MEDICAL POLICY STATEMENT		
Original Effective Date	**Next Annual Review Date**	**Last Review / Revision Date**
02/22/2011	**02/22/2016**	**8/25/2015**
Policy Name		**Policy Number**
Inflammatory Bowel Disease: Biological Therapies		**SRx-0041**

Medical Policy Statements prepared by CSMG Co. and its affiliates (including CareSource) are derived from literature based on and supported by clinical guidelines, nationally recognized utilization and technology assessment guidelines, other medical management industry standards, and published MCO clinical policy guidelines. Medically necessary services include, but are not limited to, those health care services or supplies that are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part, or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative, and are not provided mainly for the convenience of the member or provider. Medically necessary services also include those services defined in any Evidence of Coverage documents, Medical Policy Statements, Provider Manuals, Member Handbooks, and/or other policies and procedures.

Medical Policy Statements prepared by CSMG Co. and its affiliates (including CareSource) do not ensure an authorization or payment of services. Please refer to the plan contract (often referred to as the Evidence of Coverage) for the service(s) referenced in the Medical Policy Statement. If there is a conflict between the Medical Policy Statement and the plan contract (i.e., Evidence of Coverage), then the plan contract (i.e., Evidence of Coverage) will be the controlling document used to make the determination.

For Medicare plans please reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

A. SUBJECT

Inflammatory Bowel Disease: Biological Therapies

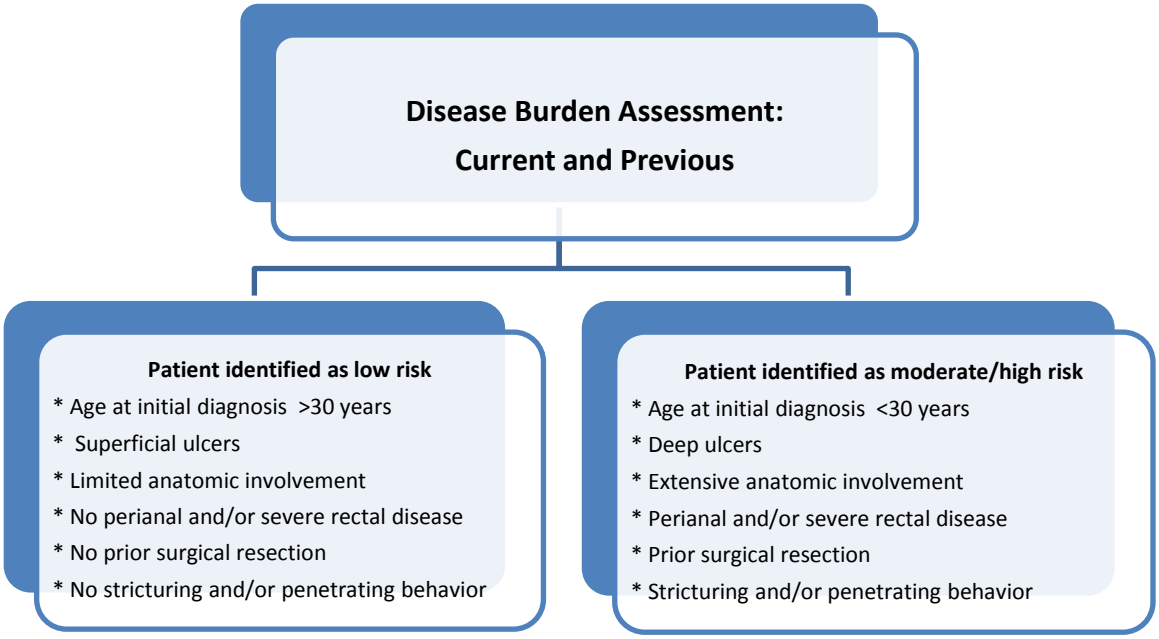
- Tumor Necrosis Factor Inhibitor
  - **Adalimumab (Humira)**
  - **Certolizumab pegol (Cimzia)**
  - **Golimumab (Simponi and Simponi Aria™)**
  - **Infliximab (Remicade)**
- Integrin receptor antagonist
  - **Vedolizumab (Entyvio)**
  - **Natalizumab (Tysabri)**

B. BACKGROUND

Tumor necrosis factor-alpha (TNF) is a messenger protein, or cytokine, produced by monocytes and macrophages that mediates inflammation and induces the destruction of some tumor cells in the body. Four TNF inhibitors have been approved for the treatment of inflammatory bowel diseases.

The α4β7 integrin is expressed on the surface of a discrete subset of memory T-lymphocytes that preferentially migrate into the gastrointestinal tract. MAdCAM-1 is mainly expressed on gut endothelial cells and plays a critical role in the homing of T-lymphocytes to gut lymph tissue. The interaction of the α4β7 integrin with MAdCAM-1 has been implicated as an important contributor to the chronic inflammation that is a hallmark of ulcerative colitis and Crohn's disease.

The intent of this pre-authorization (PA) program is to encourage the appropriate selection of preferred therapeutic agents for patients with such disorders as supported by product labeling, clinical studies and clinical guidelines.



Adapted from AGA Institute Guidelines for the Identification, Assessment and Initial Medical Treatment in Crohn's Disease: Clinical Decision Support Tool (2014).

C. DEFINITIONS

N/A

D. POLICY

CareSource will approve the use of the following medications and consider them use as **medically necessary** when the following criteria have been met:

I. **Infliximab (Remicade)** is considered **medically necessary** when criteria are met for the following indications:

A. **Crohn's Disease (CD)** when one of the following are met:

1. **Fistulizing Crohn's Disease and ALL of the following:**
   - 1.1 Age 18 years or older
   - 1.2 Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
   - 1.3 Prescribed by a gastroenterologist
2. **Moderate to severe non-fistulizing Crohn's Disease and ALL of the following:**
   - 2.1 Age 6 years or older
   - 2.2 Prescribed by a gastroenterologist
   - 2.3 Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy

2.4 Treatment needed for moderate to severe disease, as indicated by **one (1) or more** of the following:
a. Inadequate response to therapy with **one (1) or more** of the following:
(1) 6-mercaptopurine
(2) Azathioprine
(3) Corticosteroids
b. Severe disease, as indicated by **one (1) or more** of the following:
(1) Esophageal or gastroduodenal disease
(2) Extensive small-bowel disease involving more than 100cm
(3) History of colonic resection
(4) History of **two (2) or more** small-bowel resections
(5) Perianal or rectal disease

B. **Ulcerative Colitis (UC**) when **ALL** of the following are met:
1. Individual is 6 years of age or older with moderate to severe active ulcerative colitis
2. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
3. Prescribed by a gastroenterologist
4. Meets at least **one (1)** of the following:
5.1 Hospitalized with fulminant ulcerative colitis (i.e., severe ulcerative colitis with more than 10 stools per day, continuous bleeding, abdominal pain, and distension, and acute, severe toxic symptoms including fever and anoxia)
5.2 Patient hospitalized and after three days of intravenous steroids still has a CRP greater than 45 or more than 8 bloody bowel movements
5.3 Member has moderate to severe active ulcerative colitis and meets **ALL** of the following criteria:
a. Member is refractory to or requires continuous immunosuppression with corticosteroids (e.g., methylprednisolone, prednisone) at a dose of prednisone 40 to 60 mg/day (or equivalent)
b. Member is refractory to or has a contraindication to 5-aminosalicylic acid agents (e.g., balsalazide, mesalamine, sulfasalazine)
c. Member is refractory to or has a contraindication to immunosuppressants (azathioprine and 6-mercaptopurine)

II. **Adalimumab (Humira)** is considered **medically necessary** when criteria are met for the following indications:
A. **Crohn's Disease (CD)** when **ALL** of the following are met:
1. Individual is 6 years of age or older with moderately to severely active CD
2. Prescribed by a gastroenterologist
3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
4. Meets at least **one** of the following
4.1 Inadequate response to at least **one (1)** of the following:
a. 6-mercaptopurine
b. Azathioprine
c. Corticosteroids
4.2 Severe disease, as indicated by **one (1) or more** of the following:
a. Esophageal or gastroduodenal disease
b. Extensive small-bowel disease involving more than 100cm
c. History of colonic resection
d. History of **two (2) or mor**e small-bowel resections

e. Perianal or rectal disease

5. Individual lost response to or is unable to tolerate infliximab

B. **Ulcerative Colitis (UC)** when **ALL** of the following are met:
   1. Individual is 18 years of age or older with moderately to severely active UC
   2. Prescribed by a gastroenterologist
   3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
   5. Meets at least **one (1)** of the following:
      5.1 Hospitalized with fulminant ulcerative colitis (i.e., severe ulcerative colitis with more than 10 stools per day, continuous bleeding, abdominal pain, and distension, and acute, severe toxic symptoms including fever and anoxia)
      5.2 Patient hospitalized and after three days of intravenous steroids still has a CRP greater than 45 or more than 8 bloody bowel movements
      5.3 Member has moderate to severe active ulcerative colitis and meets **ALL** of the following criteria:
         a. Member is refractory to or requires continuous immunosuppression with corticosteroids (e.g., methylprednisolone, prednisone) at a dose of prednisone 40 to 60 mg/day (or equivalent)
         b. Member is refractory to or has a contraindication to 5-aminosalicylic acid agents (e.g., balsalazide, mesalamine, sulfasalazine)
         c. Member is refractory to or has a contraindication to immunosuppressants (azathioprine and 6-mercaptopurine

III. **Certolizumab Pegol (Cimzia)** is considered **medically necessary** when criteria is met for the following indication:
   A. **Crohns' Disease (CD)** when **ALL** of the following are met:
      1. Individual is 18 years of age or older with moderately to severely active CD
      2. Prescribed by a gastroenterologist
      3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
      4. Meets at least **one (1)** of the following
         4.1 Documented inadequate response to at least one of the following:
            a. 6-mercaptopurine
            b. Azathioprine
            c. Methotrexate
         4.2 Severe disease, as indicated by **one (1) or more** of the following:
            a. Esophageal or gastroduodenal disease
            b. Extensive small-bowel disease involving more than 100cm
            c. History of colonic resection
            d. History of **two (2) or mor**e small-bowel resections
            e. Perianal or rectal disease

IV. **Golimumab (Simponi & Simponi Aria)** is considered **medically necessary** when criteria is met for the following indication:
   A. **Ulcerative Colitis (UC)** when **ALL** of the following are met:
      1. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
      2. Prescribed by a gastroenterologist
      3. Individual is 18 years of age or older with moderately to severely active UC

4. Meets at least **one (1)** of the following:
   4.1 Hospitalized with fulminant ulcerative colitis (i.e., severe ulcerative colitis with more than 10 stools per day, continuous bleeding, abdominal pain, and distension, and acute, severe toxic symptoms including fever and anoxia)
   4.2 Patient hospitalized and after three days of intravenous steroids still has a CRP greater than 45 or more than 8 bloody bowel movements
   4.3 Member has moderate to severe active ulcerative colitis and meets **ALL** of the following criteria:
      a. Member is refractory to or requires continuous immunosuppression with corticosteroids (e.g., methylprednisolone, prednisone) at a dose of prednisone 40 to 60 mg/day (or equivalent)
      b. Member is refractory to or has a contraindication to 5-aminosalicylic acid agents (e.g., balsalazide, mesalamine, sulfasalazine)
      c. Member is refractory to or has a contraindication to immunosuppressants (azathioprine and 6-mercaptopurine)

V. **Vedolizumab (Entyvio)** is considered **medically necessary** when criteria are met for ANY of the following indications:
   A. **Crohn's Disease (CD)** when **ALL** of the following are met::
      1. Individual is 18 years of age or older with moderately to severely active CD
      2. Prescribed by a gastroenterologist
      3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
      5. Meets at least **one (1)** of the following
         5.1 Documented inadequate response to at least one of the following:
            a. 6-mercaptopurine
            b. Azathioprine
            c. Methotrexate
            d. Tumor necrosis factor blocker (TNF)
         5.2 Severe disease, as indicated by **one (1) or more** of the following:
            a. Esophageal or gastroduodenal disease
            b. Extensive small-bowel disease involving more than 100cm
            c. History of colonic resection
            d. History of **two (2) or mor**e small-bowel resections
            e. Perianal or rectal disease
   B. **Ulcerative colitis** when **ALL** of the following are met:
      1. Individual is 18 years of age or older with moderately to severely active UC with demonstrated corticosteroid dependence
      2. Prescribed by a gastroenterologist
      3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
      4. Meets at least **one (1)** of the following:
         4.1 Hospitalized with fulminant ulcerative colitis (i.e., severe ulcerative colitis with more than 10 stools per day, continuous bleeding, abdominal pain, and distension, and acute, severe toxic symptoms including fever and anoxia)
         4.2 Patient hospitalized and after three days of intravenous steroids still has a CRP greater than 45 or more than 8 bloody bowel movements
         4.3 Member has moderate to severe active ulcerative colitis and meets **ALL** of the following criteria:

a. Member is refractory to or requires continuous immunosuppression with corticosteroids (e.g., methylprednisolone, prednisone) at a dose of prednisone 40 to 60 mg/day (or equivalent)
b. Member is refractory to or has a contraindication to 5-aminosalicylic acid agents (e.g., balsalazide, mesalamine, sulfasalazine)
c. Member is refractory to or has a contraindication to immunosuppressants (azathioprine and 6-mercaptopurine
d. Member has had an inadequate response with, lost response to, or was intolerant to a tumor necrosis factor blocker (TNF)

VI. **Natalizumab (Tysabri)** is considered **medically necessary** when **ALL** criteria are met for the following indication:
   A. **Crohn's Disease (CD)** when **ALL** of the following are met:
      1. Prescribed by a gastroenterologist
      2. Member is 18 years or older
      3. Member has had anti-JCV antibody testing with ELISA prior to initiating treatment with natalizumab and annually thereafter
      4. Provider and patient are registered with Crohn Disease Tysabri Outreach Unified Commitment to Health (CD TOUCH) program
      5. Diagnosis of moderately- to severely-active Crohn's Disease
      6. Agent is **not** being used in combination with immunosuppressant's or TNF-alpha inhibitors
      7. Failure of **two (2)** different therapies such as:
         7.1 Methotrexate (eg, Rheumatrex)
         7.2 Systemic corticosteroids (eg, budesonide (Entocort), prednisone)
         7.3 Immunosuppressants (eg, 6-mercaptopurine (Purinethol))
         7.4 Azathioprine (Imuran) or cyclosporine (Neoral, Sandimmune, Gengraf)
         7.5 Tumor necrosis factor blocker (TNF) (Humira, Enbrel, etc.)

ALL other uses of Adalimumab, Certolizumab pegol, Golimumab, Infliximab, Natalizumab, or Vedolizumab are considered experimental/investigational and therefore, will follow CareSource's off-label policy.

Note: Patient is required to have completed the trial listed in the above criteria unless the patient is unable to tolerate, has a contraindication or a loss of response. Documentation such as chart notes or pharmacy claims may be requested.

Note: Documented diagnosis must be confirmed by portions of the individual's medical record which will confirm the presence of disease and will need to be supplied with prior authorization request. These medical records may include, but not limited to test reports, chart notes from provider's office or hospital admission notes.

Refer to the product package insert for dosing, administration and safety guidelines.

For Medicare Plan members, reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

If there is no NCD or LCD present, reference the CareSource Policy for coverage.

CONDITIONS OF COVERAGE

HCPCS J0135 Adalimumab **(Humira)**
J0717 Certolizumab pegol **(Cimzia)**
J3590, C9399 Golimumab SC **(Simponi)**
J1602 Golimumab IV **(Simponi Aria)**
J1745 Infliximab **(Remicade)**
J3590, C9026 Vedolizumab **(Entyvio)**
J2323 Natalizumab **(Tysabri)**

CPT

Step Therapy
Under some plans, including plans that use an open or closed formulary, some of the medications in this policy may be subject to step-therapy. Refer to the CareSource formulary tool or PDL for further guidance.

PLACE OF SERVICE
Office, Outpatient, Home
**Preferred place of service is in the home.
This medication can be self-administered and can be billed through the pharmacy benefit.
Note: CareSource supports administering inject able medications in various setting, as long as those services are furnished in the most appropriate and cost effective setting that are supportive of the patient's medical condition and unique needs and condition. The decision on the most appropriate setting for administration is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of the specific medication.

AUTHORIZATION PERIOD
Approved initial authorizations are valid for 12 months. Continued treatment may be considered when the member has shown biological response to treatment. **ALL** authorizations are subject to continued eligibility.

E. RELATED POLICIES/RULES

- SRx-0042 Autoimmune Disease: Biologic Therapies
- SRx-0043 Psoriasis Biologic Therapies

F. REVIEW/REVISION HISTORY

Date Issued: 06/22/2011
Date Reviewed: 06/22/2011, 12/22/2012, 12/22/2013, 10/22/2014, 02/22/2015, 04/21/2015
Date Revised: 12/22/2012
12/22/2013 – Added detail to criteria, changed agents to fail
10/22/2104 – Add indication Crohn's Disease
02/22/2015 – Combine TNF and Stelara policies; revised diagnoses for Certolizumab, Infliximab & Adalimumab, changed duration of initial authorization
04/21/2015 – Add Entyvio & criteria, Xeljanz, trial length added for UC CD
08/25/2015 – Removed all criteria, information and references for disease states other than IBD, updated

G. REFERENCES

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2. Feagan, BG, Rutgeerts, P, Sands, BE, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. The New England journal of medicine. 2013 Aug 22;369(8):699-710. PMID: 23964932
3. Sands, BE, Feagan, BG, Rutgeerts, P, et al. Effects of Vedolizumab Induction Therapy for Patients With Crohn's Disease in Whom Tumor Necrosis Factor Antagonist Treatment Had Failed. Gastroenterology. 2014 May 21. PMID: 24859203
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5. Humira [prescribing information]. North Chicago, IL; AbbVie Inc.: Revised December 2014.
6. Cimzia [prescribing information]. Smyrna, GA; UCB, Inc.: Revised October 2013.
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9. Wolters Kluwer. Facts & Comparisons. www.factsandcomparisons.com, 2015.
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14. Simponi [prescribing information]. Horsham, PA; Janssen Biotech, Inc.; Revised: June 2015

This guideline contains custom content that has been modified from the standard care guidelines and has not been reviewed or approved by MCG Health, LLC.

The medical Policy Statement detailed above has received due consideration as defined in the Medical Policy Statement Policy and is approved.

Independent Medical Review - 2015