

Origination Date: 5/01	Revision Date(s): 7/03, 10/04, 9/05, 11/05, 11/06, 12/07, 1/09, 3/11
Developed By: Medical Criteria Committee	

*Robert Neal Mills MD M.D.M.B.A.*

Approved: **Robert Neal Mills, MD** Date: 03/04/11

ODS Rx <sup>1.0</sup> <input type="checkbox"/>	ODS Rx <sup>2.0</sup> <input checked="" type="checkbox"/>	OEBB <input checked="" type="checkbox"/>	OHP <input type="checkbox"/>
NON-SPECIALTY <input type="checkbox"/>	SPECIALTY <input checked="" type="checkbox"/>		
PA <input checked="" type="checkbox"/>	QLL <input type="checkbox"/>	STEP THERAPY <input type="checkbox"/>	

**PURPOSE:** To ensure the appropriate and safe use of Remicade for FDA approved indications.

**DESCRIPTION:** Tumor necrosis factor (TNF) antagonists inhibit binding of tumor necrosis factor alpha which results in a decrease of circulating pro-inflammatory cytokines involved in inflammatory responses in rheumatoid arthritis (RA), ankylosing spondylitis, psoriasis, and psoriatic arthritis.

**INDICATIONS:**

- Treatment in combination with methotrexate, of moderately to severely active RA.
- Treatment of psoriatic arthritis.
- Treatment of active ankylosing spondylitis
- Use of Remicade off-label in psoriasis
- Reduction of signs and symptoms and inducement and maintenance of clinical remission in patients with moderately to severely active Crohn's disease.
- Reduction in the number of fistulas and maintenance of fistula closure in patients with fistulizing Crohn's disease.
- Reduction in signs and symptoms, promotion of clinical remission, mucosal healing, and elimination of corticosteroid use in patients with moderately to severely active UC with an inadequate response to conventional therapy.

**PRODUCT AVAILABILITY:**

Remicade (infliximab): 100mg injection, solution reconstituted

**QUANTITY LIMITS:**

- Crohn's Disease, Ulcerative Colitis, Plaque Psoriasis or Psoriatic Arthritis: 15x100mg vials per 6 weeks one time, then 5x100mg vials per 8 weeks
- Rheumatoid Arthritis: 9x100mg vials per 6 weeks one time, then 5x100mg vials per 8 weeks
- Ankylosing Spondylitis: 15x100mg vials per 6 weeks one time, then 3x100mg vials per 6 weeks

**GUIDELINES FOR USE:**

- 1) **Has the treatment been prescribed by or is it being supervised by a dermatologist, gastroenterologist or rheumatologist?**
  - a) **If yes, go to #2**
  - b) **If no, forward to clinical for review**
- 2) **Does the patient have a clinically important active infection?**
  - a) **If yes, forward to clinical for review**

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- b) If no, go to #3 (It is relatively contraindicated for patients with a chronic or recurrent infection to receive TNF antagonists. These medications may place patients at greater risk for developing serious infections.)
- 3) Has the patient had a **NEGATIVE** tuberculin skin test, or if positive, has treatment for latent TB been initiated prior to anti-TNF therapy?
- a) If yes go to #4  
b) If no, forward to clinical for review
- 4) Has the patient previously been treated with Remicade?
- a) If yes, go to #31  
b) If no, go to #5
- 5) Has the patient tried and failed a self injectable tumor necrosis factor (TNF)-alpha blocker such as Humira or Enbrel?
- a) If yes, go to #6  
b) If no, forward to clinical for review
- 6) Will the patient be using the Remicade drug with Rituxan, Orencia, Kineret, Amevive, or Enbrel?
- a) If yes, forward to clinical for review  
b) If no, go to #7
- 7) Does the patient have moderate to severe congestive heart failure (ie. NYHA Functional Class III or IV)?
- a) If yes, go to #8  
b) If no, go to #9
- 8) Is the prescribed Remicade dose greater than 5 mg/kg?
- a) If yes, forward to clinical for review  
b) If no, go to #9 (Caution prescriber about risks of cardiovascular adverse events, hospitalizations and death with doses > 5 mg/kg in patients with Class III or IV heart failure. Must consider whether benefits outweigh risks and be aware not to increase dose > 5 mg/kg).
- 9) What is the indication for use?
- i) Rheumatoid Arthritis, go to #10  
ii) Psoriasis, go to #13  
iii) Psoriatic Arthritis, go to #17  
iv) Ankylosing Spondylitis, go to #19  
v) Crohn's Disease, go to #24  
vi) Ulcerative Colitis, go to #30  
vii) None of the above, forward to clinical for review

**Rheumatoid Arthritis:**

- 10) Does the patient have at least four of the following for at least 6 weeks duration:
- i) Prolonged morning stiffness in the joints ( $\geq 45$  minutes duration)  
ii) Arthritis of 3 or more joint areas- wrist, elbow, knee, subtalar, MTP, or hands (MCP or PIP)  
iii) Arthritis of hand joints  
iv) Symmetric arthritis  
v) Rheumatoid nodules under the skin  
vi) Elevated levels of serum rheumatoid factor  
vii) Radiographic changes in the joints
- a) If yes, go to #11  
b) If no, forward to clinical for review

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- 11) Has the patient met at least two of the following criteria:
- i) Failure of optimal dosing/adequate duration of methotrexate (at least 3 months)
  - ii) Failure of optimal dosing/adequate duration of a DMARD other than methotrexate
  - iii) Contraindication or intolerance to methotrexate
- a) If yes, go to #12
  - b) If no, forward to clinical for review

- 12) Is Remicade being co-prescribed with methotrexate?
- a) If yes, go to #31
  - b) If no, forward to clinical for review

Psoriasis:

- 13) Does the patient have documented chronic ( $\geq 12$  months) plaque psoriasis which covers  $\geq 10\%$  of the body surface area or involves areas of the face, ears, hands, feet or genitalia?
- a) If yes, go to #14
  - b) If no, forward to clinical for review
- 14) Is the patient at least 18 years of age?
- a) If yes, go to #15
  - b) If no, forward to clinical for review
- 15) Is the patient a candidate for systemic therapy and/or phototherapy?
- a) If yes, go to #16
  - b) If no, forward to clinical for review
- 16) Does the patient have documented relative contraindication to or failure/intolerance of optimal dosing/adequate duration of systemic therapy (i.e. methotrexate, cyclosporine, acitretin) and/or phototherapy (i.e. PUVA, UVB)?
- a) If yes, go to #31
  - b) If no, forward to clinical for review

Psoriatic Arthritis

- 17) Has the patient received  $> 1,000$  joules cumulative dosage of PUVA?
- a) If yes, go to #18 (Note: Patients have a 6-fold increased risk of nonmelanoma skin cancer if they have received  $> 1,000$  joules cumulative dosage of PUVA and are treated with anti-TNF agents. It is recommended that these patients receive annual skin checks from a dermatologist.)
  - b) If no, go to #18
- 18) Does the patient have active disease and failed optimal dosing or an adequate trial duration of at least two different DMARDs?
- i) Adequate trial:
    - (1) Treatment for  $\geq 6$  months, of which 2 months is at standard target dose
    - OR
    - (2) Treatment for  $< 6$  months where treatment was withdrawn because of intolerance, toxicity, or contraindicated
    - OR
    - (3) If treatment is withdrawn because of drug intolerance or toxicity after  $> 2$  months, at least 2 months should have been at therapeutic doses
  - a) If yes, go to #31
  - b) If no, forward to clinical for review

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Ankylosing Spondylitis

19) Does the patient have:

- i) Active disease defined by BASDAI score  $\geq 4$  cms AND spinal pain VAS (within last week)  $\geq 4$  cms, both having been measured on two occasions at least 4 weeks apart without a change in treatment  
AND
  - ii) Radiologic evidence of Sacroiliitis  $\geq$  grade II bilaterally or grade III to IV unilaterally  
AND
  - iii) One of the following three criteria:
    - (1) Low back pain and stiffness for  $> 3$  months that improves with exercise but is not relieved by rest
    - (2) Limitation of motion of the lumbar spine in both the sagittal and frontal planes
    - (3) Limitation of chest expansion relative to normal values correlated for age and sex
- a) If yes, go to #20
  - b) If no, forward to clinical for review

20) Has the patient failed adequate trial of at least two different NSAID treatments?

- i) Adequate trial:
    - (1) Treatment for  $\geq 3$  months of maximal recommended or tolerated anti-inflammatory dose unless contraindicated
    - OR
    - (2) Treatment for  $< 3$  months where treatment was withdrawn because of intolerance, toxicity, or contraindicated
- a) If yes, go to #21
  - b) If no, forward to clinical for review

21) Is the disease manifested as axial disease, peripheral arthritis or enthesitis?

- a) If enthesitis or axial disease, go to #31
- b) If peripheral arthritis, go to #22

22) Has patient failed intra-articular corticosteroid treatment (at least one injection)?

- a) If yes, go to #23
- b) If no, forward to clinical for review

23) Has the patient failed three months trial of at least 2 g/day oral sulfasalazine, unless contraindicated?

- a) If yes, go to #31
- b) If no, forward to clinical for review

Crohn's Disease

24) Is the patient being treated for:

- a) Moderate to Severe Crohn's Disease, go to #25
- b) Fistulizing Crohn's Disease go to #28

25) Has the patient failed or is intolerant to optimal dosing and adequate duration of corticosteroids?

- a) If yes, go to #26
- b) If no, forward to clinical for review

26) Has the patient failed or is intolerant to optimal dosing and adequate duration of mesalamine or sulfasalazine?

- a) If yes, go to #27
- b) If no, forward to clinical for review

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- 27) Has the patient failed or is intolerant to optimal dosing and adequate duration of an immunomodulator (i.e., methotrexate, 6-mercaptopurine or azathioprine)?
- If yes, go to #29
  - If no, forward to clinical for review

- 28) Has the patient failed or is intolerant to optimal dosing and adequate duration of corticosteroids or an immunomodulator (6-mercaptopurine and/or azathioprine)?
- If yes, go to #31
  - If no, forward to clinical for review

Ulcerative Colitis:

- 29) Is the patient being treated for moderate to severe ulcerative colitis?
- If yes, go to #30
  - If no, forward to clinical for review

- 30) Does the patient have a documented failure of an aminosalicylate, corticosteroid, and/or immunomodulator (i.e., mesalamine, sulfasalazine, balsalazide, mercaptopurine, or azathioprine) at optimal dosing/adequate duration?
- If yes, go to #31
  - If no, forward to clinical for review

- 31) Initial Approval - Approve 8 weeks initial therapy

RENEWAL CRITERIA

- 32) What is the indication for use?
- Rheumatoid Arthritis, go to #33
  - Psoriasis, go to #34
  - Psoriatic Arthritis, go to #35
  - Ankylosing Spondylitis, go to #36
  - Crohn's Disease, go to #37
  - Ulcerative Colitis, go to #40
  - None of the above, forward to clinical for review

Rheumatoid Arthritis

- 33) Has the patient had:
- ≥ 20% improvement in the number of tender joints AND
  - ≥ 20% improvement in the number of swollen joints AND
  - ≥ 20% improvement in three of the following five measures:
    - Pain
    - Global assessment of disease activity by the physician
    - Global assessments of disease activity by the patient
    - Patient assessment of physical function
    - Levels of acute phase reactant (ESR or CRP)
  - OR achieved an equivalent therapeutic response as indicated by scoring using the DAS28, SDAI or CDAI indices.
- If yes, approved for 12 months for maintenance therapy
  - If no, forward to clinical for review

Psoriasis Renewal

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- 34) Did the patient receive clinical benefit on the therapy as measured by PASI improvement ( $\geq 50\%$  improvement in PASI score) or a significant improvement in Quality of Life observed by the physician and patient (i.e. Dermatology Life Quality Index)?
- If yes, approve 50 mg subcutaneously once weekly for 12 months
  - If no, forward to clinical for review

Psoriatic Arthritis Renewal

- 35) For Psoriatic Arthritis, has the patient had:
- $\geq 20\%$  improvement in the number of tender joints AND
  - $\geq 20\%$  improvement in the number of swollen joints AND
  - $\geq 20\%$  improvement in three of the following five measures:
    - Pain
    - Global assessment of disease activity by the physician
    - Global assessments of disease activity by the patient
    - Patient assessment of physical function
    - Levels of acute phase reactant (ESR or CRP)
- If yes, approved for 12 months of maintenance therapy
  - If no, forward to clinical for review

Ankylosing Spondylitis Renewal

- 36) For Ankylosing Spondylitis, have the patient's symptoms improved  $\geq 50\%$  relative to baseline or experienced an absolute change of 2 points (scale 0-10) in the BASDAI score?
- If yes, approved for 12 months of maintenance therapy
  - If no, forward to clinical for review

Crohn's Disease Renewal

- 37) Has the patient shown clinical improvement (i.e. decreased number of draining fistulas, decreased rectal bleeding, diarrhea and abdominal pain; maintenance of remission) after induction therapy with Remicade as documented in medical records of treating physician?
- If yes, go to #39
  - If no, forward to clinical for review
- 38) Has it been at least 8 weeks since the last Remicade treatment?
- If yes, approved 12 months for maintenance therapy. Refer to guide below for appropriate number of vials to dispense.
  - If no, go to #40
- 39) Is the prescribed dose an increase from the last dose? If it has been less than 8 weeks from the last dosage signifying inadequate response, the dosage should be increased from 5 mg/kg.
- If yes, approve for 12 months of maintenance therapy. Refer to guide below for appropriate number of vials to dispense.
  - If no, forward to clinical for review

Ulcerative Colitis

- 40) Did the patient experience a positive response (i.e. decreased rectal bleeding, mucosal healing, corticosteroid discontinuation) post-induction or during maintenance therapy as documented in medical records of treating physician?
- If yes, go to #41
  - If no, forward to clinical for review

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- 41) Has it been at least 8 weeks since the last Remicade treatment?
- a) If yes, approved for 12 months maintenance therapy. Refer to guide below for appropriate number of vials to dispense
  - b) If no, forward to clinical for review

<b>Remicade Appropriate Vial Provision Guide</b>	
If prescribed dose is within 10% of an incremental vial size, the pharmacist may round down to the nearest vial size to provide cost-savings while not compromising clinical efficacy.	
<i>ie. Pt = 66kg. MD writes for 5 mg/kg = 330mg; Round down to give 300 mg (3 vials)</i>	
Patient Weight Range	Remicade dose (# vials) (based on 5 mg/kg ± 10%)
< 40 kg	5 mg/kg (up to 2 vials)
40 kg to 44 kg	200 mg (2 vials)
> 44 kg to 60 kg	5 mg/kg (up to 3 vials)
60 kg to 66 kg	300 mg (3 vials)
> 66 kg to 80 kg	5 mg/kg (up to 4 vials)
> 80 kg to 88 kg	400 mg (4 vials)
> 88 kg to 100 kg	5 mg/kg (up to 5 vials)
> 100 kg to 110 kg	500 mg (5 vials)
> 110 kg to 120 kg	5 mg/kg (up to 6 vials)
> 120 kg to 132 kg	600 mg (6 vials)
> 132 kg to 140 kg	5 mg/kg (up to 7 vials)
> 140 kg to 154 kg	700 mg (7 vials)
> 154 kg to 160 kg	5 mg/kg (up to 8 vials)
> 160 kg to 176 kg	800 mg (8 vials)

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<ul style="list-style-type: none"> <li>• <b>Duration of Approvals:</b></li> <li>• <b>Dosing:</b></li> <li>• Pregnancy category B</li> <li>• Remicade is indicated for adults (<math>\geq</math> 18 years of age)</li> <li>• Treatment with Remicade in patients with moderate to severe heart failure (NYHA Class III or IV) has resulted increased cardiovascular adverse events, hospitalizations and death.</li> <li>• Serious infections, sepsis and fatalities have been reported with the use of anti-TNF agents. These medications should not be initiated in patients with clinically important, active infections</li> <li>• <b>Monitoring</b> - LFTs; D/C if &gt; 5x upper limit of normal</li> </ul> <p><b>Optimal Dosing and Duration</b></p> <table border="1"> <tr> <td>Sulfasalazine</td> <td>4 to 6 g/day PO</td> <td>4 weeks</td> </tr> <tr> <td>Mesalamine</td> <td>2 to 4.8 g/day PO or PR</td> <td>4 weeks</td> </tr> <tr> <td>Balsalazide</td> <td>6.75 g/day PO</td> <td>4 weeks</td> </tr> <tr> <td>Prednisone</td> <td>40 to 60 mg/day PO</td> <td>8 to 12 weeks</td> </tr> <tr> <td>Azathioprine</td> <td>1.5 to 2.5 mg/kg/day PO</td> <td>3 to 6 months</td> </tr> <tr> <td>Mercaptopurine</td> <td>individualized</td> <td>3 to 6 months</td> </tr> </table>	Sulfasalazine	4 to 6 g/day PO	4 weeks	Mesalamine	2 to 4.8 g/day PO or PR	4 weeks	Balsalazide	6.75 g/day PO	4 weeks	Prednisone	40 to 60 mg/day PO	8 to 12 weeks	Azathioprine	1.5 to 2.5 mg/kg/day PO	3 to 6 months	Mercaptopurine	individualized	3 to 6 months	<p><b>Special Instructions:</b></p> <p>Induction – 2 months                  Maintenance - 12 months</p> <p>(RA) 3 mg/kg IV infusion at 0, 2, and 6 weeks then q 8 wks, in combination with methotrexate.                  (AS) 5 mg/kg IV infusion at 0, 2, and 6 weeks then q 6 wks. With/Without methotrexate.                  (PsA) 5mg/kg IV infusion at 0, 2, and 6 weeks then q 8 wks. With/Without methotrexate.                  (CD) Induction: 5 mg/kg at 0, 2 and 6 weeks as an IV infusion  <i>Maintenance: 5 mg/kg IV every 8 weeks thereafter induction</i>  <i>For responders that lose response: consider 10mg/kg</i>                  If patient has not responded by week 14, consider discontinuing medication since response is unlikely.                  (UC) Induction: 5 mg/kg IV at 0, 2 and 6 weeks  <i>Maintenance: 5 mg/kg IV every 8 weeks thereafter induction</i></p>
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