Policy Statement:

Physicians Health Plan, PHP Insurance & Service Company, and Sparrow PHP will cover Aubagio, Gilenya, Tecfidera, and Ampyra through the Pharmacy Benefit, and Ocrevus through the Medical Benefit based on approval by the Clinical Pharmacist or Medical Director using the following determination guidelines.

Drugs and Applicable Coding:

J Code: Ocrevus - J2350 (1u/1mg)

Clinical Determination Guidelines:

Document the following with chart notes:

A. Oral MS Agents:
   1. Agents
      a. Aubagio® (teriflunomide oral)
      b. Gilenya® (fingolimod oral)
      c. Tecfidera® (dimethyl fumarate oral)
   2. Diagnosis & severity: Relapsing-remitting multiple sclerosis
   3. Prescribing provider: Neurologist
   4. Dosage regimen (see Appendix II)
   5. Approval
      a. Initial: 6 mons.
      b. Re-approval: 12 mons.
B. IV MS Agent: Ocrevus® IV (ocrelizumab)
   1. Diagnosis & severity: Relapsing-remitting MS or primary-progressive MS
   2. Prescribing provider: Neurologist
   3. Dosage Regimen (see Appendix II)
   4. Other therapies: Failure of significant adverse effects to 2 preferred MS agents
   5. Approval:
      a. Initial: 12 mons.
      b. Re-approval: 12 mons.

C. Ampyra® (dalfampridine oral)
   1. Age ≥18
   2. Prescriber: Neurologist
   3. Diagnosis & severity: MS w documented difficulty walking, resulting in significant limitations of activities of daily living
   4. Walk-speed
      a. Clinical notes documenting 3 measurements & average score.
      b. Timed 25-foot walk speed (T25FW): Baseline 25 feet in 8 - 45 seconds
   5. Other therapies: No prior treatment & failure w Ampyra
   6. Dosage regimen (see Appendix II)
   7. Approval
      a. Initial approval: 4 mons
      b. Re-approval: 6 mons.; meet all the below:
         • **Responder:** Shows benefit after the initial 4-mon. trial period while on medication. *(Ongoing & future coverage of Ampyra will not be authorized for non-responders)*
         • T25FW: Improved/maintained >20% above baseline
         • Significant limitations in activities of daily living: Improved or resolved as a result of ↑ speed of ambulation as documented in clinical notes
   8. Exclusions:
      a. History of seizures
      b. Moderate to severe renal impairment (CrCl < 50 ml/min)
## Appendix I: Patient Safety and Monitoring

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adverse Reactions</th>
<th>Monitoring &amp; Contraindications</th>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ampyra</strong> dalfampridine</td>
<td>• CNS: Asthenia (7%), balance disorder (5%), Dizziness (7%), HA (7%), insomnia (9%)&lt;br&gt;• GI: Nausea (7%)&lt;br&gt;• Misc.: UTI (12%)&lt;br&gt;• Preg.: Adverse events seen in animal repro. studies (↓growth &amp; death)</td>
<td>• Lab: CrCl pre. &amp; annually</td>
<td>• Medication guide</td>
</tr>
<tr>
<td><strong>Aubagio</strong> teriflunomide</td>
<td>• CNS: Paraesthesia (9-10%),&lt;br&gt;• Derm: Alopecia (10-13%)&lt;br&gt;• GI: Diarrhea (15-18%), nausea (9-14%)&lt;br&gt;• Hepatic: ↑ALT (black box warning)&lt;br&gt;• Misc.: Influenza (9-12%)&lt;br&gt;• Preg.: Based on animal data, may cause major birth defects if used in preg. Contraindicated in preg. or childbearing potential (not using contraception).</td>
<td>• Labs: transaminase &amp; bilirubin - 6 mons pre &amp; post, periodically; CBC 6 mons pre. &amp; w signs of infection; K as needed&lt;br&gt;• Blood pressure: Pre. &amp; intermittently</td>
<td>• Medication guide</td>
</tr>
<tr>
<td><strong>Gilenya</strong> fingolimod HCl</td>
<td>• CNS: HA (25%)&lt;br&gt;• GI: Diarrhea (12%), ↑ALT/AST&lt;br&gt;• Resp.: Cough (10%)&lt;br&gt;• Misc.: Back pain (12%), Influenza (13%)&lt;br&gt;• Preg.: Adverse events seen in animal repro. studies</td>
<td>• Labs: CBC - pre. &amp; periodically; LFT’s - 6 mons pre &amp; periodically&lt;br&gt;• Bradycardia: HR, blood pressure - hrly. X 6 ; continue watch w EKG if HR &lt; 45 or new 2nd degree AV block&lt;br&gt;• Ophth. exam: Pre, 3-4 mons. during &amp; intermittently&lt;br&gt;• Resp: FEV1 if needed&lt;br&gt;• Misc: VZV antibodies, S&amp;S of infection</td>
<td>• Medication guide</td>
</tr>
<tr>
<td><strong>Tecfidera</strong> dimethyl fumarate</td>
<td>• GI: Abdominal pain (18%), diarrhea (14%)&lt;br&gt;• Misc.: Flushing (40%)&lt;br&gt;• Preg.: Adverse events seen in animal repro. studies</td>
<td>• Labs: CBC - pre. 6 mons &amp; annually,&lt;br&gt;• Infusion rx.: 1 hr end of infusion&lt;br&gt;• S &amp; Sx of infection, malignancy &amp; PML</td>
<td>• Medication guide</td>
</tr>
<tr>
<td><strong>Ocrevus</strong> (ocrelizumab)</td>
<td>• Derm: Skin infection (14%)&lt;br&gt;• Hem/Onco: ↓IgM (17%), ↓neutrophils&lt;br&gt;• Resp: URI (40-49%)&lt;br&gt;• Misc: Infusion rxs. (34-40%)&lt;br&gt;• Preg.: Monoclonal IgG known to cross the placenta</td>
<td>• Hep B screen prior to tx&lt;br&gt;• Infusion rx.: 1 hr end of infusion</td>
<td>• Medication guide</td>
</tr>
</tbody>
</table>
Appendix II: Dosage Regimen

<table>
<thead>
<tr>
<th>Drug</th>
<th>Standard maintenance dosing regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aubagio® 7 or 14 mg PO daily</td>
<td></td>
</tr>
<tr>
<td>Gilenya® 0.5 mg PO daily</td>
<td></td>
</tr>
<tr>
<td>Tecfidera® 240 mg PO BID</td>
<td></td>
</tr>
<tr>
<td>Ocrevus® 300 mg IV at wk 0 &amp; 2; then 600 mg IV q6 mons. subsequently 600 mg IV q6months</td>
<td></td>
</tr>
<tr>
<td>Ampyra® 10 mg PO BID</td>
<td></td>
</tr>
</tbody>
</table>

References and Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Ampyra, Aubagio, Gilenya, Tecfidera, Ocrevus, accessed June 2018
4. Assessing dalfampridine efficacy in the physician’s office. Multiple Sclerosis Journal 2014:20(1);24-26

Approved By:

Peter Graham, MD – PHP Executive Medical Director

Human Resources (Kurt Batteen)