Multiple Sclerosis Step Therapy and Quantity Limit Criteria

Tysabri (natalizumab) will NOT be included in this step therapy program for Blue Cross and Blue Shield of Illinois because this plan does not cover Tysabri under the pharmacy benefit.

FDA APPROVED INDICATIONS AND DOSAGE\(^1\)-\(^7\)

<table>
<thead>
<tr>
<th>Available Products</th>
<th>Indication</th>
<th>Dosage and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avonex (interferon (\beta)-1a) intramuscular injection</td>
<td>RRMS(^b)</td>
<td>30 mcg intramuscularly once weekly</td>
</tr>
<tr>
<td>Betaseron, Extavia (interferon (\beta)-1b)</td>
<td>RRMS(^b)</td>
<td>Patients should be started at 0.0625 mg subcutaneously every other day, and increased over a six-week period to 0.25 mg every other day. See recommended titration table:</td>
</tr>
<tr>
<td></td>
<td>EUR.M.S.</td>
<td>Dosage and Volume</td>
</tr>
<tr>
<td></td>
<td>Weeks 1-2</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td>Weeks 3-4</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>Weeks 5-6</td>
<td>75%</td>
</tr>
<tr>
<td></td>
<td>Week 7+</td>
<td>100%</td>
</tr>
<tr>
<td>Copaxone (glatiramer acetate) subcutaneous injection</td>
<td>RRMS</td>
<td>20 mg subcutaneously daily</td>
</tr>
<tr>
<td>Gilenya (fingolimod) tablet</td>
<td>RRMS</td>
<td>0.5 mg orally once daily</td>
</tr>
<tr>
<td>Rebif (interferon (\beta)-1a) subcutaneous injection</td>
<td>RRMS</td>
<td>22 mcg or 44 mcg injected subcutaneously three times per week. Patients should be started at 20% of the prescribed dose three times a week and increased over a 4-week period to the targeted dose, either 22 mcg or 44 mcg three times a week. See recommended titration table:</td>
</tr>
<tr>
<td></td>
<td>EUR.M.S.</td>
<td>Dosage and Volume</td>
</tr>
<tr>
<td></td>
<td>Weeks 1-2</td>
<td>20%</td>
</tr>
<tr>
<td></td>
<td>Weeks 3-4</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>Weeks 5+</td>
<td>100%</td>
</tr>
<tr>
<td>Tysabri (natalizumab) intravenous infusion</td>
<td>RRMS,</td>
<td>300 mg infused intravenously over approximately 1 hr, given at CONSIDEROUT 4-week (28-day) intervals(^a),(^c)</td>
</tr>
<tr>
<td>Moderate to severe CD</td>
<td>EUR.M.S.</td>
<td>Dosage and Volume</td>
</tr>
</tbody>
</table>

RRMS- Relapsing-remitting multiple sclerosis
CD- Crohn’s disease
\(^a\)- In Crohn’s disease, discontinue in patients that have not experienced therapeutic benefit by 12 weeks of induction therapy, and in patients that cannot discontinue chronic concomitant steroids within six months of starting therapy.
\(^b\)- approved for patients with first clinical event suggestive of multiple sclerosis
\(^c\)- in adult patients with moderately to severely active disease who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of tumor necrosis factor-alpha (TNF-a)
**CLINICAL RATIONALE**

**Injectable Disease Modifying Agents (DMAs) for Multiple Sclerosis (MS)**

DMAs for the treatment of MS reduce the number and severity of relapses, reduce the number of new lesions appearing on magnetic resonance imaging, and may reduce long-term progression of MS.8,9 Guidelines from the United States and Europe recommend treatment for RRMS be initiated with either glatiramer or interferon beta (INFβ). Although the INFβ agents differ in route of administration (intramuscular or subcutaneous) and in dosing frequency, studies have not shown clinical differences in efficacy between the different types of INFβ. The INFβ agents are considered appropriate for patients at high risk of developing clinically definite MS, or those who already have RRMS or secondary progressive MS and are experiencing relapses. There is a probable dose or frequency of dosing response curve associated with use of INFβ agents. Interferon beta-1a (Avonex, Rebif) has been associated with less neutralizing antibody formation than interferon beta-1b (Betaseron, Extavia). The clinical effects of these neutralizing antibodies are uncertain. Their presence has been associated with a possible decrease in interferon efficacy. The route of administration of the INFβ agents does not have apparent effects on efficacy but side effect profiles differ between routes of administration. Because glatiramer works by a different mechanism than interferons, the side effect profile is different from interferons and may make this agent an option for some patients unable to tolerate interferons.9 Glatiramer is considered an appropriate option for patients with RRMS. Natalizumab is recommended for patients with relapsing forms of MS who have had an inadequate response to, or are unable to tolerate other MS therapies.8,9

Concurrent use of more than one injectable DMA has been studied in clinical trials. The combinations of INFβ with natalizumab and glatiramer with natalizumab have been studied. Although a beneficial effect was seen (such as improved magnetic resonance imaging (MRI) parameters), there may be more adverse reactions associated with combination therapies. The study with a combination of INFβ and natalizumab was halted due to reported cases of progressive multifocal leukoencephalopathy (PML).21 The adverse effects seen with combination therapies are similar to those reported with the individual agents, but it is unclear if the risk for developing these adverse effects is higher in combination therapy. Some of the clinical effects of glatiramer may occur by entry of regulatory glatiramer-reactive cells into the central nervous system (CNS) across a disrupted blood-brain-barrier (BBB) and effects on CNS resident cells. It is possible that combining glatiramer with therapies that close the BBB like INFβ and natalizumab may limit the effectiveness of glatiramer.21 There is an ongoing double-blind, placebo-controlled, phase III study looking at a combination of INFβ and glatiramer. The benefits of combination therapies and the safety concerns associated with concurrent therapy still need further investigation.

**Oral DMAs for MS**10

Fingolimod, a sphingosine 1 phosphate (S1P) receptor modulator, is the first oral disease modifying therapy for RRMS. Fingolimod works by trapping lymphocytes (T-cells and B-cells) in the lymph nodes so that they cannot attack the central nervous system. Clinical studies have shown fingolimod to be effective in preventing MS relapses, and fingolimod was superior to Avenox in one comparative study. However, its place in therapy is undetermined. Fingolimod has not been studied in combination with (concurrently with) other DMAs. Higher doses (1.25 mg compared to 0.5 mg) of fingolimod were studied in clinical trials, but there was not a statistical difference in efficacy. More serious adverse events, including increased bradycardia, were reported with 1.25 mg.1 Dose-related first dose bradycardia and atrioventricular heart block has been reported. Patients should receive their first dose of fingolimod under medical supervision and be monitored for six hours post dose.5 Ophthalmic exams are recommended to detect macular edema as a greater incidence of macular edema was seen in the fingolimod-treated group compared to the placebo group in clinical trials. Dose-dependent decrease of pulmonary function (forced expiratory volume within one second [FEV1]) was observed in clinical trials with fingolimod. It is unclear whether pulmonary function changes will continue to
worsen over time with uninterrupted fingolimod dosing. Long term safety data is not available for fingolimod as the longest phase 3 trial to date was 2 years in duration.

A National MS Society consensus statement recommends changing from one disease modifying therapy to another only for medically appropriate reasons (e.g., lack of efficacy, adverse effects, or if better treatments options become available).8

**Crohn’s Disease**
The American College of Gastroenterology (ACG) practice guidelines for CD in adults (2009)13 recommend treatment for mild to moderate CD with oral aminosalicylates (mesalamine and sulfasalazine), antibiotics (metronidazole or ciprofloxacin), and corticosteroid treatment (controlled-release budesonide or other conventional corticosteroids).13,14 For moderate to severe disease, azathioprine or 6-mercaptopurine (6-MP) are effective.13 Infliximab is recommended by ACG, the American Gastroenterological Association (AGA), and the British Society of Gastroenterology as a second-line treatment option in patients with moderately to severely active, refractory CD (including fistulizing disease).12,13,15,16 The 2009 ACG guidelines for CD13 state that infliximab, adalimumab, and certolizumab are all effective in the treatment of moderate to severely active CD in patients who have not responded despite complete and adequate therapy with a corticosteroid or an immunosuppressive agent. Natalizumab is effective in patients who have had an inadequate response or are unable to tolerate conventional CD therapy and anti-TNF-α monoclonal antibody therapy.13

**Natalizumab and Progressive Multifocal Leukoencephalopathy (PML)**
Tysabri (natalizumab) has a black box warning for increasing the risk of PML, an opportunistic viral infection of the brain that usually leads to death or severe disability. The FDA MedWatch alert on February 5, 2010 notified healthcare professionals and patients that the risk of developing PML increases with the number of natalizumab infusions received. Information about the occurrence of Immune Reconstitution Inflammatory Syndrome (IRIS) in patients who have developed PML and subsequently discontinued natalizumab has also been added to the drug label. IRIS is a rare condition characterized by a severe inflammatory response that can occur during or following immune system recovery, causing an unexpected decline in a patient’s condition after return of immune function.20 Revisions to the drug label and patient Medication Guide, with the continued use of the TOUCH Prescribing Program, are intended to maximize the safe use of Tysabri (natalizumab) and the identification of new PML cases.20

For additional clinical information see Prime Therapeutics Formulary Chapter 9.6C Multiple Sclerosis Agents.

**REFERENCES**


**Document History**

Original Prime Standard criteria approved by P&T UM Committee 02/2009
Annual Review Prime Standard criteria with changes approved by P&T UM Committee 02/2010
Administrative Action (addition of Actemra to list of biologics) 04/2010
Mid-year Review Prime Standard Criteria (addition of Gilenya) reviewed by P&T UM Committee 11/2010
Multiple Sclerosis Step Therapy with Gilenya™ Quantity Limit

OBJECTIVE
The intent of the Multiple Sclerosis Step Therapy (ST) program is to encourage the use of preferred multiple sclerosis agents before the nonpreferred agents for patients initiating therapy and accommodate for use of nonpreferred multiple sclerosis agents when preferred agents cannot be used due to previous trial and failure, allergy, intolerance, or contraindication. Tysabri (natalizumab) will also be reviewed for use in patients with moderate to severe Crohn’s disease (CD) who have had inadequate response to or unable to tolerate conventional CD therapies (aminosalicylates, sulfasalazine, metronidazole, ciprofloxacin, corticosteroids, methotrexate, or immunomodulators such as azathioprine or 6-mercaptopurine) and inhibitors of tumor necrosis factor- alpha (TNF-α) [Cimzia (certolizumab), Humira (adalimumab), or Remicade (infliximab)]. Requests for the nonpreferred agents will be reviewed when patient-specific documentation has been provided.

The intent of the Gilenya Quantity Limit (QL) program is to encourage appropriate prescribing quantities as recommended by Food and Drug Administration (FDA)-approved product labeling and/or clinical studies and/or guidelines. Requests for larger quantities will be reviewed if the prescriber provides evidence that dosing outside of FDA labeling is appropriate for the patient.

TARGET DRUGS – STEP THERAPY
Betaseron® (interferon β-1b)
Extavia® (interferon β-1b)
Gilenya™ (fingolimod)
Tysabri® (natalizumab)

QUANTITY LIMIT TARGET DRUG - RECOMMENDED LIMIT

<table>
<thead>
<tr>
<th>Brand (generic)</th>
<th>GPI</th>
<th>Quantity Limit Per Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gilenya™ (fingolimod)</td>
<td>62407025100120</td>
<td>1 tablet</td>
</tr>
</tbody>
</table>

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Gilenya will be approved when ONE of the following is met:
   1. ALL of the following:
      a. Gilenya is being used for FDA approved indication
         AND
      b. ONE of the following:
         i. The patient’s medication history indicates current use of the requested nonpreferred multiple sclerosis agent OR
         ii. The patient’s medication history indicates use of a preferred multiple sclerosis agent OR
         iii. The patient has a documented allergy, contraindication, or intolerance to a preferred multiple sclerosis agent
         AND
      b. ONE of the following:
         i. The patient is not currently being treated with any other disease modifying agent (DMA) for MS OR
         ii. The patient is currently being treated with a DMA for MS AND the DMA will be discontinued before starting Gilenya (fingolimod)
         AND
      c. ONE of the following:
i. The quantity requested is less than or equal to the program quantity limit OR
ii. The quantity (dose) requested is greater than the maximum dose recommended in FDA-approved labeling, and the prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist

OR

2. The physician has submitted documentation in support of therapy with Gilenya (fingolimod) for the patient or for a higher dose (above FDA-approved labeling) for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist

**Betaseron or Extavia** will be approved when ONE of the following is met:

1. **ALL** of the following:
   a. **ONE** of the following:
      i. The patient’s medication history indicates current use of the requested nonpreferred multiple sclerosis agent **OR**
      ii. The patient’s medication history indicates use of a preferred multiple sclerosis agent **OR**
      iii. The patient has a documented allergy, contraindication, or intolerance to a preferred multiple sclerosis agent **AND**
   b. **ONE** of the following:
      i. The patient is not currently being treated with a disease modifying agent (DMA) for multiple sclerosis (MS) **OR**
      ii. The patient is currently being treated with a DMA for MS AND the DMA will be discontinued before starting the requested agent

OR

2. The physician has submitted documentation in support of therapy with the nonpreferred agent for the patient which has been reviewed and approved by the Clinical Review pharmacist

**Tysabri** will be approved when **ONE** of the following is met:

*NOTE: Tysabri (natalizumab) will NOT be included in this step therapy program for Blue Cross and Blue Shield of Illinois, because this plan does not cover Tysabri under the pharmacy benefit.*

1. **ALL** of the following:
   a. **ONE** of the following:
      i. The patient’s medication history indicates current use of the requested nonpreferred multiple sclerosis agent **OR**
      ii. The patient’s medication history indicates use of a preferred multiple sclerosis agent **OR**
      iii. The patient has a documented allergy, contraindication, or intolerance to a preferred multiple sclerosis agent **AND**
   b. **ONE** of the following:
      i. The patient is not currently being treated with a disease modifying agent (DMA) for multiple sclerosis (MS) **OR**
      ii. The patient is currently being treated with a DMA for MS AND the DMA will be discontinued before starting the requested agent

OR

2. **ALL** of the following:
   a. Tysabri (natalizumab) is prescribed for use in patients with moderate to severe Crohn’s disease (CD) **AND**
b. The patient has had an inadequate response to, a documented allergy, intolerance, or contraindication to conventional CD therapies (aminosalicylates, sulfasalazine, metronidazole, ciprofloxacin, corticosteroids, methotrexate, or immunomodulators such as azathioprine or 6-mercaptopurine) AND
c. The patient has had an inadequate response to, a documented allergy, intolerance, or contraindication to inhibitors of TNF-a [Cimzia (certolizumab), Humira (adalimumab), or Remicade (infliximab)] AND
d. ONE of the following
   i. The patient is not currently being treated with any other biologic immunomodulator OR
   ii. The patient is currently being treated with a biologic immunomodulator AND the biologic immunomodulator will be discontinued before starting Tysabri (natalizumab)

OR

3. The physician has submitted documentation in support of therapy with the nonpreferred agent for the patient which has been reviewed and approved by the Clinical Review pharmacist

Length of approval: 12 months
Multiple Sclerosis Step Therapy with Gilenya™ Quantity Limit

**ELECTRONIC EDIT**
For the Multiple Sclerosis step therapy edit, a 90-day look-back period was chosen to capture recent or current therapy for the identical agent. A 365-day look-back period was chosen to capture past, recent, or current therapy for one prerequisite for multiple sclerosis (MS) or two prerequisite agents for Crohn’s disease (CD).

For patients who have previously been on a biologic immunomodulator that are requesting Tysabri (natalizumab) or for patients who have previously been on a disease modifying agent (DMA) for MS that are requesting any targeted agent, a washout period will be required before initiating the targeted agent. For the automatic functionality, a 30-day look-back timeframe will be used to capture current therapy of other biologic immunomodulators or other DMAs.

**SUMMARY OF MULTIPLE SCLEROSIS STEP THERAPY**
NOTE: Tysabri (natalizumab) will NOT be included in this step therapy program for Blue Cross and Blue Shield of Illinois because this plan does not cover Tysabri under the pharmacy benefit.

<table>
<thead>
<tr>
<th>Targeted Agent(s)</th>
<th>Betaseron, Extavia, Gilenya, Tysabri</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is auto-grandfathering implemented? (with look-back time frame)</td>
<td>Yes (90 days*)</td>
</tr>
<tr>
<td>Prerequisite Agent(s) for MS</td>
<td>Avonex, Copaxone, Rebif</td>
</tr>
<tr>
<td>Number of prerequisites required</td>
<td>1</td>
</tr>
<tr>
<td>Prerequisite look-back time frame</td>
<td>365 daysb</td>
</tr>
<tr>
<td>Prerequisite Agent(s) for CD</td>
<td>One conventional agent: aminosalicylates, budesonide EC, methotrexate (oral or injection), azathioprine, 6-mercaptopurine AND One TNF-α inhibitor: Cimzia (certolizumab), Humira (adalimumab), Remicade (infliximab)</td>
</tr>
<tr>
<td>Number of prerequisites required</td>
<td>2</td>
</tr>
<tr>
<td>Prerequisite look-back time frame</td>
<td>365 daysb</td>
</tr>
<tr>
<td>Age-related edit?</td>
<td>NA</td>
</tr>
<tr>
<td>Additional comments</td>
<td>Tysabri will NOT pay if a claim for another biologic product is found in the previous 30 days. All targeted agents will NOT pay if a claim for another DMA for MS is found in the previous 30 days.</td>
</tr>
</tbody>
</table>

*a - The system searches for a claim with a days supply that begins or ends in the past 90 days. For claims with a 30 day supply the system would be able to identify a claim processed for payment between 1 and 120 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 180 days.*

*b - The system searches for a claim with a days supply that begins or ends in the past 365 days. For claims with a 30 day supply the system would be able to identify a claim processed for payment between 1 and 395 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 455 days.*
### DETAILS OF BETASERON, EXTAVIA, AND GILENYA STEP THERAPY

<table>
<thead>
<tr>
<th>Targeted Agents</th>
<th>GPIs (multisource code)</th>
<th>Prior Agents</th>
<th>GPIs (multisource code)</th>
<th>Look-back Time frames</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ANY ONE of:</strong></td>
<td></td>
<td><strong>Contraindicated Therapy</strong> – must NOT have any other DMA except the identical agent:</td>
<td></td>
<td><strong>Contraindicated Therapy look-back time frame:</strong></td>
</tr>
<tr>
<td>Betaseron (interferon β-1b)</td>
<td>624030605021**</td>
<td>Avonex (interferon β-1a)</td>
<td>624030604564**</td>
<td>30 days&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Extavia (interferon β-1b)</td>
<td>624070251001** (M, N, or O)</td>
<td>Betaseron (interferon β-1b)</td>
<td>624030605021**</td>
<td></td>
</tr>
<tr>
<td>Gilenya (fingolimod)</td>
<td></td>
<td>Extavia (interferon β-1b)</td>
<td>624070251001**</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Copaxone (glatiramer)</td>
<td>62400030******</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gilenya (fingolimod)</td>
<td>624030604520**</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rebif (interferon β-1a)</td>
<td>6240505000***** (M, N, O, or Y)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tysabri (natalizumab)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ANY ONE of a preferred agent:</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>Prerequisite look-back time frame:</strong></td>
</tr>
<tr>
<td>Avonex (interferon β-1a)</td>
<td>624030604564**</td>
<td></td>
<td>365 days&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Copaxone (glatiramer)</td>
<td>62400030******</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rebif (interferon β-1a)</td>
<td>624030604520** (M, N, O, or Y)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>For auto-grandfathering, ANY ONE of:</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>Auto-grandfathering look-back time frame:</strong></td>
</tr>
<tr>
<td>Betaseron (interferon β-1b)</td>
<td>624030605021**</td>
<td></td>
<td>90 days&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Extavia (interferon β-1b)</td>
<td>624070251001** (M, N, or O)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gilenya (fingolimod)</td>
<td>Set up at drug or GPI 12 level</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> - The system searches for a claim with a days supply that begins or ends in the past 30 days. For claims with a 30 day supply the system would be able to identify a claim processed for payment between 1 and 60 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 120 days.

<sup>b</sup> - The system searches for a claim with a days supply that begins or ends in the past 365 days. For claims with a 30 day supply the system would be able to identify a claim processed for payment between 1 and 395 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 455 days.

<sup>c</sup> - The system searches for a claim with a days supply that begins or ends in the past 90 days. For claims with a 30-day supply the system would be able to identify a claim processed for payment between 1 and 120 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 180 days.
DETAILS OF TYSAHRI STEP THERAPY
NOTE: Tysabri (natalizumab) will NOT be included in this step therapy program for Blue Cross and Blue Shield of Illinois because this plan does not cover Tysabri under the pharmacy benefit.

<table>
<thead>
<tr>
<th>Targeted Agents</th>
<th>GPIs (multisource code)</th>
<th>Prior Agents</th>
<th>GPIs (multisource code)</th>
<th>Look-back Time frames</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANY ONE of: Tysabri (natalizumab)</td>
<td>6240505000**** (M, N, or O)</td>
<td>Contraindicated Therapy – must NOT have: Actemra (tocilizumab), Amevive (alefacept), Cimzia (certolizumab), Enbrel (etanercept), Humira (adalimumab), Kineret (anakinra), Orencia (abatacept), Remicade (infliximab), Rituxan (rituximab), Simponi (golimumab), Stelara (ustekinumab), Avonex (interferon β-1a), Betaseron (interferon – 1b), Extavia (interferon – 1b), Copaxone (glatiramer), Gilenya (fingolimod), Rebif (interferon β-1a)</td>
<td>6650007000**** 9025051500**** 5250502010**** 6629003000**** 6627001500**** 6626001000**** 664001000**** 5250504000**** 2135306000**** 6672004000**** 9025058500**** 624030604564** 624030605021** 62400030****** 624070251001** 624030604520** (M, N, O, or Y) 6240505000**** (M, N, or O)</td>
<td>Contraindicated Therapy look-back time frame: 30 days^a</td>
</tr>
</tbody>
</table>

For prerequisites, For MS, ANY ONE of: Avonex (interferon β-1a), Copaxone (glatiramer), Rebif (interferon β-1a)

<table>
<thead>
<tr>
<th>GPIs (multisource code)</th>
<th>Pre-requisite look-back time frame: 365 days^b</th>
</tr>
</thead>
<tbody>
<tr>
<td>624030604564** 62400030****** 624030604520** (M, N, O, or Y)</td>
<td></td>
</tr>
</tbody>
</table>

For CD, ANY ONE of: aminosalicylates, budesonide EC, methotrexate (oral or injection), azathioprine, 6-mercaptopurine

<table>
<thead>
<tr>
<th>GPIs (multisource code)</th>
<th>Pre-requisite look-back time frame: 365 days^b</th>
</tr>
</thead>
<tbody>
<tr>
<td>525000****** 2210001200**** 66250050****** 21300050****** 99406010****** 2130004000**** (M, N, O, or Y)</td>
<td></td>
</tr>
</tbody>
</table>

AND one of: Cimzia (certolizumab), Humira (adalimumab), Remicade (infliximab)

<table>
<thead>
<tr>
<th>GPIs (multisource code)</th>
<th>Auto-grandfathering look-back time frame: 90 days^c</th>
</tr>
</thead>
<tbody>
<tr>
<td>5250502010**** 6627001500**** 5250504000**** (M, N, O, or Y)</td>
<td></td>
</tr>
</tbody>
</table>

For auto-grandfathering, ANY ONE of: Tysabri (natalizumab)

<table>
<thead>
<tr>
<th>GPIs (multisource code)</th>
<th>Auto-grandfathering look-back time frame: 90 days^c</th>
</tr>
</thead>
<tbody>
<tr>
<td>6240505000**** (M, N, or O)</td>
<td></td>
</tr>
</tbody>
</table>

Set up at drug or GPI 10 level

---

^a - The system searches for a claim with a days supply that begins or ends in the past 30 days. For claims with a 30 day supply the system would be able to identify a claim processed for payment between 1 and 60 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 120 days.

^b - The system searches for a claim with a days supply that begins or ends in the past 365 days. For claims with a 30 day supply the system would be able to identify a claim processed for payment between 1 and 395 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 455 days.

^c - The system searches for a claim with a days supply that begins or ends in the past 90 days. For claims with a 30-day supply the system would be able to identify a claim processed for payment between 1 and 120 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 180 days.
**Quantity Limits**

The quantity limit edit for Gilenya (fingolimod) allows an automatic approval for patients prescribed quantities at or below the program limits. This product is also subject to the step therapy criteria.

**PRIOR AUTHORIZATION CRITERIA QUESTION SET**

**Betaseron (interferon β-1b) or Extavia (interferon β-1b)**

**Initial and Renewal Evaluation**

1. Is the patient currently being treated with any other disease modifying agent (DMA) for MS other than the requested agent?  
   If yes, continue to 2. If no, continue to 3.

2. Will the DMA be discontinued before starting the requested agent?  
   If yes, continue to 3. If no, deny.

3. Is the patient currently being treated with requested medication?  
   If yes, approve for 12 months. If no, continue to 4.

4. Does the patient’s medication history include current or past use of Avonex (interferon β-1a), Copaxone (glatiramer), or Rebif (interferon β-1a)?  
   If yes, approve for 12 months. If no, continue to 5.

5. Does the patient have a documented allergy, contraindication, or intolerance to Avonex (interferon β-1a), Copaxone (glatiramer), or Rebif (interferon β-1a)?  
   If yes, approve for 12 months. If no, continue to 6.

6. Has the prescriber submitted and the pharmacist reviewed documentation in support of the requested therapeutic use for Betaseron, Extavia (interferon β-1b) in this patient?  
   If yes, pharmacist must review and may approve for 12 months based on review of information provided. If no, deny.

**Gilenya (fingolimod)**

**Initial and Renewal Evaluation**

1. Is Gilenya being prescribed for FDA approved indication?  
   If yes, continue to 2. If no, deny.

2. Has Gilenya (fingolimod) been previously approved under step therapy criteria and now is rejecting for a quantity over the set limit?  
   If yes, continue to 8. If no, continue to 3.

3. Is the patient currently being treated with any other disease modifying agent (DMA) for multiple sclerosis (MS)?  
   If yes, continue to 4. If no, continue to 5.

4. Will the DMA be discontinued before starting Gilenya (fingolimod)?  
   If yes, continue to 5. If no, deny.

5. Is the patient currently being treated with Gilenya (fingolimod)?  
   If yes, continue to 8. If no, continue to 6.

6. Does the patient’s medication history include current or past use of Avonex (interferon β-1a), Copaxone (glatiramer), or Rebif (interferon β-1a)?  
   If yes, continue to 8. If no, continue to 7.
7. Does the patient have a documented allergy, contraindication, or intolerance to Avonex (interferon \( \beta \)-1a), Copaxone (glatiramer), or Rebif (interferon \( \beta \)-1a)?
   If yes, continue to 8. If no, continue to 9.

8. Is the quantity requested greater than the maximum dose recommended in FDA-approved labeling?
   If yes, continue to 9. If no, approve for 12 months.

9. Has the prescriber submitted and the pharmacist reviewed documentation in support of the requested therapeutic use for Gilenya (fingolimod) in this patient or for a higher dose (above FDA-approved labeling) for the intended diagnosis?
   If yes, pharmacist must review and may approve for 12 months based on review of information provided. If no, deny.

**Tysabri (natalizumab)**

NOTE: Tysabri (natalizumab) will NOT be included in this step therapy program for Blue Cross and Blue Shield of Illinois because this plan does not cover Tysabri under the pharmacy benefit.

**Initial and Renewal Evaluation**

1. What is the patient’s diagnosis?
   a. Multiple Sclerosis
   b. Crohn’s disease
   c. Other
   If a, continue to 2. If b, continue to 7. If c, continue to 13.

2. Is the patient currently treated with any other disease modifying agent (DMA) for MS?
   If yes, continue to 3. If no, continue to 4.

3. Will the DMA be discontinued before starting Tysabri (natalizumab)?
   If yes, approve for 12 months. If no, deny.

4. Is the patient currently being treated with Tysabri (natalizumab)?
   If yes, approve for 12 months. If no, continue to 5.

5. Does the patient’s medication history include current or past use of Avonex (interferon \( \beta \)-1a), Copaxone (glatiramer), or Rebif (interferon \( \beta \)-1a)?
   If yes, approve for 12 months. If no, continue to 6.

6. Does the patient have a documented allergy, contraindication, or intolerance to Avonex (interferon \( \beta \)-1a), Copaxone (glatiramer), or Rebif (interferon \( \beta \)-1a)?
   If yes, approve for 12 months. If no, continue to 13.

7. Has the patient tried and failed treatment with conventional therapy (aminosalicylates, sulfasalazine, metronidazole, ciprofloxacin, corticosteroids, methotrexate, or immunomodulators such as azathioprine or 6-mercaptopurine) for Crohn’s disease?
   If yes, continue to 11. If no, continue to 8.

8. Does the patient have a documented allergy, intolerance or contraindication to conventional therapy for Crohn’s disease?
   If yes, continue to 9. If no, continue to 13.

9. Has the patient tried and failed treatment with a TNF-\( \alpha \) inhibitor [Cimzia (certolizumab), Humira (adalimumab), or Remicade (infliximab)] indicated for Crohn’s disease?
If yes, continue to 11. If no, continue to 10.

10. Does the patient have a documented allergy, intolerance or contraindication to TNF-α inhibitors indicated for Crohn’s disease?
   If yes, continue to 11. If no, continue to 13.

11. Is the patient currently being treated with any other biologic immunomodulator?
   If yes, continue to 12. If no, approve for 12 months.

12. Will the biologic immunomodulator be discontinued before starting Tysabri (natalizumab)?
   If yes, approve for 12 months. If no, deny.

13. Has the prescriber submitted and the pharmacist reviewed documentation in support of the requested therapeutic use for Tysabri (natalizumab) in this patient?
   If yes, pharmacist must review and may approve for 12 months based on review of information provided. If no, deny.

---

**Document History**

Original Prime Standard criteria approved by P&T UM Committee 02/2009
Initial Client Review Prime Standard criteria approved by HCSC Corporate Clinical Committee 06/2009
Annual Review Prime Standard criteria with changes approved by P&T UM Committee 02/2010
Client Specific Annual Review Prime Standard criteria with changes approved by HCSC Corporate Clinical Committee 04/2010
Client Specific Annual Review Prime Standard criteria with changes approved by HCSC Corporate Clinical Committee 11/2010
(addition of Gilenya)