Biologic Therapy for Gastroenterology
Prior Authorization Criteria

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Benefit</th>
<th>Coverage Status</th>
<th>Quantity per month: maintenance therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infliximab (Remicade®, Inflectra®)</td>
<td>Medical</td>
<td>Restricted</td>
<td>N/A</td>
</tr>
<tr>
<td>Natalizumab (Tysabri®)</td>
<td>Medical</td>
<td>Restricted</td>
<td>N/A</td>
</tr>
<tr>
<td>Vedolizumab (Entyvio®)</td>
<td>Medical</td>
<td>Restricted</td>
<td>N/A</td>
</tr>
<tr>
<td>Ustekinumab (Stelara®)</td>
<td>Medical</td>
<td>Restricted</td>
<td>Single Dose</td>
</tr>
</tbody>
</table>

**Quantity Limits:**
- Induction therapy: Ustekinumab: weight-based infusion X1
- Maintenance therapy: As listed in the table
- Approval Limits: None

**CRITERIA FOR COVERAGE:**
- Prescribed by a Gastroenterologist
- Diagnosis of inflammatory bowel disease as described below:

**1. Diagnosis of moderate to severely active Crohn’s disease AND**

**In a low-risk individual:**
- Intolerance/contraindication to 2 conventional therapies
  OR
- Inadequate disease control or inability to achieve remission after an adequate trial of 3 months with 2 conventional therapies
  OR
- Demonstrated steroid dependence

**Therapy options**
- **Infliximab**: failure/intolerance/contraindication to a first-line self-injectable anti-TNF medication
- **Vedolizumab** (in adults): failure/intolerance/contraindication to 2 anti-TNF medications
- **Ustekinumab** (in adults): failure/intolerance/contraindication to 2 anti-TNF medications
- **Natalizumab** (in adults): failure/intolerance/contraindication of 2 anti-TNF medications AND failure/intolerance/contraindication to vedolizumab AND not being used concurrently with immunomodulatory therapy (must be used as monotherapy).

**In a high-risk individual:**

**Therapy options**
- **Infliximab**: failure/intolerance/contraindication to a first-line self-injectable anti-TNF medication OR if fistulizing disease
- **Vedolizumab** (in adults): failure/intolerance/contraindication 2 anti-TNF medications AND inflammation still present
- **Ustekinumab** (in adults): failure/intolerance/contraindication to a first-line self-injectable anti-TNF medication AND infliximab
• **Natalizumab** (in adults) - failure/intolerance/contraindication of 2 anti-TNF medications AND failure/intolerance/contraindication to vedolizumab AND not being used concurrently with immunomodulatory therapy (must be used as monotherapy).

In a **hospitalized patient with acute flare** of severely active Crohn’s disease with a lack of response to IV corticosteroids (dose equivalents of 60mg methylprednisolone) after 3-5 days in attempt to avoid surgical intervention with documentation of inflammatory component

**Therapy options**

• **Infliximab** - failure/intolerance/contraindication to a preferred first-line self-injectable biologic DMARD OR the patient has fistulizing disease

• **Vedolizumab** - failure/intolerance/contraindication to two first-line self-injectable biologic DMARD

• **Ustekinumab** (in adults) - failure intolerance/contraindication of a first-line self-injectable anti-TNF AND infliximab

• **Natalizumab** (in adults) - failure/intolerance/contraindication of 2 anti-TNF medications AND failure/intolerance/contraindication to vedolizumab AND not being used concurrently with immunomodulatory therapy (must be used as monotherapy).

For persons already established on biologic therapy prior to admission, consider dose escalation, addition of immunomodulator or change in biologic therapy (different anti-TNF or different class) as appropriate based on drug concentrations and antibody levels as noted below-

- If remission not achieved or disease relapsed on a TNF inhibitor or infliximab and subtherapeutic drug concentration with high antibody level then change to drug within the same class (i.e. Infliximab to a TNF inhibitor OR a TNF inhibitor to infliximab)
- If remission not achieved or disease relapsed on a TNF inhibitor and subtherapeutic drug concentration with low or absent antibody level then-
  - Increase dose of TNF inhibitor
  - Decrease the dosing interval
  - Add immunomodulator to anti-TNF therapy
- If remission not achieved or disease relapsed on anti-TNF therapy based on therapeutic drug concentrations and lack of anti-drug antibodies (primary non-response or secondary loss of response) AND inflammation still present, then change to different drug class

2. **Diagnosis of moderate to severely active Ulcerative Colitis AND**

In a **high-risk individual**

**Therapy options** (after short course of corticosteroids plus azathioprine (unless contraindicated))

• **Infliximab** - pediatrics (age<18) OR failure/intolerance/contraindication to a first-line self-injectable anti-TNF medication

• **Vedolizumab** (in adults) - failure/intolerance/contraindication of a first-line self-injectable anti-TNF medication
In a **hospitalized patient with acute flare of** severely active ulcerative colitis with lack of response to IV corticosteroids (dose equivalents of 60mg methylprednisolone) after 3-5 days in attempt to avoid surgical intervention with documentation of inflammatory component

**Therapy options**
- Infliximab
- Vedolizumab - failure/intolerance/contraindication to an anti-TNF medication

- For persons already established on biologic therapy prior to admission, consider dose escalation, addition of immunomodulator or change in biologic therapy (different anti-TNF or different class) as appropriate based on drug concentrations and antibody levels as noted below
  - If remission not achieved or disease relapsed on a TNF inhibitor or infliximab and subtherapeutic drug concentration with high antibody level then change to drug within the same class (i.e. Infliximab to a TNF inhibitor OR a TNF inhibitor to infliximab)
  - If remission not achieved or disease relapsed on a TNF inhibitor and subtherapeutic drug concentration with low or absent antibody level then
    - Increase TNF inhibitor dose
    - Decrease the dosing interval
    - Add immunomodulator to anti-TNF therapy
  - If remission not achieved or disease relapsed on TNF inhibitor therapy based on therapeutic drug concentrations (primary non-response or secondary loss of response)
    - Vedolizumab (contraindication to anti-TNF therapy OR failure/intolerance of anti-TNF trial based on drug concentrations and antibody levels) in attempt to avoid surgical intervention

**CRITERIA FOR CONTINUATION OF THERAPY:**
- For persons new to the plan: must have a clinical assessment provided by the gastroenterologist (or other specialist if co-managed by Rheumatology) within previous 12 months and prescriber documents individual response to therapy, including individual improvement in functional status related to therapeutic response. Provision of recent labs, current symptoms and change in status should be provided to review for improvement and demonstrate effectiveness. Examples of documentation include laboratory assessment (i.e. CRP, hemoglobin, ESR, WBC, albumin, etc), symptom assessment (i.e. bleeding, stooling pattern, abdominal pain, extraintestinal complaints, fatigue, fever, etc) or recent endoscopy results.
- Continuation of therapy/coverage criteria will not be applied to persons who were not previously approved for coverage whose therapy was initiated using a manufacturer-sponsored free drug program, provider samples, and/or vouchers.

**IMPORTANT INFORMATION:**
- While the anti-TNF agents are category B in pregnancy, certolizumab does not appear to cross the placenta and therefore, it may pose less risk to a fetus. For pregnant women established on anti-TNF therapy, therapy interruptions prior to delivery are recommended with infliximab (8-10 weeks prior) and adalimumab (4-5 weeks prior). For pregnant women established on anti-TNF therapy and requiring an adjustment to anti-TNF therapy, consideration will be given to use of certolizumab.
DEFINITIONS OF TERMS:

Inadequate Disease Control:
Worsening of baseline symptoms (i.e. bowel frequency, presence of blood, abdominal pain or tenderness, fever, etc), extraintestinal manifestations (i.e. fatigue, joint pain, skin rash, and ocular symptoms), laboratory assessment (i.e. C-reactive protein (CRP), hemoglobin, ESR white blood count (WBC), albumin, platelets, fecal calprotectin, etc) and/or recent endoscopy results demonstrating ongoing inflammation.

High Risk in Ulcerative Colitis:
- Patient with extensive colitis, deep ulcers, age<40 years, High CRP and ESR, steroid-requiring disease, history of hospitalization, C difficile infection, CMV infection
- Low risk patient (with limited anatomic disease or mild endoscopic disease) AND inability to achieve remission on induction and maintenance therapy with conventional agents OR achieved remission on induction and maintenance therapy but has relapsed after steroid taper (primary non-response or secondary loss of response)

High Risk in Crohn’s Disease:
- Age<30 at diagnosis, extensive anatomic involvement, perianal and/or severe rectal disease, deep ulcers, prior surgical resection, stricturing and/or penetrating behavior, fistulizing disease, extraintestinal manifestations of inflammation (i.e. uveitis, erythema nodosum, pyoderma gangrenosum, spondyloarthropathy, etc)

Induction and Maintenance Therapy with Conventional Agents:
- Conventional therapy with immunomodulator therapy such as azathioprine, balsalazide, corticosteroids, mesalamine, mercaptopurine, methotrexate, sulfasalazine

Steroid Dependence:
- Demonstrated steroid dependence (defined as equivalent to prednisone 10mg daily for >3 months) with the inability to taper or when tapering of dose leads to loss of symptom control

Inflammatory status: Signs/Symptoms/Labs/Endoscopy for diagnosis
- Bloody diarrhea, weight loss, tenesmus, urgency, abdominal pain, fever, joint swelling/redness, localized abdominal tenderness, anemia, cutaneous signs
- CBC, CMP, CRP, ESR, stool cultures, C difficile assay, fecal calprotectin
- Endoscopy, colonoscopy, sigmoidoscopy

Ulcerative Colitis Disease Severity:
Based on the degree of presentation of the signs and symptoms and change in baseline inflammatory status
- Moderate disease- more than four stools per day with minimal signs of toxicity, anemia, abdominal pain, low grade fever
- Severe disease- more than six bloody stools per day, fever, tachycardia, anemia or elevated ESR or CRP

Primary non-response to anti-TNF therapy:
Lack of response to therapy as assessed after induction regimen, (i.e. approximately 12 weeks into therapy), and the inability to achieve steroid-free complete remission, despite dose optimization. This can be managed by evaluation of inflammation (is there evidence of inflammatory activity causing lack of perceived response or something else?), dose escalation, addition of immunomodulator or by changing to a different drug.
Secondary loss of response to anti-TNF therapy:
Re-emerging symptoms appear where they were previously controlled and are due to inflammation and not other causes. (i.e. irritable bowel disease, infection, non-inflammatory component of IBD, etc).
The inability to maintain steroid-free complete remission after achieving symptomatic response.
This can be managed by assessment of drug concentrations and antibody levels to determine if dose increase or therapy change.

Crohn's Disease Classification:
Stricturing- narrowing of bowel that may cause bowel obstruction
Penetrating- fistulae may form between bowel and other structures
Inflammatory- nonstricturing, nonpenetrating- inflammation without strictures or fistula

References: