POLICY Document for TYSABRI (natalizumab)

The overall objective of this policy is to support the appropriate and cost-effective use of the medication, specific to use of preferred medication options, and overall, clinically appropriate use. This document provides specific information to both sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 3: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

CAREFIRST: EXCEPTIONS CRITERIA
AUTOIMMUNE CONDITIONS

PRIMARY PREFERRED PRODUCTS: ENTYVIO, SIMPONI ARIA, SKYRIZI, STELARA

Client Requested: The intent of the criteria is to ensure that patients follow selection elements as established by CareFirst.

POLICY
This policy informs prescribers of preferred products and provides an exception process for targeted products through prior authorization.

I. PLAN DESIGN SUMMARY

This program applies to the autoimmune drug products specified in this policy. Coverage for targeted product is provided based on clinical circumstances that would exclude the use of the preferred products and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. This program applies to all members requesting treatment with a targeted product.

Each referral is reviewed based on all utilization management (UM) programs implemented for the client.

Table. Autoimmune Products

	Product(s)
Preferred	• **Entyvio** (vedolizumab) • **Simponi Aria** (golimumab, intravenous) • **Skyrizi** (risankizumab-rzaa) • **Stelara** (ustekinumab)
Targeted	• **Actemra** (tocilizumab) • **Cimzia** (certolizumab pegol)

	• **Cosentyx** (Secukinumab) • **Ilumya** (tildrakizumab-asmn) • **Orencia** (abatacept) • **Tofidence** (Tocilizumab-bavi) • **Tremfya** (guselkumab) • **Tyenne** (Tocilizumab-aazg) • **Tysabri** (natalizumab)

*: Medications considered formulary or preferred on your plan may still require a clinical prior authorization review

II. EXCEPTION CRITERIA

This program applies to members requesting treatment for an indication that is FDA-approved for the preferred products.

Coverage for a targeted product is provided when any of the following criteria is met:

A. For Actemra, Tofidence, or Tyenne when any of the following criteria is met:
   1. When the request is for Systemic Juvenile Idiopathic Arthritis
   2. When the request is for Giant Cell Arteritis
   3. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
   4. Member has a documented inadequate response, contraindication, or intolerable adverse event to Simponi Aria.

B. For Cimzia, when any of the following criteria is met:
   1. When the request is for Axial Spondylarthritis
   2. Member is pregnant, breastfeeding, or of childbearing potential
   3. Member suffers from Trypanophobia (needle-phobic) and cannot self-inject
   4. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
   5. Member has a documented inadequate response, contraindication, or intolerable adverse event to Simponi Aria, Stelara, Entyvio, and Skyrizi.

C. For Cosentyx, when any of the following criteria is met:
   1. When the request is for Axial Spondylarthritis
   2. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
   3. Member has a documented inadequate response, contraindication, or intolerable adverse event to Simponi Aria, Stelara, and Skyrizi.

D. For Ilumya, when any of the following criteria is met:
   1. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
   2. Member has a documented inadequate response, contraindication, or intolerable adverse event to Stelara and Skyrizi

E. For Orencia, when any of the following criteria is met:
   1. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
   2. Member has a documented inadequate response, contraindication, or intolerable adverse event to Simponi Aria, Stelara, and Skyrizi.

F. For Tremfya, when any of the following criteria is met:
   1. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
   2. Member has a documented inadequate response, contraindication, or intolerable adverse event to Simponi Aria, Stelara, Entyvio, and Skyrizi.

G. For Tysabri, when any of the following criteria is met:
   1. When the request is for Multiple Sclerosis
   2. Member is currently receiving treatment with the requested targeted product, excluding when the requested targeted product is obtained as samples or via manufacturer's patient assistance programs.
   3. Member has a documented inadequate response, contraindication, or intolerable adverse event to Stelara, Entyvio, and Skyrizi.

Section 2: Site of Care

Site of Care Criteria
Administration of Intravenous Natalizumab

Tyruko, Tysabri

POLICY

I. CRITERIA FOR APPROVAL FOR ADMINISTRATION IN OUTPATIENT HOSPITAL SETTING

This policy provides coverage for administration of natalizumab in an outpatient hospital setting for up to 45 days when ANY of the following criteria are met:
   A. The member is new to therapy or reinitiating therapy after not being on therapy for at least 6 months
   B. The member has experienced a gap in therapy of greater than 2 infusions.

This policy provides coverage for administration of natalizumab in an outpatient hospital setting for a longer course of treatment when ANY of the following criteria are met:
   A. The member has experienced an adverse reaction to the medication that did not respond to conventional interventions (eg, acetaminophen, steroids, diphenhydramine, fluids or other pre-medications) or a severe adverse event (anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures) during or immediately after an infusion.
   B. The member has developed antibodies to natalizumab which increases the risk for infusion related reactions.
   C. The member is medically unstable (eg respiratory, cardiovascular, or renal conditions).
   D. The member has severe venous access issues that require the use of special interventions only available in the outpatient hospital setting.
   E. The member has significant behavioral issues and/or physical or cognitive impairment that would impact the safety of the infusion therapy AND the patient does not have access to a caregiver.
   F. Alternative infusion sites (pharmacy, physician office, ambulatory care, etc.) are greater than 30 miles from the member's home.
   G. The member is less than 14 years of age.

For situations where administration of natalizumab does not meet the criteria for outpatient hospital infusion, coverage for natalizumab is provided when administered in alternative specially certified sites such as; physician office or ambulatory care. Natalizumab is not indicated for home infusion.

II. REQUIRED DOCUMENTATION

The following information is necessary to initiate the site of care prior authorization review (where applicable):

A. Medical records supporting the member has experienced an adverse reaction that did not respond to conventional interventions or a severe adverse event during or immediately after an infusion
B. Medical records supporting the member has developed antibodies to natalizumab
C. Medical records supporting the member is medically unstable
D. Medical records supporting the member has severe venous access issues that require specialized interventions only available in the outpatient hospital setting
E. Medical records supporting the member has behavioral issues and/or physical or cognitive impairment and no access to a caregiver
F. Records supporting alternative infusion sites are greater than 30 miles from the member's home
G. Medical records supporting the member is new to therapy

Section 3: Clinical Criteria

Specialty Guideline Management
Tysabri-Tyruko

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Tysabri	natalizumab
Tyruko	natalizumab-sztn

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-approved Indications[1,2]

Indicated 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 alpha (TNF-α). Tysabri and Tyruko should not be used in combination with immunosuppressants (e.g., 6-mercaptopurine, azathioprine, cyclosporine, or methotrexate) or inhibitors of TNF-α.

Indicated as monotherapy for the treatment of relapsing forms of multiple sclerosis, to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Tysabri and Tyruko increase the risk of progressive multifocal leukoencephalopathy (PML). When initiating and continuing treatment with Tysabri or Tyruko, physicians should consider whether the expected benefit of Tysabri or Tyruko is sufficient to offset this risk.

All other indications are considered experimental/investigational and not medically necessary.

Documentation

Submission of the following information is necessary to initiate the prior authorization review:

Crohn's Disease (CD)

Initial Requests

Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy.

Continuation Requests

Chart notes or medical record documentation supporting positive clinical response to therapy or remission.

Prescriber Specialties

This medication must be prescribed by or in consultation with one of the following:

- Crohn's disease: gastroenterologist
- Multiple sclerosis: neurologist

Coverage Criteria

Crohn's Disease (CD)[1-5]

Authorization of 12 months may be granted for adult members who have received any other biologic indicated for the treatment of moderately to severely active Crohn's disease and who have been tested for anti-JCV antibodies.

Relapsing Forms of Multiple Sclerosis (MS)[1,2]

Authorization of 12 months may be granted to members who have been diagnosed with a relapsing form of multiple sclerosis (including relapsing-remitting and secondary progressive disease for those who continue to experience relapse) and those who have been tested for anti-JCV antibodies.

Clinically Isolated Syndrome (CIS)[1,2]

Authorization of 12 months may be granted to members for the treatment of clinically isolated syndrome of multiple sclerosis and those who have been tested for anti-JCV antibodies.

Continuation of Therapy

Crohn's Disease (CD)[1-3,5]

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active Crohn's disease and who achieve or maintain remission.

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active Crohn's disease and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

- Abdominal pain or tenderness
- Diarrhea
- Body weight
- Abdominal mass
- Hematocrit
- Appearance of the mucosa on endoscopy, computed tomography enterography (CTE), magnetic resonance enterography (MRE), or intestinal ultrasound
- Improvement on a disease activity scoring tool (e.g., Crohn's Disease Activity Index [CDAI] score)

Relapsing Forms of Multiple Sclerosis (MS) or Clinically Isolated Syndrome (CIS)[1,2]

Authorization of 12 months may be granted for all members (including new members) who achieve or maintain a positive clinical response with the requested drug as evidenced by experiencing disease stability or improvement.

Other

For all indications: Members cannot use the requested drug concomitantly with any other disease modifying multiple sclerosis agents (Note: Ampyra and Nuedexta are not disease modifying), immunosuppressants, or TNF inhibitors (e.g., adalimumab, infliximab).

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

REFERENCES:

SECTION 1

1. Actemra [package insert]. South San Francisco, CA: Genentech, Inc.; September 2024.
2. Tofidence {package insert] Cambridge, MA: Biogen MA Inc; July 2024.
3. Tyenne [package insert] Lake Zurich, IL: Fresenius Kabi USA, LLC; September 2024.
4. Cimzia [package insert]. Smyrna, GA: UCB, Inc.; September 2019.
5. Cosentyx [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2024.
6. Entyvio [package insert]. Lexington, MA: Takeda Pharmaceuticals U.S.A., Inc.; April 2024.
7. Ilumya [package insert]. Cranbury, NJ: Sun Pharma Global FZE; April 2024.
8. Orencia [package insert]. Princeton, NJ: Bristol-Meyers Squibb Company; May 2024.
9. Simponi Aria [package insert]. Horsham, PA: Janssen Biotech, Inc.; February 2021.
11. Stelara [package insert]. Horsham, PA: Janssen Biotech, Inc.; March 2024.
12. Tysabri [package insert]. Cambridge, MA: Biogen Inc.; October 2023.
13. Tremfya [package insert]. Horsham, PA; Janssen Biotech, Inc; September 2024

Skyrizi [package insert]. North Chicago, IL; AbbVie Inc.; June 2024.

SECTION 2

1. Tysabri [package insert]. Cambridge, MA: Biogen Inc.; October 2023.
2. Tyruko [package insert]. Princeton, NJ: Sandoz Inc.; August 2023.
3. O'Connor P, Goodman A, Kappos L, et al. Long-term safety and effectiveness of natalizumab redosing and treatment in the STRATA MS Study. *Neurology.* 2014;83(1):78-86.
4. Polman CH, O'Connor PW, Havrdova E, et al. A randomized, placebo-controlled trial of natalizumab for relapsing multiple sclerosis. *N Engl J Med*. 2006;354(9):899-910.

SECTION 3

1. Tysabri [package insert]. Cambridge, MA: Biogen Inc.; October 2023.
2. Tyruko [package insert]. Princeton, NJ: Sandoz Inc.; August 2023.
3. Talley NJ, Abreu MT, Achkar J, et al. An evidence-based systematic review on medical therapies for inflammatory bowel disease. Am J Gastroenterol. 2011;106(Suppl 1):S2-S25.
4. Lichtenstein GR, Loftus Jr EV, Isaacs KI, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2018;113:481-517.
5. Feuerstein JD, Ho EY, Shmidt E, et al. AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease. Gastroenterology. 2021;160:2496- 2508.