another on the basis of clinical trial evidence. ^[2, 7]
- The relationship between neutralizing antibody (NAb) formation and subsequent effects on clinical efficacy and safety of the interferon products is not entirely understood and remains controversial. However, studies suggest that the presence of NABs against interferon beta reduce the clinical efficacy of the drug and should therefore play a role in treatment decisions. ^[3]
- According to FDA approved package labeling of the three commercially available interferon beta products, the immunogenicity of each product (formation of NABs) in controlled clinical trials are as follows:
 - * Interferon beta-1b (Betaseron[®], Extavia[®]): 45% ^[4]
 - * Interferon beta-1a (Rebif[®]): 24% ^[5]
 - * Interferon beta-1a (Avonex[®]): 5% ^[6]
- There is no reliable evidence to support superior clinical outcomes when interferon beta-1b is given in dosages greater than what is recommended in the prescribing information (package insert) and approved by the Food and Drug Administration (FDA). The recommended dosage is 0.25 mg injected subcutaneously every other day. ^[4]

Cross References
Self Administered Injectables dru110
Extavia [®] , interferon beta-1b, dru200

Codes	Number	Description
HCPCS	J1830	Injection, Interferon beta 1b, 0.25mg

References

1. Vartanian T. "An examination of the results of the EVIDENCE, INCOMIN and phase III studies of interferon beta products in the treatment of multiple sclerosis." *Clin Ther* 2003;25 (1):105-18.
2. Goodin DS, Frohman EM, Garmany GP, et al. "Disease modifying therapies in multiple sclerosis; report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines." *Neurology* 2002;58:169-78.
3. Sorensen PS, Ross C, Clemmesen KM, et al. "Clinical importance of neutralizing antibodies against interferon beta in patients with relapsing-remitting multiple sclerosis." *Lancet* 2003;362:1184-91.
4. Betaseron[®] (interferon beta-1b) Prescribing Information. Berlex Laboratories; Montville, NJ, April 2008.
5. Rebif[®] (interferon beta-1a) Prescribing Information. Serono, Inc.; Rockland, MA, December 2008.
6. Avonex[®] (interferon beta-1a) Prescribing Information. Biogen IDEC, Inc.; Cambridge, MA, October 2008.
7. Rice G PA, Incurvaia B, Munari L, Ebers G, Polman C, D'Amico R, Filippini G. Interferon in relapsing-remitting multiple sclerosis. *The Cochrane Database of Systematic Reviews* 2001, Issue 4. Art. No.: CD002002. DOI: 10.1002/14651858.CD002002.

8. Munari L, Lovati R, Boiko A. Therapy with glatiramer acetate for multiple sclerosis. *The Cochrane Database of Systematic Reviews* 2003, Issue 4. Art. No.: CD004678. DOI: 10.1002/14651858.CD004678.
9. Durelli L, Verdun E, Barbero P, Bergui M, Versino E, et al.; Independent Comparison of Interferon (INCOMIN) Trial Study Group. Every-other-day interferon beta-1b versus once-weekly interferon beta-1a for multiple sclerosis: results of a 2-year prospective randomized multicentre study (INCOMIN). *Lancet*. 2002;359(9316):1453-60.
10. Koch-Henriksen N, Sørensen PS, Christensen T, Frederiksen J, Ravnborg M, et al.; Danish Multiple Sclerosis Group. A randomized study of two interferon-beta treatments in relapsing-remitting multiple sclerosis. *Neurology*. 2006;66(7):1056-60. Epub 2006 Mar 1.
11. Etemadifar M, Janghorbani M, Shaygannejad V. Comparison of Betaferon, Avonex, and Rebif in treatment of relapsing-remitting multiple sclerosis. *Acta Neurol Scand*. 2006;113(5):283-7.
12. Copaxone[®] (glatiramer acetate) Prescribing Information. TEVA Neuroscience, Inc., Kansas City, MO. February 2009.
13. Extavia (interferon beta-1b) Prescribing Information. Novartis Pharmaceuticals Corp.: East Hanover, NJ; August 2009.