OVERVIEW

Clinical Justification:
All multiple sclerosis drugs are restricted to use by neurologists. This is to ensure that patients are being monitored for disease progression and side effects by a specialist. Interferon and glatiramer have a long history of use, and proven safety and tolerability profile, which is why they are first line therapy for HPSJ members. Newer agents, such as Tecfidera, Aubagio, and Gilenya have more risk of potentially serious adverse effects. Though they are more convenient to administer (oral), they have had less time on the market, and will require robust post-marketing data to ensure patient safety. Both Novantrone and Tysabri are restricted as last line disease modifying therapy, due to the risks involved with these drugs. They both have black box warnings. Novantrone for myocardial toxicity, and Tysabri for Progressive Multifocal Leukoencephalopathy. Both are potentially fatal conditions. Lemtrada is reserved for last line due to the same reason, mixed efficacy results and potential safety concerns.
**Triage:**
1. Appropriate diagnosis
2. Prescribed by a neurologist
3. List of previous MS drugs tried, reaction, type/severity, or documentation of disease progression in chart notes.

**EVALUATION CRITERIA FOR APPROVAL / EXCEPTION CONSIDERATION**
Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

**1st Line Disease Modifying Therapy**

- **Interferon β -1b (Betaseron), Interferon β -1a (Avonex), Interferon β -1a (Rebif), Glatiramer (Glatopa)**
  - **Coverage Criteria:** Restricted to patients with a verified diagnosis of MS with therapy initiated by a neurologist. Avonex, Copaxone, Rebif, and Betaseron are first line therapy for multiple sclerosis.
  - **Limits:** None
  - **Required Information for Approval:** Prescription must be written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis.
  - **Notes:** Copaxone 20mg and 40mg are non-formulary.

**2nd Line Disease Modifying Therapy**

- **Fingolimod (Gilenya), Teriflunomide (Aubagio), Dimethyl Fumarate (Tecfidera)**
  - **Coverage Criteria:** Reserved for second line therapy after treatment failure of Avonex, Glatopa, Rebif, or Betaseron. Restricted to patients with a verified diagnosis of MS with therapy initiated by a neurologist.
  - **Limits:** None
  - **Required Information for Approval:** Prescription written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis, and must have pharmacy fill history, and chart note documentation of treatment failure of one First-Line Disease Modifying Treatment.

**3rd Line Disease Modifying Therapy**

- **Mitoxantrone (Novantrone), Natalizumab (Tysabri)**
  - **Coverage Criteria:** Reserved as third line therapy for MS behind [1] Betaseron / Avonex / Rebif / Glatopa, AND [2] Gilenya or Aubagio or Tecfidera due to increased risk of developing progressive multifocal leukoencephalopathy (PML). Documentation of a negative anti-JCV antibody test is required at initiation and annually for continuation.
  - **Limits:** None
  - **Required Information for Approval:** Prescription must be written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis. Additionally, patient must have documented treatment failure of the above two categories (1st line and 2nd line MS drugs).

**Alemtuzumab (Lemtrada)**
  - **Coverage Criteria:** Reserved for patients with relapsing remitting MS with inadequate treatment response to one drug from the following two categories: [1] Betaseron / Avonex / Rebif / Glatopa, AND [2] Gilenya or Aubagio. Members must have no previous history of malignancy, and documentation of negative HIV, HBV, HCV, and TB tests.
  - **Limits:** None
  - **Required Information for Approval:** Prescription must be written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis. Additionally, patient must have documented treatment failure of the above two categories (1st line and 2nd line MS drugs). Documentation that the member is negative for latent or active infections.
  - **Other Notes:** Daclizumab (Zinbryta) was discontinued by the manufacturer in March 2018 due to the drug’s concerning benefit/risk profile.

**Ocrelizumab (Ocrevus)**
  - **Coverage Criteria:** For patients with Relapsing MS (RMS), Ocrevus is reserved for patients with inadequate treatment response to one drug from the following two categories: [1] Betaseron / Avonex / Rebif / Glatopa, AND [2] Gilenya or Aubagio. Prescription must be written by a neurologist and members must have no previous history of malignancy, and documentation of negative HIV, HBV, HCV, and TB tests.
tests. It must also be documented that the member is negative for latent or active infections and a negative anti-JCV antibody test is required at initiation and annually for continuation.

- For patients with **Primary Progressive Multiple Sclerosis (PPMS)**, members must have no previous history of malignancy, and documentation of negative HIV, HBV, HCV, and TB tests. Prescription must be written by a neurologist and patient must have chart notes showing a diagnosis of PPMS. Additionally, there must have documented treatment failure of the above two categories (1st line and 2nd line MS drugs). Documentation that the member is negative for latent or active infections and a negative anti-JCV antibody test is required at initiation and annually for continuation.

| **Required Information for Approval:** Prescription must be written by a neurologist. Patient must have chart notes showing a diagnosis of Multiple Sclerosis. Additionally, patient must have documented treatment failure of the above two categories (1st line and 2nd line MS drugs). Documentation that the member is negative for latent or active infections and a negative anti-JCV antibody test is required at initiation and annually for continuation.

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### References

1. Ocrevus (ocrelizumab) [prescribing information]. South San Francisco, CA: Genentech Inc; March 2017.

**REVIEW & EDIT HISTORY**

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<thead>
<tr>
<th>Document Changes</th>
<th>Reference</th>
<th>Date</th>
<th>P&amp;T Chairman</th>
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<tr>
<td>Creation of Policy</td>
<td>MS Drug Class Review 5-21-2013.docx</td>
<td>5/2013</td>
<td>Jonathan Szkotak, PharmD BCACP</td>
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<tr>
<td>Updated Policy</td>
<td>Tecfidera Monograph 2014-09-16.docx</td>
<td>9/2014</td>
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<td>Updated Policy</td>
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<td>9/2015</td>
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<td>Updated Policy</td>
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<td>Matthew Garrett, PharmD</td>
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*Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy*