



Therapeutic Class ReviewSM

Self-injectable biologic agents for treatment of Multiple Sclerosis

February 2006

Glatiramer acetate (Copaxone[®]) [TEVA]
Interferon beta-1a (Avonex[®]) [Biogen Idec, Inc]
Interferon beta-1a (Rebif[®]) [Serono, Inc]
Interferon beta-1b (Betaseron[®]) [Chiron, Inc]

Dossier Evaluation: 0

Dossier Evaluation: 0

Dossier Evaluation: 0

Dossier Evaluation: 2

0 - Dossier requested but not received

1 - Dossier with missing components

2 - Dossier with all components, except pharmacoeconomic model

3 - All components present (comprehensive)

Executive Summary

- Avonex, Rebif, and Betaseron are interferons, while Copaxone is structurally different from interferons.
- The best evidence for efficacy in this class is in the treatment of relapsing-remitting multiple sclerosis (RRMS).
- All of the agents are promoted for their potential benefits in decreasing exacerbations in RRMS, while Avonex and Rebif are also promoted for slowing the progression of disability.
- Comparative efficacy among these products is difficult to determine because:
 - There are few well-designed RCTs comparing these agents.
 - The severity and duration of disease in patients at study entry is highly variable between trials.
- Formation of antibodies occurs with all medications in this class, however the clinical relevance of this observation has not been established in well-designed randomized control trials (RCTs).

Evidence:

- Interferon beta products (Avonex, Rebif, Betaseron) provide the best evidence of efficacy for the treatment of RRMS based on the:
 - proportion of patients who continued to experience exacerbations during the first two years of treatment, and
 - proportion of patients with progression of disease in the first two years of treatment.
- In one analysis of the interferon beta trials, the statistical difference observed between treatment and placebo groups disappeared when dropouts were assigned to the groups with continued exacerbations or progression of disease.
- Copaxone failed to show efficacy in the treatment of RRMS in pooled data from 3 placebo-controlled trials based on the endpoints:

- proportion of patients who continued to experience exacerbations during the first two years of treatment, and
- proportion of patients with progression of disease in the first two years of treatment.
- There have been no direct comparisons between Copaxone and interferon beta products to date.
- There is no useful evidence to distinguish between the efficacy of the different interferon beta products used in the treatment of RRMS.
- The clinical relevance of MRI findings as outcome measures in MS patients is not known.
- Injection site reactions are the most prevalent adverse effects reported with the subcutaneously administered products (Copaxone, Rebif, Betaseron).
- There is no useful evidence to support any differences in tolerability between any of these agents.

Decision

- Betaseron (interferon beta-1b) is non-preferred/non-formulary status because:
 - There are no clinical advantages with Betaseron over other interferon beta products.
 - Changing Betaseron to non-formulary/non-preferred status will have minimal impact on members and prescribers due to its low use relative to other products.
 - Maintaining Betaseron as preferred/formulary would increase overall costs in this class.
- Rebif and Avonex are preferred/formulary interferon beta product options for MS.
- Although current evidence for efficacy is poor, maintain Copaxone as a preferred/formulary agent pending review of results from an ongoing comparative trial between Rebif and Copaxone (slated for completion in 2007), and evaluation of member impact.

Products

Drug Product	Date of FDA Approval	FDA Approved Indication	Dose/Route	Potential Off-Label Uses ⁵
glatiramer acetate (Copaxone [®]) ¹	12/1996	Reduction of frequency of relapses in patients with relapsing-remitting multiple sclerosis (RR-MS)	20 mg subQ daily	<ul style="list-style-type: none"> ▪ none.
interferon beta-1a (Avonex [®]) ²	5/1996	Treatment of relapsing forms of multiple sclerosis to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations.	30 mcg IM q week.	<ul style="list-style-type: none"> ▪ first demyelinating event with likely MS.⁶ ▪ condyloma acuminatum ▪ adjunct to IVIG in CIDP[†] ▪ motor neuropathy w/ multiple conduction block ▪ moderately severe ulcerative colitis.
interferon beta-1a (Rebif [®]) ³	3/2002	Treatment of relapsing forms of multiple sclerosis to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations.	22 or 44 mcg subQ three times per week.	<ul style="list-style-type: none"> ▪ Progressive relapsing MS (PRMS) ▪ condyloma acuminatum ▪ adjunct to IVIG in CIDP[†] ▪ motor neuropathy w/ multiple conduction block ▪ moderately severe ulcerative colitis.

interferon beta-1b (Betaseron®) ⁴	7/1993	Treatment of relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations.	0.25 mg subQ every other day.	<ul style="list-style-type: none"> ▪ Secondary progressive MS (SPMS) ▪ Kaposi's sarcoma ▪ recurrent malignant gliomas.
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† CIDP = chronic demyelinating polyradiculoneuropathy.

References

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