Medication Policy Manual

Topic: Betaseron®, Extavia®, interferon beta-1b

Date of Origin: June 18, 2004

Committee Approval Date: December 11, 2015

Next Review Date: December 2016

Effective Date: January 1, 2016

IMPORTANT REMINDER

This Medication 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 medication policy is to provide a guide to coverage. Medication 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

Interferon beta-1b (Betaseron and Extavia) is an immunotherapy used in the treatment of multiple sclerosis (MS). It is administered subcutaneously and helps to reduce the number of clinical exacerbations associated with this condition.
Policy/Criteria

I. Most contracts require prior authorization approval of interferon beta-1b (Betaseron, Extavia) prior to coverage. Interferon beta-1b (Betaseron, Extavia) may be considered medically necessary in patients with relapsing-remitting or secondary-progressing multiple sclerosis when treatment with one of the following is ineffective or not tolerated:

A. Avonex® (interferon beta-1a).

OR

B. Rebif® (interferon beta-1a).

II. Administration, Quantity Limitations and Authorization Period

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

B. When prior authorization is approved, interferon beta-1b (Betaseron, Extavia) 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.

III. Interferon beta-1b is considered investigational when used for all other conditions, including but not limited to: clinically isolated syndrome.

Position Statement

Summary

- All interferon beta 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.

- Interferon beta-1b (Betaseron, Extavia) is approved at the titrated dose of 0.25 mg (one 0.3 mg vial) injected subcutaneously every other day.

Clinical efficacy

- There are several randomized, controlled trials comparing the efficacy of the different interferon beta products in the treatment of relapsing-remitting multiple sclerosis. The studies contain sufficient flaws (e.g., open-label design, large proportion of patients not included in the efficacy analysis) rendering conclusions regarding the comparative efficacy unreliable. \[9-11, 14\]
- 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.
- Evidence for interferon beta-1b in clinically isolated syndrome is limited to one small randomized trial. Long-term data from large randomized, controlled trials are needed to adequately assess efficacy and safety of interferon beta-1b in this population.\[^{15}\]

**Background on Multiple Sclerosis (MS)\[^{2}\]**

- There are four clinical courses of multiple sclerosis (characterized in Table 1 below).
- Relapsing-remitting forms of multiple sclerosis account for up to 85% of cases.

<table>
<thead>
<tr>
<th>Table 1: Multiple Sclerosis Forms/Clinical Course Definitions [^{2}]</th>
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<tbody>
<tr>
<td><strong>Relapsing-remitting</strong> (RRMS)</td>
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<tr>
<td><strong>Secondary progressive</strong> (SPMS)</td>
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<td><strong>Primary progressive</strong> (PPMS)</td>
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<tr>
<td><strong>Progressive relapsing</strong> (PRMS)</td>
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**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). [14] The recommended dosage is 0.25 mg injected subcutaneously every other day. [4]

### Appendix A: Disease-Modifying Agents Used in the Treatment of Multiple Sclerosis (MS)

<table>
<thead>
<tr>
<th>Agent</th>
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<tbody>
<tr>
<td>Alemtuzumab (Lemtrada®)</td>
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<tr>
<td>Fingolimod (Gilenya®)</td>
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<tr>
<td>Dimethyl fumarate (Tecfidera®)</td>
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<tr>
<td>Glatiramer acetate (Copaxone®)</td>
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<tr>
<td>Interferon beta-1a (Avonex®, Rebif®)</td>
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<tr>
<td>Interferon beta-1b (Betaseron®, Extavia®)</td>
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<tr>
<td>Mitoxantrone (Novantrone®)</td>
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<tr>
<td>Natalizumab (Tysabri®)</td>
</tr>
<tr>
<td>Peginterferon beta-1a (Plegridy®)</td>
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<tr>
<td>Teriflunomide (Aubagio®)</td>
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</tbody>
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Cross References

Self-Administered Injectables, Medication Manual, Policy No. 110

Aubagio®, teriflunomide, Medication Manual, Policy No. 283

Tecfidera®, dimethyl fumarate, Medication Manual, Policy No. 299

Gilenya®, fingolimod, Medication Manual, Policy No. 229

Lemtrada™, alemtuzumab, Medication Manual, Policy No. 381

Plegridy®, peginterferon beta-1a, Medication Policy Manual, Policy No. 376

Tysabri®, natalizumab, Medication Manual, Policy No. 111

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
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<tbody>
<tr>
<td>HCPCS</td>
<td>J1830</td>
<td>Injection, Interferon beta 1b, 0.25mg</td>
</tr>
<tr>
<td>HCPCS</td>
<td>J2323</td>
<td>Injection, natalizumab, 1 mg</td>
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<tr>
<td>ICD-10</td>
<td>G35</td>
<td>Multiple Sclerosis</td>
</tr>
</tbody>
</table>

References


13. Extavia (interferon beta-1b) Prescribing Information. Novartis Pharmaceuticals Corp.: East Hanover, NJ; March 2012.


<table>
<thead>
<tr>
<th>Revision Date</th>
<th>Revision Summary</th>
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<tbody>
<tr>
<td>12/11/2015</td>
<td>No Criteria Changes</td>
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