Clinical Policy: Infliximab (Remicade, Inflectra, Renflexis)

Reference Number: PA.CP.PHAR.254
Effective Date: 01/18
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Coding Implications
Revision Log

Description
Infliximab (Remicade®), infliximab-dyyb (Inflectra®) and infliximab-abda (Renflexis™) are chimeric monoclonal antibodies 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 rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), plaque psoriasis (PsO), Crohn's disease (CD) and ulcerative colitis (UC).

FDA approved indication
Remicade, Inflectra* and Renflexis* are indicated for the treatment of:

- 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 (Remicade only): 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.

**Inflectra and Renflexis are FDA approved for all indications above except pediatric UC.*

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria
It is the policy of Pennsylvania Health and Wellness® that Remicade, Inflectra and Renflexis are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of CD and (a or b):
   a. Member is identified as moderate/high risk based on one of the following:
      i. Age at initial diagnosis < 30 years;
      ii. Extensive anatomic involvement (e.g., ileocecal disease, continuous ileocolonic disease, small bowel disease);
      iii. Perianal and/or severe rectal disease;
      iv. Deep ulcers;
      v. Prior surgical resection;
      vi. Stricturing and/or penetrating disease;
   b. Member has failed both of the following, unless contraindicated or clinically significant adverse effects are experienced (i and ii):
      i. An immunomodulator (e.g., azathioprine, mercaptopurine (6MP), methotrexate (MTX)) used for ≥ 3 months;
      ii. Adalimumab *(Humira is preferred)* used for ≥ 3 consecutive months;
      **Prior authorization is required for adalimumab*
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 6 years;
4. If request is for Remicade or Renflexis, member has failed or experienced clinically significant adverse effects from Inflectra;
5. Tuberculosis (TB) test within the past 12 months is negative, or if positive, active TB has been ruled out and the member has received treatment for latent TB infection;
6. Dose does not exceed the following:
   a. Initial: 5 mg/kg at weeks 0, 2, and 6;
   b. Maintenance: adults - 10 mg/kg every 8 weeks; children and adolescents – 5 mg/kg every 8 weeks.

Approval duration: 6 months

B. Ulcerative Colitis (must meet all):

1. Diagnosis of UC;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 6 years;
4. Failure of a thiopurine (e.g., azathioprine, 6MP), used for ≥ 3 months, unless contraindicated or clinically significant adverse effects are experienced;
5. If age is ≥ 18 years, member has failed or experienced clinically significant adverse effects to Inflectra;
6. TB test within the past 12 months is negative, or if positive, active TB has been ruled out and the member has received treatment for latent TB infection;
7. Dose does not exceed the following:
   a. Initial: 5 mg/kg at weeks 0, 2, and 6;
   b. Maintenance: 5 mg/kg every 8 weeks.

Approval duration: 6 months

C. Rheumatoid Arthritis (must meet all):

1. Diagnosis of RA per American College of Rheumatology (ACR) criteria (refer to *Appendix B*);
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. If request is for Remicade or Renflexis, member has failed or experienced clinically significant adverse effects to Inflectra;
5. Member meets one of the following (a or b):
   a. Failure of MTX for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effect are experienced;
   b. If intolerance or contraindication to MTX, failure of sulfasalazine, leflunomide, or hydroxychloroquine for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effect are experienced;
6. Failure of etanercept *(Enbrel is preferred)* and adalimumab *(Humira is preferred)*, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for etanercept and adalimumab*
7. TB test within the past 12 months is negative, or if positive, active TB has been ruled out and the patient has received treatment for latent TB infection;
8. Dose does not exceed the following:
   a. Initial: 3 mg/kg at weeks 0, 2, and 6;
   b. Maintenance: 10 mg/kg every 4 weeks.

Approval duration: 6 months

D. Ankylosing Spondylitis (must meet all):

1. Diagnosis of active AS;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. If request is for Remicade or Renflexis, member has failed or experienced clinically significant adverse effects to Inflectra;
5. Failure of at least TWO non-steroidal anti-inflammatory drugs (NSAIDs) each trialed for ≥ 4 weeks unless contraindicated or clinically significant adverse effect are experienced;
6. Failure of etanercept *(Enbrel is preferred)* and adalimumab *(Humira is preferred)*, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for etanercept and adalimumab*
7. TB test within the past 12 months is negative, or if positive, active TB has been ruled out and the member has received treatment for latent TB infection;
8. Dose does not exceed the following:
   a. Initial: 5 mg/kg at weeks 0, 2, and 6;
   b. Maintenance: 5 mg/kg every 6 weeks.

Approval duration: 6 months

E. Psoriatic Arthritis (must meet all):

1. Diagnosis of PsA;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;

3. Age ≥ 18 years;
4. If request is for Remicade or Renflexis, member has failed or experienced clinically significant adverse effects to Inflectra;
5. Member meets one of the following (a or b):
    a. For Axial Disease
        i. A documented history of therapeutic failure of a six (6) week trial of two (2) NSAIDs or
        ii. A documented contraindication or intolerance to NSAIDs
    b. For Peripheral Disease:
        i. A documented history of therapeutic failure of a six (6) week trial of two (2) NSAIDs AND
        ii. A documented history of therapeutic failure of a three (3) or more month trial of methotrexate OR an alternate DEMARD OR
        iii. A documented contraindication or intolerance to NSAIDs, methotrexate, or an alternate DMARD.
6. Failure of etanercept *(Enbrel is preferred)* and adalimumab *(Humira is preferred)*, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization is required for etanercept and adalimumab*
7. TB test within the past 12 months is negative, or if positive, active TB has been ruled out and the member has received treatment for latent TB infection;
8. Dose does not exceed the following:
    a. Initial: 5 mg/kg at weeks 0, 2, and 6;
    b. Maintenance: 5 mg/kg every 8 weeks.

Approval duration: 6 months

F. Plaque Psoriasis (must meet all):

1. Diagnosis of chronic severe (i.e., extensive and/or disabling) 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;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 18 years;
4. If request is for Remicade or Renflexis, member has failed or experienced clinically significant adverse effects to Inflectra;
5. Failure of phototherapy and a topical therapy (e.g., calcipotriene, coal tar preparations, medium-to-high potency corticosteroids, anthralin, tazarotene), unless contraindicated or clinically significant adverser effects are experienced;
6. Failure of at least one systemic therapy (e.g., MTX, cyclosporine, acitretin, thioguanine) for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effect are experienced;
7. TB test within the past 12 months is negative, or if positive, active TB has been ruled out and the member has received treatment for latent TB infection;
8. Dose does not exceed the following:
    a. Initial: 5 mg/kg at weeks 0, 2, and 6;

b. Maintenance: 5 mg/kg every 8 weeks.

Approval duration: 6 months

G. Other diagnoses/indications: Refer to PA.CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Approval

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, member has not responded adequately to current dose and requested dose does not exceed the following
    a. RA and CD: 10mg/kg/dose;
    b. All other indications: 5mg/kg/dose;
4. Prescribed regimen for Remicade/Inflectra does not exceed the following (a, b or c):
    a. AS: dosing frequency of every 6 weeks;
    b. RA: dosing frequency of every 4 weeks; if the request represents an increase in dosing frequency from the current regimen, documentation supports both of the following (i and ii):
        i. Member has had an inadequate response to adherent use of Remicade/Inflectra concurrently with MTX or another disease-modifying antirheumatic drug (DMARD);
        ii. One of the following (a) or b)):
            a) Current dosing frequency is every 8 weeks: member has received at least 4 doses (14 weeks of total therapy) of Remicade/Inflectra;
            b) Current dosing frequency is < every 8 weeks: member has received at least 2 doses of Remicade/Inflectra at the current dosing frequency;
    c. All other indications: dosing frequency of every 8 weeks.

Approval duration: 12 months *(If new dosing regimen, approve for 6 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 the Continuity of Care policy (PA.LTSS.PHAR.01) applies.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

6MP: mercaptopurine
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

Appendix B: The 2010 ACR Classification Criteria for RA
Add score of categories A through D. A score of ≥ 6 out of 10 is needed for classification of a patient as having definite RA.

A	**Joint Involvement**	**Score**
	1 large joint	0
	2-10 large joints	1
	1-3 small joints (with or without involvement of large joints)	2
	4-10 small joints (with or without involvement of large joints)	3
	> 10 joints (at least one small joint)	5
B	**Serology (at least one test result is needed for classification)**	
	Negative rheumatoid factor (RF) *and* negative anti-citrullinated protein antibody (ACPA)	0
	Low positive RF *or* low positive ACPA * *Low: < 3 x upper limit of normal*	2
	High positive RF *or* high positive ACPA * *High: ≥ 3 x upper limit of normal*	3
C	**Acute phase reactants (at least one test result is needed for classification)**	
	Normal C-reactive protein (CRP) and normal erythrocyte sedimentation rate (ESR)	0
	Abnormal CRP or normal ESR	1
D	**Duration of symptoms**	
	< 6 weeks	0
	≥ 6 weeks	1

Appendix C: Definition of MTX or disease-modifying antirheumatic drug (DMARD) failure
In RA, failure of MTX or DMARD is defined as ≤ 50% decrease in swollen joint count, ≤ 50% decrease in tender joint count, and ≤ 50% decrease in ESR, or ≤ 50% decrease in CRP.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
RA	3 mg/kg IV initially and at weeks 2 and 6, then every 8 weeks	10 mg/kg every 4 weeks
AS	5 mg/kg IV initially and at weeks 2 and 6, then every 6 weeks	5 mg/kg every 6 weeks
CD, UC, PsO, PsA	5 mg/kg IV initially and at weeks 2 and 6, then every 8 weeks	CD (adults): 10 mg/kg every 8 weeks PsO, PsA, UC, CD (children and adolescents): 5 mg/kg every 8 weeks

V. Product Availability

Drug	Availability
infliximab (Remicade), infliximab-dyyb (Inflectra) infliximab-abda (Renflexis)	Single-use vial: 100 mg

VI. References

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15. Gladman DD, Ritchlin C. Treatment of psoriatic arthritis. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at www.UpToDate.com. Accessed June 16, 2016.
16. Feldman SR. Treatment of psoriasis. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2016. Available at www.UpToDate.com. Accessed June 15, 2016.
17. Infliximab Drug Monograph. Clinical Pharmacology. Accessed June 2017. http://www.clinicalpharmacology-ip.com.
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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, excludes biosimilar, 10 mg
Q5102	Injection, infliximab, biosimilar, 10 mg

Reviews, Revisions, and Approvals	Date	Approval Date