

POLICY Document for ENTYVIO

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, lower cost site of care and overall clinically appropriate use. This document provides specific information to each of the three 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

EXCEPTIONS CRITERIA DISEASE-MODIFYING ANTIRHEUMATIC DRUGS PRODUCTS

PREFERRED PRODUCTS: ENTYVIO, ILUMYA, REMICADE, SIMPONI ARIA, STELARA IV

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 disease-modifying antirheumatic drug (DMARD) products specified in this policy. Coverage for targeted products is provided based on clinical circumstances that would exclude the use of the preferred product and may be based on previous use of a product. The coverage review process will ascertain situations where a clinical exception can be made. For psoriasis, this program applies to all adult members requesting treatment with a targeted product. For all other indications, this program applies to adult members who are new to treatment with a targeted product for the first time.

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

Table. Disease-modifying antirheumatic drugs for autoimmune conditions

	Products	
Preferred	<ul style="list-style-type: none"> Entyvio (vedolizumab) Ilumya (tildrakizumab-asmn) Remicade (infliximab) 	<ul style="list-style-type: none"> Simponi Aria (golimumab, intravenous) Stelara IV (ustekinumab)*
Targeted	<ul style="list-style-type: none"> Actemra (tocilizumab) Avsola (infliximab-axxq) Cimzia (certolizumab pegol) 	<ul style="list-style-type: none"> Inflectra (infliximab-dyyb) Orencia (abatacept) Renflexis (infliximab-abda)

*Stelara IV is indicated for a one time induction dose for Crohn's disease and ulcerative colitis.

II. EXCEPTION CRITERIA

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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 Avsola, Inflectra and Renflexis, when member meets both of the following:
 - 1. Member has a documented intolerable adverse event with the preferred product, Remicade, and the adverse event was not an expected adverse event attributed to the active ingredient as described in the prescribing information.
 - 2. Member has a documented inadequate response or intolerable adverse event with Entyvio, Ilumya, and Simponi Aria where the product's indications overlap.
- B. For Cimzia, when any of the following criteria are 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, unless the request is for psoriasis.
 - 2. Member has a documented inadequate response or intolerable adverse event with Entyvio, Ilumya, Remicade, and Simponi Aria where the product's indications overlap
 - 3. Member is currently pregnant or breastfeeding
- C. For all other targeted products, when any of the following criteria are 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 or intolerable adverse event with Entyvio, Ilumya, Remicade, and Simponi Aria where the product's indications overlap, unless there is a documented clinical reason to avoid TNF inhibitors (Appendix)

III. Appendix: Clinical reasons to avoid TNF inhibitors

- History of demyelinating disorder
- History of congestive heart failure
- History of hepatitis B virus infection
- Autoantibody formation/lupus-like syndrome
- Risk of lymphoma

Section 2: Site of Care

GUIDELINES FOR HOSPITAL OUTPATIENT SPECIALTY MEDICATION INFUSION

I. INTRODUCTION

There is a wide variation in the site-of-service utilization patterns for specific medications and therapy classes. This is driven by several factors. Some of these specialty medications are derived from pooled blood plasma, and therefore have the potential for an increased risk of infusion-related complications. These differences can affect patient tolerance and a physician's decision to utilize a more acute site of care such as the outpatient hospital. However, many patients that have been established on this treatment with one to several infusions safely administered may be candidates for infusions in a less acute lower-cost site of care.

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Outpatient hospital infusion costs may be 2-3 times more compared to other sites of care suggesting an immediate opportunity exists for lowering spend on select specialty medications that require infusion.

Services for patients requiring infused specialty medications may be provided through a physician's in office infusion program or free standing ambulatory infusion center. These options provide access to quality care at a lower cost that may be more convenient for the patient. In addition, many patients who receive home or in office infusion therapy have been shown to experience better outcomes, fewer complications and, improved quality of life and preference, including more personalized attention which helps avoid stress.

This document describes the medical necessity criteria required for hospital outpatient infusion of the medications included in this policy.

II. GENERAL REQUIREMENTS: OUTPATIENT MEDICAL NECESSITY

Infusion in a hospital outpatient setting may be considered medically necessary for medications included in this policy when the criteria below OR individual medication policy criteria are met as outlined Section III.

A. Clinical documentation that supports one or more of the following:

1. History of repeated moderate adverse reactions not responding to conventional interventions OR,
2. Laboratory confirmation of autoantibody development (autoantibodies to IgA, anti-infliximab, etc)
3. The patient is medically unstable which may include respiratory, cardiovascular, or renal conditions that may predispose the member to a severe adverse event that cannot be managed in an alternate setting without appropriate medical personnel and equipment.
4. The patient has previously experienced a severe adverse event during or immediately after an infusion including but not limited to: anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures.
5. Significant venous access issues requiring phlebotomy

B. Patient specific criteria that meets the following:

1. All alternate non-hospital outpatient settings are not within a reasonable distance from the member's home (10-30miles) AND,
2. The patient's home has been determined to be inappropriate for home infusion by a social worker, case manager or previous home nurse assessment or home infusion services are not available due to limited network access

III. MEDICATION SPECIFIC CRITERIA FOR HOSPITAL OUTPATIENT MEDICAL NECESSITY

In addition to the general criteria in Section II, the following guidelines will be applied:

A. VEDOLIZUMAB

One or more of the following criteria must be met:

1. To determine tolerance of the therapy, the first two infusions may be permitted in the hospital outpatient setting.
2. Pediatric patients who are less than 21 years of age. The use of non-hospital based alternate site infusion services are at the discretion of the prescribing physician.
3. Patients who have experienced moderate infusion reactions including hypertension, hypotension, tachycardia, syncope, etc that have not responded to standard interventions including infusion rate adjustment and premedication.

IV. GENERAL CONSIDERATIONS: HOME INFUSION

Home Infusion therapy has the potential to deliver cost-effective, quality care.

Efforts to support patients who can receive infused medications care in a lower-cost setting versus an inpatient or clinic-based setting seems appealing, particular if that lower-cost setting is the patient's home.

The home infusion provider will complete an assessment to determine the appropriateness of a patient, caregiver if applicable, and their home prior to initiating care. This assessment may include an evaluation of the following:

- A. Accessibility to 911 services and urgent care. Volunteer services may be acceptable if urgent care is readily available.
- B. Adequate refrigeration is available if required.
- C. Home is not located in a high crime area as determined by local authorities
- D. Home environment does not meet general cleanliness standards determined by onsite home nursing assessment

V. BACKGROUND

Therapeutic monoclonal antibodies are laboratory-engineered substances that recognize and bind to a protein on the surface of a cell. Each mAB recognizes a different protein, or antigen. mAB's may be administered alone, in combination with other drugs, or as a carrier of agents. There are four types of antibodies defined by their source: Murine, chimeric (30:70 ratio of mouse to human sequences), humanized (~90% human sequences) and human. Monoclonal antibodies induce moderate acute infusion reactions in 5-10% of patients. Reactions may occur with any dose of therapy; however, they are more common with the first two doses. The mAB's with the highest risk include murine and chimeric. The humanized and human mAB's carry a lesser risk because they carry fewer non-human components.

Vedolizumab is a monoclonal antibody that reduces chronically inflamed gastrointestinal parenchymal tissue associated with ulcerative colitis and Crohn disease by binding specifically to the alpha-4-beta-7-integrin receptor and blocking its interaction with mucosal addressin cell adhesion molecule-1. This inhibits the movement of memory T-lymphocytes across the endothelium into inflamed gastrointestinal tissue.

Vedolizumab is indicated for inducing and maintaining clinical response and remission and achieving corticosteroid-free remission in adults who have had inadequate response with, lost response to, or were intolerant to tumor necrosis factor blocker or immunomodulator; or had inadequate response with, were intolerant to, or demonstrated dependence on corticosteroids.

The risk of infusion related reactions (IRRs) with vedolizumab was evaluated in 2 randomized double blind, placebo-controlled trials in patients with UC or CD. In these studies, GEMINI I and GEMINI II respectively, clinically important reactions were few. In GEMINI I 3 cases resulted in study discontinuation and in GEMINI II only 1 patient discontinued study drug because of a serious adverse reaction. IRRs were evaluated in a post hoc analysis using data from GEMINI I and GEMINI II for patients who received continuous treatment with vedolizumab or placebo. The evaluation included time of onset and use of premedications. The authors identified that IRRs occurred in 5% of patients with UC and 4% of patients with CD compared to <1% and 5% who received placebo infusions respectively. In addition, >70% of all IRRs occurred within 2 hours of the end of the infusion.

Section 3: Clinical Criteria

ENTYVIO (vedolizumab)

POLICY

I. 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. Moderately to severely active ulcerative colitis (UC)
2. Moderately to severely active Crohn's disease (CD)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active ulcerative colitis (UC)

1. Authorization of 4 months may be granted for members who are 18 years of age or older who have previously received Entyvio or any other biologic or targeted synthetic drug (e.g., Xeljanz) indicated for moderately to severely active ulcerative colitis.
2. Authorization of 4 months may be granted for treatment of moderately to severely active UC in members who are 18 years of age or older who had an inadequate response, intolerance or contraindication to EITHER of the following:
 - a. At least ONE conventional therapy option (See Appendix A)
 - b. At least ONE TNF-alpha inhibitor indicated for UC:
 - i. Humira (adalimumab)
 - ii. Remicade (infliximab)
 - iii. Simponi (golimumab)

B. Moderately to severely active Crohn's disease (CD)

1. Authorization of 4 months may be granted for members who are 18 years of age or older who have previously received Entyvio or any other biologic indicated for the treatment of Crohn's disease.
2. Authorization of 4 months may be granted for treatment of moderately to severely active CD in members who are 18 years of age or older who had an inadequate response, intolerance or contraindication to EITHER of the following:
 - a. At least ONE conventional therapy option (See Appendix B)
 - b. At least ONE TNF-alpha inhibitor indicated for CD:
 - i. Cimzia (certolizumab)
 - ii. Humira (adalimumab)
 - iii. Remicade (infliximab)

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 4 months of therapy with Entyvio as evidenced by low disease activity or improvement in signs and symptoms of the condition.

IV. APPENDICES

Appendix A: Examples of Conventional Therapy Options for UC

1. Mild to moderate disease – induction of remission:
 - a. Oral mesalamine (e.g., Asacol, Asacol HD, Lialda, Pentasa), balsalazide, olsalazine
 - b. Rectal mesalamine (e.g., Canasa, Rowasa)
 - c. Rectal hydrocortisone (e.g., Colocort, Cortifoam)
 - d. Alternatives: prednisone, azathioprine, mercaptopurine, sulfasalazine
2. Mild to moderate disease – maintenance of remission:
 - a. Oral mesalamine, balsalazide, olsalazine, rectal mesalamine
 - b. Alternatives: azathioprine, mercaptopurine, sulfasalazine
3. Severe disease – induction of remission:
 - a. Prednisone, hydrocortisone IV, methylprednisolone IV
 - b. Alternatives: cyclosporine IV, tacrolimus, sulfasalazine
4. Severe disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternative: sulfasalazine
5. Pouchitis: Metronidazole, ciprofloxacin
 - a. Alternative: rectal mesalamine

Appendix B: Examples of Conventional Therapy Options for CD

1. Mild to moderate disease – induction of remission:
 - a. Oral budesonide
 - b. Alternatives: metronidazole, ciprofloxacin, rifaximin
2. Mild to moderate disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternatives: oral budesonide, methotrexate intramuscular (IM) or subcutaneous (SC), sulfasalazine
3. Moderate to severe disease – induction of remission:
 - a. Prednisone, methylprednisolone intravenously (IV)
 - b. Alternatives: methotrexate IM or SC
4. Moderate to severe disease – maintenance of remission:
 - a. Azathioprine, mercaptopurine
 - b. Alternative: methotrexate IM or SC
5. Perianal and fistulizing disease – induction of remission
 - a. Metronidazole ± ciprofloxacin, tacrolimus
6. Perianal and fistulizing disease – maintenance of remission
 - a. Azathioprine, mercaptopurine
 - b. Alternative: methotrexate IM or SC

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