Inflectra™ (infliximab-dyyb)

FDA approval: April 5th, 2016
HCPCS: Q5102
Benefit: Medical

Policy/Criteria:

Note: Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when FDA approved indications below are met:
   a. Trial and failure of preferred therapy
   b. Crohn’s disease
      i. Diagnosis established by or in consultation with a specialist in gastroenterology
         1. Active Crohn’s disease
            1. Treatment with an adequate course of systemic corticosteroid (e.g., prednisone, or prednisolone per day for 7 to 14 days) has been ineffective or is contraindicated
               OR
            2. The patient has been unable to taper off an adequate course of systemic corticosteroids without experiencing worsening of disease
               OR
            3. The patient is experiencing breakthrough disease (e.g., active disease flares) while stabilized for at least 2 months on immunomodulatory medication (such as azathioprine, mercaptopurine, cyclosporine, or methotrexate)
      2. Fistulizing Crohn’s disease
   c. Pediatric Crohn’s disease
      i. Diagnosis established by or in consultation with a specialist in gastroenterology
      ii. The patient has had an inadequate response to conventional therapy
   d. Ulcerative colitis
      i. Diagnosis established by or in consultation with a specialist in gastroenterology
      ii. Treatment with an adequate course of systemic corticosteroid (e.g., prednisone, or prednisolone per day for 7 to 14 days) has been ineffective or is contraindicated
         OR
      iii. The patient has been unable to taper off an adequate course of systemic corticosteroids without experiencing worsening of disease
         OR
iv. The patient is experiencing breakthrough disease (e.g., active disease flares) while stabilized for at least 2 months on immunomodulatory medication (such as azathioprine, mercaptopurine, cyclosporine, or methotrexate)

e. Pediatric ulcerative colitis
  i. Diagnosis established by or in consultation with a specialist in gastroenterology
  ii. The patient has had an inadequate response to conventional therapy

f. Rheumatoid arthritis
  i. Diagnosis established by or in consultation with a specialist in rheumatology
  ii. There is clinical documentation that an oral DMARD (such as methotrexate) was not effective after at least a 6 to 12 week treatment course
  iii. Inflectra is administered with methotrexate

g. Psoriatic arthritis
  i. Diagnosis established by or in consultation with a specialist in dermatology or rheumatology

h. Plaque psoriasis
  i. Diagnosis established by or in consultation with a specialist in dermatology or rheumatology
  ii. Diagnosis of chronic severe (i.e., extensive and/or disabling) plaque psoriasis:
     1. Clinical documentation supports involvement of at least 10% of the body surface area OR
     2. There is significant functional disability
  iii. Treatment with phototherapy (for example, UVB) or photochemotherapy was not effective, not tolerated, or is contraindicated
  iv. Treatment with at least one oral systemic agent for psoriasis was ineffective or not tolerated, unless all are contraindicated. Examples of systemic agents include, but are not limited to, cyclosporine, methotrexate, and acitretin

i. Ankylosing spondylitis
  i. Diagnosis established by or in consultation with a specialist in rheumatology

B. Quantity Limitations, Authorization Period, and Renewal Criteria
   a. Initial: 5 mg/kg at 0, 2, and 6 weeks except 3 mg/kg for rheumatoid arthritis
   b. Continued: 3 mg/kg every 8 weeks for rheumatoid arthritis and 5 mg/kg every 8 weeks except every 6 weeks for ankylosing spondylitis
   c. Approval duration: 1 year
   d. Renewal: 1 year
   e. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective:
      i. Crohn’s disease:
         1. Active Crohn’s disease:
            a. Reducing signs and symptoms, inducing, and maintaining clinical remission
         2. Fistulizing Crohn’s disease
            a. Reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing disease
      ii. Pediatric Crohn’s disease:
         1. Reducing signs and symptoms, inducing, and maintaining clinical remission
      iii. Ulcerative colitis:
         1. Reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients
      iv. Pediatric ulcerative colitis:
         1. Reducing signs and symptoms, inducing, and maintaining clinical remission
      v. Rheumatoid arthritis: 
1. Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function

vi. Psoriatic arthritis:
1. Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function

vii. Plaque psoriasis:
1. Documentation of beneficial clinical response defined as achieving a PASI 75 response or equivalent response such as greater than 50% reduction in Body Surface Area (BSA) covered by psoriasis compared to baseline

viii. Ankylosing spondylitis:
1. Reducing signs and symptoms in patients with active disease

C. Inflectra is considered investigational when used for all other conditions, including but not limited to:

a. Behçet syndrome uveitis
b. Celiac sprue
c. Chronic obstructive pulmonary disease (stable)
d. Giant cell arteritis
e. Graft versus host disease (adults)
f. Graft versus host disease (children/adolescents)
g. Hidradenitis suppurativa (adults)
h. Juvenile idiopathic arthritis
i. Pustular psoriasis
j. Pyoderma gangrenosum
k. Sarcoidosis
l. Uveitis
m. Wegener granulomatosis

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia

Therapeutic considerations:

A. FDA approved indication / Diagnosis:
Inflectra is a tumor necrosis factor (TNF) blocker that is indicated for Crohn’s disease, ulcerative colitis, rheumatoid arthritis, psoriatic arthritis, plaque psoriasis, and ankylosing spondylitis.

*Please refer to most recent prescribing information.

B. Background Information
- Crohn’s disease (CD) is a chronic inflammatory disorder that is characterized by focal, asymmetric, transmural, and granulomatous inflammation which primarily affects the gastrointestinal tract.
  o Therapeutic recommendations are individualized and depend on disease location, severity, and complications present. Treatment options for CD include: glucocorticoids (conventional steroids and budesonide), immunosuppressants (azathioprine, mercaptopurine, methotrexate), 5-aminosalicylates (5-ASA), and biologic agents [infliximab (Remicade®), adalimumab (Humira®), natalizumab (Tysabri®), certolizumab (Cimzia®), and vedolizumab (Entyvio™)].

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• Ulcerative colitis (UC) is an inflammatory bowel disease (IBD) that causes long-lasting inflammation and ulcers (sores) in the digestive tract.
  o Treatment options for UC include: glucocorticoids (conventional steroids and budesonide), immunosuppressants (azathioprine, mercaptopurine, methotrexate), 5-aminosalicylates (5-ASA), and biologic agents (Remicade, Humira, Tysabri, Cimzia, and Entyvio).
• Rheumatoid arthritis (RA) is an autoimmune disease that most commonly affects the wrists, fingers, knees, feet, and ankle joints symmetrically.
  o Treatment options for RA include: glucocorticoids (most often used for short-term management of flares), disease-modifying anti-rheumatic drugs (DMARDs): hydroxychloroquine, leflunomide, methotrexate, minocycline, and sulfasalazine; and biologic agents [non-TNF: abatacept (Orencia®), rituximab (Rituxan®), tocilizumab (Actemra®); anti-TNF: Humira, entanercept (Enbrel®), Remicade, Cimzia, and golimumab (Simponi®)].
• Psoriatic Arthritis (PsA) is a chronic inflammatory disease often associated with psoriasis. Psoriasis is an autoimmune disease affecting the skin, resulting in scaly red and white patches.
  o Treatment options include NSAIDS, DMARDs, and anti-TNF biologic agents. If PsA does not respond to the initial treatment [NSAIDs, DMARDs (sulfasalazine, methotrexate, cyclosporine, and leflunomide)] as monotherapy, combination therapy may be used. Hydroxychloroquine should be avoided due to exacerbation of psoriasis. Anti-TNF agents may be utilized when initial treatment has been ineffective. Anti-TNF agents approved for PsA include: Humira, Enbrel, Remicade, Cimzia and Simponi.
• Psoriasis is a complex autoimmune inflammatory disease that occurs in genetically susceptible individuals and presents with the development of inflammatory plaques on the skin.
  o Treatment options include: phototherapy or photochemotherapy, DMARDs: cyclosporine, methotrexate, and acitretin. Anti-TNF agents may be utilized when initial treatment has been ineffective. Anti-TNF agents approved for plaque psoriasis include: Humira, Enbrel, and Remicade.
• Ankylosing Spondylitis (AS) belongs to a group of chronic rheumatic diseases affecting the bones and joints connecting the spine and pelvis known as spondyloarthritis.
  o Treatment options include NSAIDs, corticosteroids, DMARDs, and anti-TNF biologic agents. Anti-inflammatory agents such as NSAIDs may be used to reduce swelling; however, they do not affect disease progression. DMARDs (sulfasalazine and methotrexate) have not been proven effective for the treatment of axial disease. Anti-TNF agents (Enbrel, Humira, Remicade, Cimzia or Simponi) target the pathophysiologic mechanism of AS and have been shown to be beneficial and effective.

C. Efficacy:

*Please refer to most recent prescribing information.

D. Medication Safety Considerations

Boxed Warning: Yes

*Please refer to most recent prescribing information.

E. Dosing and administration

a. Dosing:
  i. Crohn’s disease
     1. Initial: 5 mg/kg at 0, 2, and 6 weeks
     2. Maintenance: 5 mg/kg every 8 weeks

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ii. Ulcerative colitis
   1. Initial: 5 mg/kg at 0, 2, and 6 weeks
   2. Maintenance: 5 mg/kg every 8 weeks

iii. Rheumatoid arthritis in conjunction with methotrexate
   1. Initial: 3 mg/kg at 0, 2, and 6 weeks
   2. Maintenance: 3 mg/kg every 8 weeks

iv. Psoriatic arthritis and plaque psoriasis
   1. Initial: 5 mg/kg at 0, 2, and 6 weeks
   2. Maintenance: 5 mg/kg every 8 weeks

v. Ankylosing spondylitis
   1. Initial: 5 mg/kg at 0, 2, and 6 weeks
   2. Maintenance: 5 mg/kg every 6 weeks

*Please refer to most recent prescribing information.

F. How supplied

   a. Solution Reconstituted, intravenous containing 100 mg of infliximab-dyyb

References:

1. Inflectra™ [prescribing information]. Lake Forest, IL: ©CELLTRION, Inc; April 2016.
2. FDA News Release. FDA approves Inflectra, a biosimilar to Remicade. FDA. Accessed from:
   http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm494227.htm
3. American College of Rheumatology (ACR). "Rheumatology community responds to FDA approval of Inflectra
5. U.S. Biosimilar Space Reaches Its Inflectra Point. Seeking Alpha. April 2016 Accessed from:
   http://seekingalpha.com/article/3963603-u-s-biosimilar-space-reaches-inflectra-point
   http://www.reuters.com/article/us-pfizer-fda-idUSKCN0X22O1
   world-study-show-comparable-effectiveness-and-safety-of-hospira

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* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is
  advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or

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