Clinical Policy: Natalizumab (Tysabri)
Reference Number: ERX.SPA.162
Effective Date: 10.01.16
Last Review Date: 11.17

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

Description
Natalizumab (Tysabri®) is an integrin receptor antagonist.

FDA Approved Indication(s)
Tysabri is indicated:
• As monotherapy for the treatment of patients with relapsing forms of multiple sclerosis (MS)
• For inducing and maintaining clinical response and remission in adult patients with moderately to severely active Crohn’s disease (CD) with evidence of inflammation who have had an inadequate response to, or are unable to tolerate, conventional CD therapies and inhibitors of tumor necrosis factor-α (TNF-α)

Limitation(s) of use:
• Tysabri increases the risk of progressive multifocal leukoencephalopathy. When initiating and continuing treatment with Tysabri, physicians should consider whether the expected benefit of Tysabri is sufficient to offset this risk.
• In CD, Tysabri should not be used in combination with immunosuppressants or inhibitors of TNF-α.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

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

I. Initial Approval Criteria
   A. Multiple Sclerosis (must meet all):
      1. Diagnosis of relapsing-remitting MS;
      2. Prescribed by or in consultation with a neurologist;
      3. Age ≥ 18 years;
      4. Failure of one of the following (a or b) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced:
         a. Tecfidera or Gilenya and any of the following: an interferon-beta agent (Betaseron and Rebif are preferred agents), glatiramer (Glatopa 20 mg and Copaxone 40 mg are preferred agents), or Aubagio;
         b. Tecfidera and Gilenya;
      5. Member will not use other disease modifying therapies for MS concurrently;
      6. Dose does not exceed 300 mg (1 vial) every 4 weeks.
      Approval duration: 6 months

   B. Crohn’s Disease (must meet all):
      1. Diagnosis of moderate-to-severe CD;
      2. Prescribed by or in consultation with a gastroenterologist;
      3. Age ≥ 18 years;
      4. Failure of a trial of a thiopurine (6-mercaptopurine or azathiopurine) or methotrexate (MTX) used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
      5. Failure of adalimumab (Humira is preferred) for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effects are experienced;
Prior authorization is required for adalimumab
6. Dose does not exceed 300 mg (1 vial) every 4 weeks.
Approval duration: 6 months

C. 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 Envolve Pharmacy Solutions or
      member has previously met initial approval criteria;
   2. Member is responding positively to therapy (e.g., improved or maintained disease control evidenced by decreased or stabilized Expanded Disability Status Scale score or reduction in relapses or magnetic resonance imaging lesions);
   3. Member is not using other disease modifying therapies for MS concurrently;
   4. If request is for a dose increase, new dose does not exceed 300 mg (1 vial) every 4 weeks.
   Approval duration: 12 months

B. Crohn's Disease (must meet all):
   1. Currently receiving medication via health plan benefit or member has previously met all initial
      approval criteria;
   2. Member is responding positively to therapy (e.g., no disease progression, no significant toxicity);
   3. If request is for a dose increase, new dose does not exceed 300 mg (1 vial) every 4 weeks.
   Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2):
   1. Currently receiving medication via a health plan affiliated with Envolve 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
6-MP: 6-mercaptopurine MS: multiple sclerosis
CD: Crohn’s disease MTX: methotrexate
FDA: Food and Drug Administration TNF-α: tumor necrosis factor-α
Appendix B: Therapeutic Alternatives

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MS agents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avonex®, Rebif®</td>
<td>Avonex: 30 mcg IM Q week Rebit: 22 mcg or 44 mcg SC TIW</td>
<td>Avonex: 30 mcg/week Rebit: 44 mcg TIW</td>
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<tr>
<td>(interferon beta-1a)</td>
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<tr>
<td>Plegidry® (peginterferon beta-1a)</td>
<td>125 mcg SC Q2 weeks</td>
<td>125 mcg/2 weeks</td>
</tr>
<tr>
<td>Betaseron®, Extavia® (interferon beta-1b)</td>
<td>250 mcg SC QOD</td>
<td>250 mg QOD</td>
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</tbody>
</table>
## Clinical Policy

**Natalizumab**

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
</table>
| Copaxone®, Glatopa® (glatiramer acetate) | Copaxone: 20 mg SC QD or 40 mg SC TIW  
Glatopa: 20 mg SC QD | Copaxone: 20 mg/day or 40 mg TIW  
Glatopa: 20 mg/day |
| Aubagio® (teriflunomide)          | 7 mg or 14 mg PO QD                                                          | 14 mg/day               |
| Gilenya™ (fingolimod)            | 0.5 mg PO QD                                                                  | 0.5 mg/day              |
| Tecfidera® (dimethyl fumarate)    | 120 mg PO BID for 7 days, followed by 240 mg PO BID                           | 480 mg/day              |

### CD agents

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
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<tbody>
<tr>
<td>6-mercaptopurine (Purixan®)*</td>
<td>2 mg/kg/day</td>
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</tbody>
</table>
| methotrexate (Otrexup®, Rasuvo®)*| IM: 25 mg/week  
SC: 15 mg/week |
| azathioprine (Azasan®, Imuran™)*  | 2 mg/kg/day             |
| adalimumab (Humira®, Amjevita®)** | See regimen            |
| infliximab (Remicade®, Renflexis™, Inflectra™)** | See regimen            |
| Cimzia® (certolizumab)**         | See regimen             |

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.

*Off-label uses

**Requires PA

### V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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</thead>
</table>
| MS, CD     | 300 mg IV every 4 weeks  
In CD, discontinue in patients who 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 | 300 mg/4 weeks |

### VI. Product Availability

Vial containing solution for dilution: 300 mg/15 mL

### VII. References


<table>
<thead>
<tr>
<th>Reviews, Revisions, and Approvals</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy split from USS.SPMN.36 Multiple Sclerosis (MS) Treatments and USS.SPMN.24 Irritable Bowel Disease (IBD) Treatments. Converted to new template. Added dosing criteria. Modified approval duration to 6 months for initial and 12 months for renewal. MS criteria: clarified monotherapy restriction. CD criteria: added requirement for trial and failure of PDL Humira as one of the two required TNF inhibitors, unless contraindicated. Modified trial/failure of immunomodulator, aminosalicylate or corticosteroid to failure of “corticosteroid, with or without immunomodulator” per 2014 AGA Clinical decision tool.</td>
<td>08.16</td>
<td>09.16</td>
</tr>
<tr>
<td>For all trial/failure requirements, indicated that member can also meet criteria if intolerant (as opposed to just contraindicated) to therapy in question. For CD, added poor prognostic indicators as alternative to trial/failure requirement and modified trial/failure requirement to indicate an immunomodulator (as opposed to a corticosteroid with or without an immunomodulator) must be trialed.</td>
<td>11.16</td>
<td>12.16</td>
</tr>
<tr>
<td>4Q17 Annual Review Converted to new template. Added age requirement as safety and efficacy have not been established in pediatric populations. MS: Removed requirement for MRI as this is not a specific diagnostic test and involvement of specialist in the care is required. Updated preferencing to require at least one of the highly effective disease-modifying therapies on formulary (Tecfidera or Gilenya). Added PPMS as a diagnosis not covered. CD: diagnostic criteria modified to require verifiable information; removed poor prognostic indicators; added trial duration of 3 months for thiopurine or MTX</td>
<td>09.12.17</td>
<td>11.17</td>
</tr>
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</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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