Clinical Policy: Infliximab (Remicade) and Infliximab-dyyb (Inflectra)

Reference Number: ERX.SPMN.150
Effective Date: 10/2016
Last Review Date: 12/2016

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Policy/Criteria

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that infliximab (Remicade®) and infliximab-dyyb (Inflectra) are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Crohn's Disease (must meet all):

1. Prescribed by or in consultation with a gastroenterologist;
2. Age ≥ 6 years;
3. Diagnosis of moderately to severely active Crohn's disease (CD) and (a or b):
   a. Has one of the following poor prognostic indicators for CD:
      i. Age < 18 years;
      ii. Perianal disease;
      iii. Upper gastrointestinal tract involvement;
      iv. Multiple extra-intestinal manifestations;
      v. Active tobacco use;
      vi. Perforating (i.e., fistulizing) disease;
   b. Member has failed one of the following therapies unless intolerant or contraindicated:
      i. A biologic for CD other than Remicade/Inflectra;
      ii. An immunomodulator (e.g., azathioprine, 6-mercaptopurine [6-MP], methotrexate [MTX]) for ≥ 3 consecutive months;
4. Member has failed Humira for ≥ 3 consecutive months unless intolerant or contraindicated;
5. After initial dosage regimen, prescribed maintenance dose frequency of Remicade/Inflectra does not exceed every 8 weeks.

Approval duration: 6 months

B. Ulcerative Colitis (must meet all):

1. Prescribed by or in consultation with a gastroenterologist;
2. Age ≥ 6 years (Remicade); age ≥ 18 years (Inflectra);
3. Diagnosis of moderately to severely active ulcerative colitis (UC);
4. Member has failed one of the following therapies unless intolerant or contraindicated:
   a. A biologic for UC other than Remicade/Inflectra;
   b. An immunomodulator (e.g., azathioprine, 6MP, MTX) for ≥ 3 consecutive months;
5. Member has failed Humira for ≥ 3 consecutive months unless intolerant or contraindicated;

6. After initial dosage regimen, prescribed maintenance dose frequency of Remicade/Inflectra does not exceed every 8 weeks.

Approval duration: 6 months

C. Rheumatoid Arthritis (must meet all):
1. Prescribed by or in consultation with a rheumatologist;
2. Age ≥ 18 years;
3. Diagnosis of moderately to severely active rheumatoid arthritis (RA) and one or more of the following:
   a. ≥ 5 inflamed joints;
   b. Elevation in the erythrocyte sedimentation rate (ESR) and/or serum C-reactive protein (CRP) concentration;
   c. Positive rheumatoid factor and/or anticyclic citrullinated peptide (CCP) antibodies (present in most patients);
   d. Evidence of inflammation on plain radiography of the hands, wrists, or feet, such as osteopenia and/or periarticular swelling;
4. Member has failed one of the following therapies unless intolerant or contraindicated:
   a. A biologic for RA other than Remicade/Inflectra;
   b. MTX for ≥ 3 consecutive months;
   c. If intolerance or contraindication to MTX, sulfasalazine, leflunomide, or hydroxychloroquine for ≥ 3 consecutive months;
5. Member has failed Humira AND Enbrel, each trialed for ≥ 3 consecutive months unless intolerant or contraindicated;
6. Prescribed concomitantly with MTX, or another disease-modifying antirheumatic (DMARD) agent if intolerance or contraindication to MTX;
7. After initial dosage regimen, prescribed maintenance dose frequency of Remicade/Inflectra does not exceed every 8 weeks.

Approval duration: 6 months

D. Ankylosing Spondylitis (must meet all):
1. Age ≥ 18 years;
2. Diagnosis of active ankylosing spondylitis (AS);
3. Member has failed one of the following therapies unless intolerant or contraindicated:
   a. A biologic for AS other than Remicade/Inflectra;
   b. Two or more non-steroidal anti-inflammatory drugs (NSAIDs) at maximum tolerated doses, each for ≥ 4 weeks;
4. Member has failed Humira AND Enbrel, each trialed for ≥ 3 consecutive months unless intolerant or contraindicated;
5. After initial dosage regimen, prescribed maintenance dose frequency of Remicade/Inflectra does not exceed every 6 weeks.

Approval duration: 6 months

E. Psoriatic Arthritis (must meet all):
1. Prescribed by or in consultation with a dermatologist or rheumatologist;
2. Age ≥ 18 years;
3. Diagnosis of active psoriatic arthritis (PsA);
4. Member has failed one of the following therapies unless intolerant or contraindicated:
   a. A biologic for PsA other than Remicade/Inflectra;
   b. MTX for ≥ 3 consecutive months;
   c. If intolerance or contraindication to MTX, sulfasalazine, leflunomide, cyclosporine, or azathioprine, for ≥ 3 consecutive months;
5. Member has failed Humira AND Enbrel, each trialed for ≥ 3 consecutive months unless intolerant or contraindicated;
6. After initial dosage regimen, prescribed maintenance dose frequency of Remicade/Inflectra does not exceed every 8 weeks.

Approval duration: 6 months

F. Plaque Psoriasis (must meet all):
1. Prescribed by or in consultation with a dermatologist or rheumatologist;
2. Age ≥ 18 years;
3. Diagnosis of chronic severe (i.e., extensive and/or disabling) plaque psoriasis (PsO) and one or more of the following (a or b):
   a. Greater than 5% of body surface area is affected;
   b. Involvement of palms, soles, face/neck, body folds, or genitalia;
4. Member has failed phototherapy and a topical therapy (e.g., calcipotriene, coal tar preparations, medium-to-high potency corticosteroids, anthralin, tazarotene);
5. Member has failed one of the following therapies unless intolerant or contraindicated:
   a. A biologic for PsO other than Remicade/Inflectra;
   b. One or more systemic therapies (e.g., MTX, cyclosporine, acitretin, thioguanine) for ≥ 3 consecutive months;
6. Member has failed Humira AND Enbrel, each trialed for ≥ 3 consecutive months unless intolerant or contraindicated;
7. After initial dosage regimen, prescribed maintenance dose frequency of Remicade/Inflectra does not exceed every 8 weeks.

Approval duration: 6 months

G. Other diagnoses/indications: Refer to ERX.SPMN.16 - Global Biopharm Policy.

II. Continued Approval

A. All Indications (must meet all)**:**
1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
2. Member responding positively to therapy;
3. Prescribed regimen for Remicade/Inflectra does not exceed the following:
   a. AS: dosing frequency of every 6 weeks;

b. All other indications: dosing frequency of every 8 weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or
2. Refer to ERX.SPMN.16 - Global Biopharm Policy**.**

Background

Description/Mechanism of Action:

Infliximab is a chimeric monoclonal antibody that binds to human tumor necrosis factor alpha (TNFα), thereby interfering with endogenous TNFα activity. Elevated TNFα levels have been found in involved tissues/fluids of patients with RA, AS, PsA, PsO, CD and UC. Biological activities of TNFα include the induction of proinflammatory cytokines (interleukins), enhancement of leukocyte migration, activation of neutrophils and eosinophils, and the induction of acute phase reactants and tissue degrading enzymes. Animal models have shown TNFα expression causes polyarthritis, and infliximab can prevent disease as well as allow diseased joints to heal.

Formulations:

Solution Reconstituted, Intravenous [preservative free]:

Remicade (infliximab): 100 mg (1 ea) [contains polysorbate 80]

Inflectra (infliximab-dyyb): 100 mg (contains polysorbate 80, sucrose 500 mg; biosimilar agent)

FDA Approved Indications:

Remicade and Inflectra* are tumor necrosis factor-alpha inhibitors/intravenous injectable formulations indicated for:

- Crohn's disease: Reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active CD who have had an inadequate response to conventional therapy. Remicade is indicated for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing CD.
- Pediatric Crohn's disease: Reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active CD who have had an inadequate response to conventional therapy.
- Ulcerative colitis: Reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients with moderately to severely active UC who have had an inadequate response to conventional therapy.
- Pediatric ulcerative colitis: Reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active UC who have had an inadequate response to conventional therapy.

- Rheumatoid arthritis in combination with methotrexate: Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active RA.
- Ankylosing spondylitis: Reducing signs and symptoms in patients with active AS.
- Psoriatic arthritis: Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with PsA.
- Plaque psoriasis: Treatment of adult patients with chronic severe (i.e., extensive and/or disabling) PsO who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.

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**Inflectra is FDA approved for all indications above except pediatric UC.*

Appendices

Appendix A: Abbreviation Key

AS: ankylosing spondylitis
CCP: citrullinated peptide
CD: Crohn's disease
CRP: C-reactive protein
DMARD: disease modifying antirheumatic drug
ESR: erythrocyte sedimentation rate
MTX: methotrexate
PsA: psoriatic arthritis
PsO: psoriasis
RA: rheumatoid arthritis
SC: subcutaneous
TB: tuberculosis
TNF: tumor necrosis factor
UC: ulcerative colitis

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1745	Injection infliximab, 10 mg

Reviews, Revisions, and Approvals	Date	Approval Date
Policy split from USS.SPMN.24 Irritable Bowel Disease (IBD) Treatments, USS.SPMN.41 Psoriasis Treatments, and USS.SPMN.44 Rheumatoid Arthritis and Ankylosing Spondylitis Treatments. Converted to new template. Added the biosimilar Inflectra (approved for all Remicade	08/16	09/16

Reviews, Revisions, and Approvals	Date	Approval Date
indications with the exception of pediatric UC). Removed all safety criteria. Added dosing per PI. Modified approval duration to 6 months for initial and 12 months for renewal with the exception of UC which is 2 months (time to clinical remission per PI) and 12 months. Shortened background section. CD: modified criteria requiring failure of immunomodulator, corticosteroids or aminosalicylate to failure of "corticosteroid, with or without immunomodulator" per 2014 AGA Clinical Decision Tool. RA: changed age requirement to 18. Modified criteria to require trial of MTX, unless contraindicated. Added sulfasalazine and hydroxychloroquine as an alternative to MTX if contraindicated. Required trial of Humira AND Enbrel instead of one or the other. Added option for other DMARD if concomitant admin of MTX contraindicated. AS: added option of trial of a different biologic in addition to NSAIDs. Required trial of Humira AND Enbrel instead of one or the other. PsA: Added requirements for failure of a different biologic or 2 or more DMARDs, not including Otezla. PsO: removed duration of trial for topical and phototherapy. Added option for trial of a different biologic. Required trial of Humira and Enbrel, instead of previous requirement of Humira or Enbrel. Re-auth: combined into All Indications. For PsO, changed efficacy criteria related to Psoriasis Area and Severity Index (PASI)-75 to general efficacy statement.		
For all trial/failure requirements, indicated that member can also meet criteria if intolerant (as opposed to just contraindicated) to therapy in question. Modified the following initial criteria sets: -CD: modified trial/failure requirement to indicate an immunomodulator (as opposed to a corticosteroid with or without an immunomodulator) must be trialed. -UC: indicated that disease must be moderately to severely active. Removed option for trial/failure of corticosteroid and aminosalicylate. -RA: indicated that disease must be moderately to severely active. -PsA: modified trial/failure requirement- instead of requiring 2 or more nonbiologic DMARDs (such as cyclosporine, sulfasalazine, azathioprine, hydoxychloroquine), criteria now requires MTX; if MTX is contraindicated, then cyclosporine, sulfasalazine, leflunomide, cyclosporine, or azathioprine may be trialed. -PsO: indicated that disease must be chronic and severe.	11/16	12/16

References

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Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.