MDWISE PRIOR AUTHORIZATION CRITERIA FOR SELF INJECTABLE DISEASE MODIFYING IMMUNOMODULATORS FOR MULTIPLE SCLEROSIS (MS)

Copaxone® (Glatiramer Acetate) 20mg kit (pre-filled syringe)
Rebif® (Interferon beta -1a): 8.8 mcg, 22 mcg, 44 mcg pre-filled syringes
Avonex® (Interferon beta -1a): 30 mcg kit (vial or pre-filled syringe)
Betaseron® (Interferon beta -1b): 0.3-mg kit (vial)
Extavia® (Interferon beta -1b): 0.3-mg pre-filled syringe

PREFERRED PRODUCTS: Copaxone® and Rebif®

PA CRITERIA FOR INITIAL APPROVAL:
- If the request is for an adult (≥ 18 y/o) member with relapsing/remitting MS (RRMS) or secondary progressive MS (SPMS) with a relapsing element, documentation was submitted confirming diagnosis in the form of MRI results and medical chart history indicating the member has had at least one clinical episode.
- If the medication request is for Avonex, Betaseron and/or any other Newly Marketed Self-Injectable Disease-Modifying Immunomodulating MS Agent, the member has a documented treatment failure to Copaxone and Rebif (see Box 1 in Glossary for definition of treatment failure) which is consistent with pharmacy claims data, OR for new members to the health plan consistent with medical chart history, indicating they had received an adequate trial (including dates, doses of 6 months or more of each therapy) of Copaxone and Rebif and/or has another documented clinically significant medical reason (i.e. intolerance, hypersensitivity, contraindication, etc) for not taking Copaxone and Rebif for a minimum of 6 months each to treat their medical condition.
- The medication is being recommended and/or prescribed by a neurologist at an FDA approved dosage.

If all of the above conditions are met, the request will be approved for up to a 6-month duration; if all of the above criteria are not met, the request is referred to a Medical Director for medical necessity review.

REAUTHORIZATION CRITERIA:
- Documentation sent indicates that the member is an adult (≥ 18 y/o) and has one of the following types of MS: RRMS or SPMS with a relapsing element.
- The medication was prescribed at an FDA approved dosage.
- Medication was recommended by a neurologist (i.e., copy of neurology consultation done within 90 days of reauthorization request) and/or prescribed by a neurologist.

If all of the above conditions are met, the request will be approved for up to a 12-month duration; if all of the above criteria are not met, the request is referred to a Medical Director for medical necessity review.

FDA INDICATIONS:
Avonex is indicated for the treatment of relapsing forms of multiple sclerosis to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations. Safety and efficacy in members with chronic progressive multiple sclerosis have not been evaluated.

Betaseron is indicated for the treatment of relapsing forms of MS to reduce the frequency of clinical exacerbations.

Copaxone is indicated for the reduction of the frequency of relapses in members with RRMS. Copaxone has NOT been formally evaluated in combination with interferon beta.

Extavia is indicated for the treatment of relapsing forms of multiple sclerosis to reduce the frequency of clinical exacerbations. Patients with multiple sclerosis in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis.

Rebif is indicated for the treatment of relapsing forms of multiple sclerosis to decrease the frequency of clinical exacerbations and delay the accumulation of physical disability. Efficacy in chronic progressive MS has not been established.

Dosage and Administration: Extavia® (Glatiramer Acetate) 20 mg/day injected SC and sites for injections include arms, abdomen, hips, and thighs.
**Extavia**: 0.25 mg subcutaneously (SC) every other day. Start dose at 0.0625 mg (0.25 mL) SQ every other day and titrate dose by increasing dose over six weeks.

**Extavia dosing titration schedule**

<table>
<thead>
<tr>
<th>Weeks 1-2</th>
<th>Recommended Titration</th>
<th>Extavia® Dose</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>25%</td>
<td>0.0625 mg</td>
<td>0.25 mL</td>
</tr>
<tr>
<td>Weeks 3-4</td>
<td>50%</td>
<td>0.125 mg</td>
<td>0.50 mL</td>
</tr>
<tr>
<td>Weeks 5-6</td>
<td>75%</td>
<td>0.1875 mg</td>
<td>0.75 mL</td>
</tr>
<tr>
<td>Week 7+</td>
<td>100%</td>
<td>0.25 mg</td>
<td>1.0 mL</td>
</tr>
</tbody>
</table>

**Rebif**: 22 mcg or 44 mcg injected SC 3 times weekly, if possible at the same time (in the late afternoon or evening) on the same 3 days at least 48 hours apart each week and to rotate SC injection sites. It is best to start members at 20% of prescribed dose 3 times/week and increase dose over a 4 week period to target dose. A titration pack containing 8.8 mcg and 22 mcg syringes is available for use during titration period.

**Rebif dosing titration schedule**

<table>
<thead>
<tr>
<th>Weeks 1-2</th>
<th>Recommended titration (% of final dose)</th>
<th>Titration dose for Rebif 22 mcg</th>
<th>Titration dose for Rebif®44 mcg</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20%</td>
<td>4.4 mcg</td>
<td>8.8 mcg</td>
</tr>
<tr>
<td>Weeks 3-4</td>
<td>50%</td>
<td>11 mcg</td>
<td>22 mcg</td>
</tr>
<tr>
<td>Weeks 5+</td>
<td>100%</td>
<td>22 mcg</td>
<td>44 mcg</td>
</tr>
</tbody>
</table>

**BOX 1: TREATMENT FAILURE:**

A member may be considered to have failed treatment if any of the following are documented:

1. Member who has an attack rate (relapse) of more than 1 per year, fails to show a reduction in relapse rate, or continues to experience attacks (relapses) at a rate similar to that found before starting therapy**

2. Member who has incomplete recovery (cumulative residual abnormalities sustained for 6 months) from repeated attacks, particularly as the EDSS score increases. **

3. Member experiences an annual increase in the EDSS (Expanded Disability Status Scale) of 1 point from a previous score of 3 to 5.5, or 0.5 point increase from a previous score of 6.0 or greater in the absence of clinical attacks or other documentation of clinically significant disability progression. **

4. Member who develops new or recurrent brainstem or spinal cord lesions as seen on MRI. **

5. Members experiencing relapses affecting multiple neurologic symptoms, and those accumulating residual impairments in multiple neurologic systems. **

6. Members who have progressive motor, cognitive or sensory impairment sufficient to disrupt their daily activities irrespective of changes on neurologic examination, provided the influence of depression, medications or superimposed concurrent disease is ruled out. Examples include: loss of endurance in sustaining activity, forced alterations in activities of daily living, muddled thinking, impaired concentration and mental processing and fatigue. **

7. Members who have new or enlarging T2 lesions, increase in brain atrophy on MRI, or new T1 Gd enhancing lesions on MRI accompanied by changes in the ability to perform daily activities.**

** These are members who have a documented treatment failure after receiving a minimum of 6 months each of Copaxone and Rebif. Diagnostic and/or clinical documentation of treatment failure will be required for the last therapy the member received. This requires that the member has failed a minimum of 6 months of (Copaxone and Rebif) and/or has a documented medical reason (i.e. intolerance) for not utilizing each of these therapies for a minimum of 6 months.

**Kurtzke Expanded Disability Status Scale (EDSS)**

<table>
<thead>
<tr>
<th>Rating</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal Neurological Exam</td>
</tr>
<tr>
<td>1.0</td>
<td>No Disability, minimal symptoms</td>
</tr>
<tr>
<td>1.5</td>
<td>No disability, minimal signs in more than one area</td>
</tr>
<tr>
<td>2.0</td>
<td>Slightly more disability in one area</td>
</tr>
<tr>
<td>2.5</td>
<td>Slightly greater disability in two areas</td>
</tr>
<tr>
<td>3.0</td>
<td>Moderate disability in one area but still walking independently</td>
</tr>
<tr>
<td>3.5</td>
<td>Walking independently but with moderate disability in one area and more than minimal disability in several others</td>
</tr>
<tr>
<td>4.0</td>
<td>Walking without aid, self-sufficient, up and about some 12 hours a day despite relatively severe disability; able to walk without aid or rest some 500 meters</td>
</tr>
<tr>
<td>4.5</td>
<td>Walking without aid, up and about much of the day, able to work a full day, may have some limitation of full activity or require some help, relatively severe disability but able to walk without aid or rest some 300 meters</td>
</tr>
</tbody>
</table>
5.0 Walking without aid or rest for about 200 meters, disability severe enough to impair full daily activities, can work a full day without special provisions

5.5 Ambulatory without aid or rest for about 100 meters; disability severe enough to prevent full daily activities

6.0 Intermittent or unilateral constant assistance (cane, crutch, brace) required to walk about 100 meters with or without resting

6.5 Needs canes, crutches, braces to walk for 20 meters without resting

7.0 Unable to walk beyond five meters even with aid; mostly confined to a wheelchair; wheels self in standard wheelchair and transfers alone; up and about in wheelchair some 12 hours a day

7.5 Unable to take more than a few steps; restricted to wheelchair; may need aid in transfer; wheels self but cannot carry on in standard wheelchair a full day; may require motorized wheelchair

8.0 Essentially restricted to bed, chair, or wheelchair, but may be out of bed itself much of the day; retains many self-care functions; generally has effective use of arms

8.5 Essentially restricted to bed much of the day; has some effective use of arms; retains some self-care functions

9.0 Helpless bed patient; can communicate and eat

9.5 Totally helpless bed patient; unable to communicate effectively or eat/swallow

10.0 Death due to MS


REFERENCES:


23. All about MS. Available at www.multi-sclerosis.org.


27. Extavia® Prescribing Information. Novartis Pharmaceuticals Corp. 8/2009

Revision/Review Date: MAC 10/12/2011
Associated Policy: Prior Authorization of Medications 236.200

NOTE: Clinical reviewer must override criteria when, in his/her professional judgment, the requested item is medically necessary.