Clinical Policy: Interferon Beta-1a (Avonex, Rebif)
Reference Number: ERX.SPA.112
Effective Date: 10.01.16
Last Review Date: 05.19

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Interferon beta-1a (Avonex®, Rebif®) is an amino acid glycoprotein.

FDA Approved Indications
Avonex and Rebif are indicated for the treatment of patients with relapsing forms of multiple sclerosis (MS) to decrease the frequency of clinical exacerbations and delay the accumulation of physical disability. Patients with MS in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have magnetic resonance imaging (MRI) features consistent with MS.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Avonex and Rebif are medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Multiple Sclerosis (must meet all):
      1. Diagnosis of one of the following (a, b, or c):
          a. Clinically isolated syndrome;
          b. Relapsing-remitting MS;
          c. Secondary progressive MS, and member has active relapsing disease;
      2. Prescribed by or in consultation with a neurologist;
      3. Age ≥ 2 years (for Rebif requests) or ≥ 18 years (for Avonex requests);
      4. For Avonex requests, member meets the following (a and b):
          a. If relapsing-remitting MS, failure of one of the following at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced: glatiramer (Copaxone®, Glatopa®), Tecfidera®, Gilenya™, Aubagio®, or Tysabri®;
          b. Failure of Rebif and Betaseron® at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced; *Prior authorization is required for all disease modifying therapies for MS
      5. Not prescribed concurrently with other disease modifying therapies for MS (see Appendix D);
      6. Dose does not exceed:
          a. Avonex: 30 mcg per week (1 vial/syringe/autoinjector per week);
          b. Rebif: 44 mcg three times per week (1 syringe/autoinjector three times per week).

   Approval duration: 6 months

   B. Other diagnoses/indications
      1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).
II. Continued Therapy
   A. Multiple Sclerosis (must meet all):
      1. Currently receiving medication via a health plan affiliated with Enolve Pharmacy Solutions or member has previously met initial approval criteria;
      2. Member is responding positively to therapy;
      3. Not prescribed concurrently with other disease modifying therapies for MS (see Appendix D);
      4. If request is for a dose increase, new dose does not exceed:
         a. Avonex: 30 mcg per week (1 vial/syringe/autoinjector per week);
         b. Rebif: 44 mcg three times per week (1 syringe/autoinjector three times per week).
   Approval duration: 12 months

   B. Other diagnoses/indications (must meet 1 or 2):
      1. Currently receiving medication via a health plan affiliated with Enolve Pharmacy Solutions and documentation supports positive response to therapy.
         Approval duration: Duration of request or 6 months (whichever is less); or
      2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:
   A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;
   B. Primary progressive MS.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   FDA: Food and Drug Administration
   MS: multiple sclerosis

   Appendix B: Therapeutic Alternatives
   This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rebif® (interferon beta-1a)</td>
<td>22 mcg or 44 mcg SC TIW</td>
<td>44 mcg TIW</td>
</tr>
<tr>
<td>Betaseron® (interferon beta-1b)</td>
<td>250 mcg SC QOD</td>
<td>250 mg QOD</td>
</tr>
<tr>
<td>glatiramer acetate (Copaxone®, Glatopa®)</td>
<td>20 mg SC QD or 40 mg SC TIW</td>
<td>20 mg/day or 40 mg TIW</td>
</tr>
<tr>
<td>Aubagio® (teriflunomide)</td>
<td>7 mg or 14 mg PO QD</td>
<td>14 mg/day</td>
</tr>
<tr>
<td>Gilenya™ (fingolimod)</td>
<td>0.5 mg PO QD</td>
<td>0.5 mg/day</td>
</tr>
<tr>
<td>Tecfidera® (dimethyl fumarate)</td>
<td>120 mg PO BID for 7 days, followed by 240 mg PO BID</td>
<td>480 mg/day</td>
</tr>
<tr>
<td>Tysabri® (natalizumab)</td>
<td>300 mg IV every 4 weeks</td>
<td>300 mg/4 weeks</td>
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   Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

   Appendix C: Contraindications/Boxed Warnings
   • Contraindication(s): history of hypersensitivity to natural or recombinant interferon beta, albumin or any other component of the formulation
   • Boxed warning(s): none reported

   Appendix D: General Information
   • Disease-modifying therapies for MS are: glatiramer acetate (Copaxone®, Glatopa®), interferon beta-1a (Avonex®, Rebif®), interferon beta-1b (Betaseron®, Extavia®), peginterferon beta-1a (Plegridy®), dimethyl fumarate (Tecfidera®), fingolimod (Gilenya™), teriflunomide (Aubagio®),
alemtuzumab (Lemtrada®, mitoxantrone (Novantrone®), natalizumab (Tysabri®), and ocrelizumab (Ocrevus™).

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon beta-1a</td>
<td>30 mcg IM Q week; may be titrated starting with 7.5 mcg for the first week, increased by 7.5 mcg each week for 3 weeks until target of 30 mcg is reached</td>
<td>30 mcg/week</td>
</tr>
<tr>
<td>(Avonex)</td>
<td></td>
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<tr>
<td>Interferon beta-1a</td>
<td>Initial dose at 20% of prescribed dose TIW increased over 4 weeks to the targeted dose of either 22 mcg or 44 mcg SC TIW</td>
<td>44 mcg TIW</td>
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<tr>
<td>(Rebif)</td>
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VI. Product Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon beta-1a</td>
<td>Single-use vial: 30 mcg</td>
</tr>
<tr>
<td>(Avonex)</td>
<td>Single-use prefilled autoinjector or syringe: 30 mcg/0.5 mL</td>
</tr>
<tr>
<td>Interferon beta-1a</td>
<td>Single-dose autoinjector or prefilled syringe: 8.8 mcg/0.2 mL, 22 mcg/0.5 mL, 44 mcg/0.5 mL</td>
</tr>
<tr>
<td>(Rebif)</td>
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</table>

VII. References

**Clinical Policy**

Interferon Beta-1a

### Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tbody>
<tr>
<td>Removed MRI requirement as it is a non-specific diagnostic test (plus, specialist involvement in care is required). Added PPMS as a diagnosis not covered.</td>
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</tr>
<tr>
<td>2Q 2018 annual review: Added coverage for SPMS per AAN guidelines. References reviewed and updated</td>
<td>01.05.18</td>
<td>05.18</td>
</tr>
<tr>
<td>2Q 2019 annual review: no significant changes; added Tysabri as a step-through option per its formulary status; references reviewed and updated.</td>
<td>02.07.19</td>
<td>05.19</td>
</tr>
</tbody>
</table>

### Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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