MEDICAL POLICY STATEMENT

Original Effective Date	Next Annual Review Date	Last Review / Revision Date
02/22/2011	02/22/2016	07/09/2015

Policy Name	Policy Number
Rheumatoid Arthritis, Inflammatory Bowel Disease, Psoriasis and Psoriatic Arthritis: Biological Therapies	**SRx-0004**

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For Medicare plans please reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

A. SUBJECT

Rheumatoid Arthritis, Inflammatory Bowel Disease, Psoriasis and Psoriatic Arthritis: Biological Therapies

- Tumor Necrosis Factor Inhibitor
  - **Adalimumab (Humira)**
  - **Certolizumab pegol (Cimzia)**
  - **Etanercept (Enbrel)**
  - **Golimumab (Simponi and Simponi Aria™)**
  - **Infliximab (Remicade)**
- Phosphodiesterase-4 Enzyme Inhibitors
  - **Apremilast (Otezla)**
- IL-12 and IL-23 Inhibitors
  - **Ustekinumab (Stelara) Injection**
- Janus Associated Kinase Inhibitors
  - **Tofacitinib (Xeljanz) Injection**
- Interleukin-1 beta (IL-1β) inhibitor
  - **Canakinumab (Ilaris) injection**
- Integrin receptor antagonist
  - **Vedolizumab (Entyvio)**

B. BACKGROUND

Tumor necrosis factor-alpha (TNF) is a messenger protein, or cytokine, produced by monocytes and macrophages that mediates inflammation and induces the destruction of some tumor cells in the body. Five TNF inhibitors have been approved for the treatment of selected rheumatic and inflammatory bowel diseases.

Phosphodiesterase 4 (PDE4) is the predominant enzyme that degrades the second messenger cAMP in many immune cells, including eosinophils, neutrophils, macrophages, T cells, and monocytes. Evidence suggests that cAMP causes a down regulatory signal in immune cells, thus suppressing the production of proinflammatory mediators, including tumor necrosis factor (TNF)-α, interleukin (IL)-17, and interferon (IFN)-γ. It is also believed that cAMP promotes the production of anti-inflammatory mediators such as IL-10.

Human IgG1κ is a monoclonal antibody that binds with specificity to the p40 protein subunit used by both the IL-12 and IL-23 cytokines. IL-12 and IL-23 are naturally occurring cytokines that are involved in inflammatory and immune responses, such as natural killer cell activation and CD4+ T-cell differentiation and activation.

Janus kinase (JAK) enzymes are intracellular enzymes are part of a signaling pathway involved in stimulating hematopoiesis and immune cell function. JAKs activate signal transducers and activators of transcription (STATs) which regulate gene expression and intracellular activity. Inhibiting JAKs prevents cytokine- or growth factor–mediated gene expression and intracellular activity of immune cells, reduces circulating CD16/56+ natural killer cells, serum IgG, IgM, IgA, and C-reactive protein, and increases B cells.

Canakinumab binds to human IL-1β and neutralizes its activity by blocking its interaction with IL-1 receptors, but it does not bind IL-1α or IL-1 receptor antagonist (IL-1ra).
CAPS refer to rare genetic syndromes generally caused by mutations in the NLRP-3 [nucleotide-binding domain, leucine rich family (NLR), pyrin domain containing 3] gene (also known as Cold-Induced Auto-inflammatory Syndrome-1 [CIAS1]). CAPS disorders are inherited in an autosomal dominant pattern with male and female offspring equally affected. Features common to all disorders include fever, urticaria-like rash, arthralgia, myalgia, fatigue, and conjunctivitis.
The NLRP-3 gene encodes the protein cryopyrin, an important component of the inflammasome. Cryopyrin regulates the protease caspase-1 and controls the activation of interleukin-1 beta (IL-1β). Mutations in NLRP-3 result in an overactive inflammasome resulting in excessive release of activated IL-1β that drives inflammation. Systemic juvenile idiopathic arthritis (SJIA) is a severe auto-inflammatory disease, driven by innate immunity by means of pro-inflammatory cytokines such as interleukin 1β (IL-1β).

The intent of this pre-authorization (PA) program is to encourage the appropriate selection of preferred therapeutic agents for patients with such disorders as supported by product labeling, clinical studies and clinical guidelines.

C. DEFINITIONS

N/A

D. POLICY

I. **Infliximab (Remicade)** is considered **medically necessary** when criteria are met for **ANY** of the following indications:
   A. **Crohn's Disease (CD)** when the following are met:
      1. Fistulizing Crohn's Disease and **ALL** of the following:
         1.1 Age 18 years or older
         1.2 No untreated latent or active tuberculosis
         1.3 Draining enterocutaneous or rectovaginal fistula
             Duration of 3 months or more
         1.4 Prescribed by or in consultant with a gastroenterologist

1.5 There is clinical documentation that treatment with adalimumab (Humira) was not effective after at least a 12-week treatment course

2. Moderate to severe non-fistulizing Crohn's Disease and **ALL** of the following:
   2.1 Age 6 years or older
   2.2 Prescribed by or in consultant with a gastroenterologist
   2.3 No untreated latent or active tuberculosis
   2.4 There is clinical documentation that treatment with adalimumab (Humira) was not effective after at least a 12-week treatment course
   2.5 Treatment needed for moderate to severe disease, as indicated by **1 or more** of the following:
      a. Inadequate response to therapy with **1 or more** of the following during a 12-week trial:
         (1) 6-mercaptopurine
         (2) Azathioprine
         (3) Methotrexate
      b. Severe disease, as indicated by **1 or more** of the following:
         (1) Esophageal or gastroduodenal disease
         (2) Extensive small-bowel disease involving more than 100cm
         (3) History of colonic resection
         (4) History of **two (2) or more** small-bowel resections
         (5) Perianal or rectal disease

B. **Ulcerative Colitis (UC)** when **ALL** of the following are met:
   1. Individual is 6 years of age or older with moderate to severe active Ulcerative Colitis
   2. No untreated latent or active tuberculosis
   3. Prescribed by or in consultant with a gastroenterologist
   4. Individual failed to respond to conventional therapy during a 4-week trial (such as 5-ASA products, sulfasalazine, systemic corticosteroids, or immunosuppressive agents)
   5. There is clinical documentation that treatment with adalimumab was not effective after at least a 12-week treatment

C. **Rheumatoid Arthritis (RA)** when **ALL** of the following are met:
   1. Individual is 18 years of age or older with moderate to severe active RA
   2. No untreated latent or active tuberculosis
   3. Prescribed by or in consultant with a rheumatologist
   4. Infliximab is given in combination with methotrexate or with another immunosuppressive agent if the individual is intolerant to methotrexate
   5. Individual has failed to respond to at least 12 weeks of **two (2) or more** non-biologic DMARDs
   6. There is clinical documentation that treatment with adalimumab or etanercept was not effective after at least a 12-week treatment

D. **Ankylosing Spondylitis (AS)** when **ALL** of the following are met:
   1. Individual is 18 years of age or older with active AS
   2. Prescribed by or in consultant with a rheumatologist
   3. No untreated latent or active tuberculosis
   4. Clinical and diagnostic imaging evidence of ankylosing spondylitis, as indicated by **ALL** of the following:
      4.1 Back pain of 3 months' or more duration and age of onset of 45 years or younger
      4.2 Sacroiliitis on imaging
      4.3 Spondyloarthritis signs or symptoms, as indicated by **1 or more** of the following:
         a. Arthritis
         b. Elevated serum C-reactive protein
         c. Enthesitis (eg, inflammation of Achilles tendon insertion)

d. HLA-B27
e. Limited chest expansion
f. Morning stiffness for 1 hour or more

5. Disease activity and treatment scenario, as indicated by **1 or more** of the following:
   5.1 Axial (spinal) disease
   5.2 Peripheral arthritis without axial involvement, and failure of 4 or more months of therapy with sulfasalazine
6. Individual has failed to respond to **two (2) or more** different NSAIDs (at maximum recommended doses) over a total period of at least 4 or more weeks of therapy
7. There is clinical documentation that treatment with adalimumab or etanercept was not effective after at least a 12-week treatment course

E. **Psoriatic Arthritis (PsA)** when **ALL** of the following are met:
1. Individual is 18 years of age or older with active PsA
2. Prescribed by or in consultant with a rheumatologist or dermatologist
3. No untreated latent or active tuberculosis
4. Moderate to severe active psoriatic arthritis, as indicated by **1 or more** of the following:
   4.1 Predominately axial disease (ie, sacroiliitis or spondylitis), as indicated by **1 or more** of the following:
      a. Radiographic evidence of axial disease (eg, sacroiliac joint space narrowing or erosions, vertebral syndesmophytes)
      b. Symptoms (eg, limited spinal range of motion, spinal morning stiffness more than 30 minutes) present for more than 3 months' duration and unresponsive to trial of two (2) different NSAIDs
   4.2 Predominately non-axial disease
      a. Individual has failed to respond after at least a 8-week trial of methotrexate and a trial of a NSAID
5. There is clinical documentation that treatment with adalimumab or etanercept was not effective after at least a 12-week treatment course

F. **Plaque Psoriasis (Ps)** when **ALL** of the following are met:
1. Individual is 18 years of age or older
2. Prescribed by or in consultant with a dermatologist or rheumatologist
3. No untreated latent or active tuberculosis
4. No concomitant systemic therapy or phototherapy
5. Chronic moderate to severe plaque Ps with the following:
   5.1 Plaque Ps involving ten percent or more of the body surface area (BSA)
   5.2 Systemic therapy or phototherapy evaluation, as indicated by **1 or more** of the following:
      a. Candidate for systemic therapy or phototherapy
      b. Previous treatment with systemic therapy or phototherapy
   5.3 Individual has failed to respond to **1 or more** of the following:
      a. Immunosuppressive treatments (eg, cyclosporine, methotrexate) for a 12-week trial
      b. Photochemotherapy (ie, psoralen plus ultraviolet A therapy)
      c. Phototherapy (ie, ultraviolet light therapy)
      d. Topical agents (eg, anthralin, calcipotriene, coal tars, corticosteroids, tazarotene) for a 4-week trial
6. There is clinical documentation that treatment with adalimumab or etanercept was not effective after at least a 12-week treatment course

G. **Behcet disease and uveitis,** as indicated by **ALL** of the following:
1. Loss of visual acuity or evidence of retinal involvement

2. No untreated latent or active tuberculosis
3. Failure to respond to a corticosteroid (e.g. prednisone)
4. Failure to respond to an immunosuppressant (e.g. azathioprine, methotrexate)

II. **Etanercept (Enbrel)** is considered **medically necessary** when criteria are met for **ANY** of the following indications:
   A. **Rheumatoid Arthritis (RA)** when **ALL** of the following are met:
      1. Individual is 18 years of age or older
      2. No untreated latent or active tuberculosis
      3. Prescribed by or in consultant with a rheumatologist
      4. Individual has failed to respond to at least 12 weeks of **two (2) or more** non-biologic DMARDs
   B. **Ankylosing Spondylitis (AS)** when **ALL** of the following are met:
      1. Individual is 18 years of age or older with active AS
      2. No untreated latent or active tuberculosis
      3. Prescribed by or in consultant with a rheumatologist
      4. Clinical and diagnostic imaging evidence of ankylosing spondylitis, as indicated by **ALL** of the following:
         4.1 Back pain of 3 months or more duration and age of onset of 45 years or younger
         4.2 Sacroiliitis on imaging
         4.3 Spondyloarthritis signs or symptoms, as indicated by **1 or more** of the following:
            a. Arthritis
            b. Elevated serum C-reactive protein
            c. Enthesitis (eg, inflammation of Achilles tendon insertion)
            d. HLA-B27
            e. Limited chest expansion
            f. Morning stiffness for 1 hour or more
      5. Disease activity and treatment scenario, as indicated by **1 or more** of the following:
         5.1 Axial (spinal) disease
         5.2 Peripheral arthritis without axial involvement, and failure of 4 or more months of therapy with sulfasalazine
         5.3 Failure of treatment with an anti-tumor necrosis factor-alpha drug after a 12-week trial
      6. Failure of **two (2) or more** different NSAIDs (at maximum recommended doses) over a total period of at least 4 or more weeks of therapy
   C. **Juvenile Idiopathic Arthritis (JIA)** when **ALL** of the following are met:
      1. Individual is two (2) years of age or older
      2. Prescribed by or in consultant with a rheumatologist
      3. No untreated latent or active tuberculosis
      4. Joint involvement and treatment scenario includes **1 or more** of the following:
         4.1 Four or fewer joints involved and inadequate response to **ALL** of the following:
            a. Glucocorticosteroid injection
            b. Methotrexate
            c. NSAIDs after a 12-week trial
         4.2 Five or more joints involved and inadequate response to methotrexate
   D. **Psoriatic Arthritis (PsA)** when **ALL** of the following are met:
      1. Individual is 18 years or older of age with active PsA
      2. Prescribed by or in consultant with a rheumatologist or dermatologist
      3. No untreated latent or active tuberculosis
      4. Moderate to severe active psoriatic arthritis, as indicated by **1 or more** of the following:

4.1 Predominantly axial disease (ie, sacroiliitis or spondylitis), as indicated by **1 or more** of the following:
    a. Radiographic evidence of axial disease (eg, sacroiliac joint space narrowing or erosions, vertebral syndesmophytes)
    b. Symptoms (eg, limited spinal range of motion, spinal morning stiffness more than 30 minutes) present for more than 3 months duration, and unresponsive to trial of **two (2)** different NSAIDs
4.2 Predominantly non-axial disease
    a. Individual has failed to respond after a least a 8-week trial of methotrexate and a trial of a NSAID

E. **Plaque Psoriasis (Ps)** when **ALL** of the following are met:
1. Individual is 18 years of age or older
2. Prescribed by or in consultant with a dermatologist or rheumatologist
3. No untreated latent or active tuberculosis
4. No concomitant systemic therapy or phototherapy
5. Chronic moderate to severe plaque Ps with the following:
    5.1 Plaque Ps involving greater than ten percent body surface area (BSA)
    5.2 Systemic therapy or phototherapy evaluation, as indicated by **1 or more** of the following:
        a. Candidate for systemic therapy or phototherapy
        b. Previous treatment with systemic therapy or phototherapy
    5.3 Individual has failed to respond to **1 or more** of the following:
        a. Immunosuppressive treatments (eg, cyclosporine, methotrexate) after a 12-week trial
        b. Photochemotherapy (ie, psoralen plus ultraviolet A therapy)
        c. Phototherapy (ie, ultraviolet light therapy)
        d. Topical agents (eg, anthralin, calcipotriene, coal tars, corticosteroids, tazarotene) after a 4 week trial

III. **Adalimumab (Humira)** is considered **medically necessary** when criteria are met for **ANY** of the following indications:

A. **Crohn's Disease (CD)** when **ALL** of the following are met:
1. Individual is 18 years of age or older with moderately to severely active CD
2. Prescribed by or in consultant with a gastroenterologist
3. No untreated latent or active tuberculosis
4. Treatment needed for moderate to severe disease, as indicated by **1 or more** of the following:
    4.1 Individual has failed to respond to, is intolerant of, or has a medical contraindication to 12 weeks of conventional therapy (such as 5-ASA products, sulfasalazine, systemic corticosteroids, or immunosuppressant agents)
    4.2 Severe disease, as indicated by **1 or more** of the following:
        a. Esophageal or gastroduodenal disease
        b. Extensive small-bowel disease involving more than 100cm
        c. History of colonic resection
        d. History of **two (2) or more** small-bowel resections
        e. Perianal or rectal disease

B. **Ulcerative Colitis (UC)** when **ALL** of the following are met:
1. Individual is 18 years of age or older with moderately to severely active UC
2. Prescribed by or in consultant with a gastroenterologist
3. No untreated latent or active tuberculosis

4. Individual has failed to respond to conventional therapy during a 4-week trial (such as 5-ASA products, sulfasalazine, systemic corticosteroids, or immunosuppressive agents)

C. **Rheumatoid Arthritis (RA)** when **ALL** of the following are met:
   1. Individual is 18 years of age or older with moderately to severely active RA
   2. Prescribed by or in consultant with a rheumatologist
   3. No untreated latent or active tuberculosis
   4. Individual has failed to respond to at least 12 weeks of, **two (2) or more** non-biologic DMARDs

D. **Ankylosing Spondylitis (AS)** when **ALL** of the following are met:
   1. Individual is 18 years of age or older with active AS
   2. Prescribed by or in consultant with a rheumatologist
   3. No untreated latent or active tuberculosis
   4. Clinical and diagnostic imaging evidence of ankylosing spondylitis, as indicated by **ALL** of the following:
      4.1 Back pain of 3 months or more duration and age of onset of 45 years or younger
      4.2 Sacroiliitis on imaging
      4.3 Spondyloarthritis signs or symptoms, as indicated by **1 or more** of the following:
         a. Arthritis
         b. Elevated serum C-reactive protein
         c. Enthesitis (eg, inflammation of Achilles tendon insertion)
         d. HLA-B27
         e. Limited chest expansion
         f. Morning stiffness for 1 hour or more
   5. Disease activity and treatment scenario, as indicated by **1 or more** of the following:
      a. Axial (spinal) disease
      b. Peripheral arthritis without axial involvement, and failure of 4 or more months of therapy with sulfasalazine
   6. Individual has failed to respond to **two (2) or more** different NSAIDs (at maximum recommended doses) over a total period of at least 4 or more weeks of therapy

E. **Juvenile Idiopathic Arthritis (JIA)** when **ALL** of the following are met:
   1. Individual is 4 years of age or older with moderately to severely active JIA
   2. No untreated latent or active tuberculosis
   3. Prescribed by or in consultant with a rheumatologist
   4. Treatment needed for disease severity, as indicated by **1 or more** of the following:
      4.1 Four or fewer joints involved and inadequate response to **ALL** of the following:
         a. Glucocorticosteroid injection
         b. Methotrexate
         c. NSAIDs after a 12 week trial
      4.2 Five or more joints involved and inadequate response to methotrexate
      4.3 Sacroiliitis, and inadequate response to methotrexate

F. **Psoriatic Arthritis (PsA)** when ALL of the following are met:
   1. Individual is 18 years of age or older with active PsA
   2. No untreated latent or active tuberculosis
   3. Prescribed by or in consultant with a rheumatologist or dermatologist
   4. Moderate to severe active psoriatic arthritis, as indicated by **1 or more** of the following:
      4.1 Predominantly axial disease (ie, sacroiliitis or spondylitis), as indicated by **1 or more** of the following:
         a. Radiographic evidence of axial disease (eg, sacroiliac joint space narrowing or erosions, vertebral syndesmophytes)

b. Symptoms (eg, limited spinal range of motion, spinal morning stiffness more than 30 minutes) present for more than 3 months duration, and unresponsive to trial of **two (2)** different NSAIDs

4.2 Predominantly non-axial disease

a. Individual has failed to respond after at least an 8-week trial of methotrexate and a trial of a NSAID

G. **Plaque Psoriasis (Ps)** when **ALL** of the following are met:

1. Individual is 18 years of age or older
2. Prescribed by or in consultant with a dermatologist or rheumatologist
3. No untreated latent or active tuberculosis
4. No concomitant systemic therapy or phototherapy
5. Chronic moderate to severe plaque Ps with the following:

5.1 Plaque Ps involving greater than ten percent body surface area (BSA)

5.2 Systemic therapy or phototherapy evaluation, as indicated by **1 or more** of the following:

a. Candidate for systemic therapy or phototherapy
b. Previous treatment with systemic therapy or phototherapy

5.3 Individual has failed to respond to **1 or more** of the following:

a. Immunosuppressive treatments (eg, cyclosporine, methotrexate) after a 12-week trial
b. Photochemotherapy (ie, psoralen plus ultraviolet A therapy)
c. Phototherapy (ie, ultraviolet light therapy)
d. Topical agents (eg, anthralin, calcipotriene, coal tars, corticosteroids, tazarotene) after a 4-week trial

H. **Uveitis** (noninfectious, chronic) as indicated by inadequate response to **ALL** of the following:

1. Failure to respond to a corticosteroid (e.g. prednisone)
2. No untreated latent or active tuberculosis
3. Failure to respond to anmmunosuppressant (eg, azathioprine, methotrexate)

IV. **Certolizumab Pegol (Cimzia)** is considered **medically necessary** when criteria are met for either of the following indications:

A. **Crohns' Disease (CD)** when **ALL** of the following are met:

1. Individual is 18 years of age or older with moderately to severely active CD
2. Prescribed by or in consultant with a gastroenterologist
3. No untreated latent or active tuberculosis
4. Treatment needed for moderate to severe disease, as indicated by **1 or more** of the following:

4.1 inadequate response to therapy with **1 or more** of the following:

a. 6-mercaptopurine after a 12-week trial
b. Azathioprine after a 12-week trial
c. Infliximab after a 4-week trial
d. Methotrexate after a 12-week trial

4.2 Severe disease, as indicated by **1 or more** of the following:

a. Esophageal or gastroduodenal disease
b. Extensive small-bowel disease involving more than 100cm
c. History of colonic resection
d. History of **two (2) or mor**e small-bowel resections
e. Perianal or rectal disease

5. There is clinical documentation that the treatment with adalimumab (Humira) was not effective after at least a 12-week treatment

B. **Rheumatoid Arthritis (RA)** when **ALL** of the following are met:

1. Individual is 18 years of age or older with moderately to severely active RA
2. Prescribed by or in consultant with a rheumatologist
3. No untreated latent or active tuberculosis
4. Individual has failed to respond to 12 weeks to **two (2) or more** non-biologic DMARDs
5. There is clinical documentation that treatment with adalimumab or etanercept was not effective after at least a 12-week treatment course

C. **Psoriatic Arthritis (PsA)** as indicated by **1 or more** of the following:
1. Initial course, as indicated by **ALL** of the following:
1.1 Age 18 years or older
1.2 No untreated latent or active tuberculosis
1.3 There is clinical documentation that treatment with adalimumab or etanercept was not effective after at least a 12-week treatment course
1.4 Prescribed by or in consultant with a rheumatologist or dermatologist
1.5 Moderate to severe active psoriatic arthritis, as indicated by **1 or more** of the following:
a. Predominately axial disease (ie, sacroiliitis or spondylitis), as indicated by **1 or more** of the following:
(1) Radiographic evidence of axial disease (eg, sacroiliac joint space narrowing or erosions, vertebral syndesmophytes)
(2) Symptoms (eg, limited spinal range of motion, spinal morning stiffness more than 30 minutes) present for more than 3 months duration, and unresponsive to trial of **two (2)** different NSAIDs
b. Predominantly non-axial disease
1.6 Individual has failed to response after at least an 8-week trial of methotrexate and a trial of a NSAID

6. **Golimumab (Simponi)** is considered **medically necessary** for individuals when criteria are met for ANY of the following indications:

A. **Ulcerative Colitis (UC)** when **ALL** of the following are met:
1. No untreated latent or active tuberculosis
2. Prescribed by or in consultation with a rheumatologist
3. Individual is 18 years of age or older with moderately to severely active UC
Intolerance of or inadequate response to **1 or more** of the following a 12 week trial:
3.1 6-mercaptopurine
3.2 Azathioprine
3.3 Oral corticosteroids or steroid dependence
3.4 Salicylates
4. There is clinical documentation that treatment with adalimumab (Humira) was not effective after at least an 8-week treatment course

B. **Rheumatoid Arthritis (RA)** when **ALL** of the following are met:
1. Individual is 18 years of age or older with moderately to severely active RA
2. Prescribed by or in consultant with a rheumatologist
3. No untreated latent or active tuberculosis
4. Golimumab is given in combination with methotrexate or with another immunosuppressive agent if the individual is intolerant to methotrexate
5. Individual has failed to respond to 12 weeks of, to **two (2) or more** non-biologic DMARDs
6. There is clinical documentation that treatment with adalimumab or etanercept was not effective after at least a 12-week treatment course

C. **Ankylosing Spondylitis (AS)** when **ALL** of the following are met:
1. Individual is 18 years of age or older with active AS
2. Prescribed by or in consultant with a rheumatologist

3. No untreated latent or active tuberculosis
4. Clinical and diagnostic imaging evidence of ankylosing spondylitis, as indicated by **ALL** of the following:
   4.1 Back pain of 3 months' or more duration and age of onset of 45 years or younger
   4.2 Sacroiliitis on imaging
   4.3 Spondyloarthritis signs or symptoms, as indicated by **1 or more** of the following:
      a. Arthritis
      b. Elevated serum C-reactive protein
      c. Enthesitis (eg, inflammation of Achilles tendon insertion)
      d. HLA-B27
      e. Limited chest expansion
      f. Morning stiffness for 1 hour or more
5. Disease activity and treatment scenario, as indicated by **1 or more** of the following:
   5.1 Axial (spinal) disease
   5.2 Peripheral arthritis without axial involvement, and failure of 4 or more months of therapy with sulfasalazine
6. Individual has failed to respond to **two (2) or more** different NSAIDs (at maximum recommended doses) over a total period of at least 4 or more weeks of therapy
7. There is clinical documentation that treatment with adalimumab or etanercept was not effective after at least a 12-week treatment course

D. **Psoriatic Arthritis (PsA)** when **ALL** of the following are met:
   1. Individual is 18 years of age or older
   2. Prescribed by or in consultant with a rheumatologist or dermatologist
   3. No untreated latent or active tuberculosis
   4. Moderate to severe active psoriatic arthritis, as indicated by **1 or more** of the following:
      4.1 Predominantly axial disease (ie, sacroiliitis or spondylitis), as indicated by **1 or more** of the following:
         a. Radiographic evidence of axial disease (eg, sacroiliac joint space narrowing or erosions, vertebral syndesmophytes)
         b. Symptoms (eg, limited spinal range of motion, spinal morning stiffness more than 30 minutes) present for more than 3 months duration, and unresponsive to trial of **two (2)** different NSAIDs
      4.2 Predominantly non-axial disease
         a. Individual has failed to respond after at least an 8-week trial of methotrexate and a trial of a NSAID
      4.3 There is clinical documentation that treatment with adalimumab or etanercept was not effective after at least a 12-week treatment course

VI. **Ustekinumab (Stelara)** is considered **medically necessary** when criteria are met for either of the following indications:

A. **Plaque Psoriasis (Ps)** when **ALL** of the following are met:
   1. No untreated latent or active tuberculosis
   2. Age 18 years or older
   3. Duration of psoriasis of 6 or more months
   4. Prescribed by or in consultant with a dermatologist or rheumatologist
   5. No concomitant systemic therapy or phototherapy
   6. Chronic moderate to severe plaque Ps with the following:
      6.1 Plaque Ps involving ten (10) percent body surface area (BSA) or more
      6.2 Systemic therapy or phototherapy evaluation, as indicated by **1 or more** of the following:
         a. Candidate for systemic therapy or phototherapy

b. Previous treatment with systemic therapy or phototherapy

6.3 Individual has failed to respond to 1 or more of the following:

a. Immunosuppressive treatments (eg, cyclosporine, methotrexate) after a 12-week trial

b. Photochemotherapy (ie, psoralen plus ultraviolet A therapy)

c. Phototherapy (ie, ultraviolet light therapy)

d. Topical agents (eg, anthralin, calcipotriene, coal tars, corticosteroids, tazarotene) after a 4-week trial

7. There is clinical documentation that treatment with adalimumab or etanercept was not effective after at least a 12-week treatment course

B. **Active Psoriatic Arthritis (PsA)** when **ALL** of the following are met:

1. Individual is 18 years or older of age with active PsA
2. Prescribed by or in consultant with a rheumatologist or dermatologist
3. No untreated latent or active tuberculosis
4. Moderate to severe active psoriatic arthritis, as indicated by **1 or more** of the following:

4.1 Predominantly axial disease (ie, sacroiliitis or spondylitis), as indicated by **1 or more** of the following:

a. Radiographic evidence of axial disease (eg, sacroiliac joint space narrowing or erosions, vertebral syndesmophytes)

b. Symptoms (eg, limited spinal range of motion, spinal morning stiffness more than 30 minutes) present for more than 3 months duration, and unresponsive to trial of **two (2)** different NSAIDs

4.2 Predominantly non-axial disease

a. Individual has failed to respond after a least a 8-week trial of methotrexate and a trial of a NSAID

5. There is clinical documentation that treatment with adalimumab or etanercept was not effective after at least a 12-week treatment course

VII**. Apremilast (Otezla)** is considered **medically necessary** for individuals when criteria are met for ANY of the following indications:

A. **Active Psoriatic Arthritis (PsA**) when **ALL** of the following are met:

1. Age over 18 years old
2. Prescribed by or in consultation with a rheumatologist or dermatologist
3. Moderate to severe active psoriatic arthritis, as indicated by **1 or more** of the following:

3.1 Predominantly axial disease (ie, sacroiliitis or spondylitis), as indicated by **1 or more** of the following:

a. Radiographic evidence of axial disease (eg, sacroiliac joint space narrowing or erosions, vertebral syndesmophytes)

b. Symptoms (eg, limited spinal range of motion, spinal morning stiffness more than 30 minutes) present for more than 3 months duration, and unresponsive to trial of **two (2)** different NSAIDs

3.2 Predominantly non-axial disease

a. Individual has failed to respond after at least an 8-week trial of methotrexate and a trial of a NSAID

4. There is clinical documentation that treatment with adalimumab or etanercept was not effective after at least a 12-week treatment course

B. **Plaque Psoriasis (Ps**) when **ALL** of the following are met:

1. Is a candidate for phototherapy
2. Prescribed by or in consultant with a dermatologist
3. Individual is 18 years of age or older
4. Chronic moderate to severe plaque Ps with the following:

4.1 Plaque Ps involving greater than ten (10) percent body surface area (BSA)

4.2 Systemic therapy or phototherapy evaluation, as indicated by **1 or more** of the following:
    a. Candidate for systemic therapy or phototherapy
    b. Previous treatment with systemic therapy or phototherapy
4.3 Individual has failed to respond to **1 or more** of the following:
    a. Immunosuppressive treatments (eg, cyclosporine, methotrexate) after a 12-week trial
    b. Photochemotherapy (ie, psoralen plus ultraviolet A therapy)
    c. Phototherapy (ie, ultraviolet light therapy)
    d. Topical agents (eg, anthralin, calcipotriene, coal tars, corticosteroids, tazarotene) after a 4-week trial

5. There is clinical documentation that treatment with adalimumab or etanercept was not effective after at least a 12-week treatment course

VIII. **Tofacitinib (Xeljanz)** is considered **medically necessary** for individuals when criteria are met for ANY of the following indications:

A. **Rheumatoid Arthritis (RA)** when **ALL** of the following are met:
1. Individual is 18 years of age or older with moderately to severely active RA
2. Prescribed by or in consultant with a rheumatologist
3. No untreated latent or active tuberculosis
4. Individual has failed to respond to 12 weeks of to **two (2) or more** non-biologic DMARDs
5. There is clinical documentation that treatment with adalimumab or etanercept was not effective after at least a 12-week treatment course

IX. **Vedolizumab (Entyvio)** is considered **medically necessary** for individuals when criteria are met for ANY of the following indications:

A. **Crohn's Disease (CD)** when established by or in consultation with a gastroenterologist, and **ALL** of the following are met:
1. Individual is 18 years of age or older with moderately to severely active CD
2. No untreated latent or active tuberculosis
3. Treatment needed for moderate to severe disease, as indicated by **1 or more** of the following:
    3.1 Individual has failed to respond to conventional therapy (such as 5-ASA products, systemic corticosteroids, or immunosuppressants 12 week trial)
    3.2 Severe disease as indicated by **1 or more** of the following:
        a. Esophageal or gastroduodenal disease
        b. Extensive small-bowel disease involving more than 100cm
        c. History of colonic resection
        d. History of **two (2) or more** small-bowel resections
        e. Perianal or rectal disease
4. There is clinical documentation that treatment with adalimumab (Humira) was not effective after at least a 12-week treatment course

B. **Ulcerative colitis** when established by or in consultation with a gastroenterologist, and **ALL** of the following are met:
1. Individual is 18 years of age or older with moderately to severely active UC with demonstrated corticosteroid dependence
2. No untreated latent or active tuberculosis
3. Individual has failed to respond to conventional therapy during a 4-week trial (such as 6-mercaptopurine, azathioprine, oral aminosalicylates, or oral corticosteroids)
4. There is clinical documentation that treatment with adalimumab (Humira) was not effective after at least an 8-week treatment course

X. **Canakinumab (Ilaris)** is considered **medically necessary** for individuals when criteria are met for **ANY** of the following indications:

A. **Cryopyrin-associated periodic syndromes (CAPS**) which include Familial Cold Auto-Inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) and criteria **ALL** below are met:
   1. There is laboratory evidence of a genetic mutation in the Cold-Induced Auto-Inflammatory Syndrome 1 (CIAS1 – sometimes referred to as the NLRP3)
   2. Age 4 years or older
   3. No untreated latent or active tuberculosis
   4. There is clinical documentation that the patient is experiencing the classic symptoms of CAPS, defined as meeting either criterion below:
      4.1 Familial Cold Auto-Inflammatory Syndrome (FCAS) – Recurrent intermittent episodes of fever and rash that primarily follow natural, artificial (eg, air conditioning) or both types of generalized cold exposure
      OR
      4.2 Muckle-Wells Syndrome (MWS) – Syndrome of chronic fever and rash that may wax and wane in intensity; sometimes exacerbated by generalized cold exposure. This syndrome may be associated with deafness or amyloidosis

B. **Juvenile Idiopathic Arthritis (JIA)** systemic, as indicated by **1 or more** of the following:
   1. As indicated by **ALL** of the following:
      1.1 Age two (2) years or older
      1.2 No untreated latent or active tuberculosis
      1.3 Prescribed by or under the recommendation of a rheumatologist
      1.4 Systemic juvenile idiopathic arthritis, as indicated by arthritis involving **two (2) or more** joints **AND 1 or more** of the following:
         a. Evanescent erythematous rash
         b. Fever for at least **two (2)** weeks
         c. Generalized lymphadenopathy
         d. Hepatomegaly or splenomegaly
         e. Pericarditis, pleuritic, or peritonitis
      1.5 Inadequate response to **ALL** of the following:
         a. Glucocorticosteroid injection
         b. Methotrexate
         c. NSAIDs
         d. Tumor necrosis factor-alpha inhibitor (eg, adalimumab (Humira))

ALL other uses of Adalimumab, Certolizumab pegol, Etanercept, Golimumab, Infliximab, Apremilast, Ustekinumab, Tofacitinib, Canakinumab, Tocilizumab, Abatacept or Vedolizumab considered experimental/investigational and therefore, will follow CareSource's off-label policy.

Note: Patient is required to have completed the trial listed in the above criteria unless the patient is unable to tolerate or has a contraindication. Documentation such as chart notes or pharmacy claims may be requested.

Note: Documented diagnosis must be confirmed by portions of the individual's medical record which will confirm the presence of disease and will need to be supplied with prior authorization request. These medical records may include, but not limited to test reports, chart notes from provider's office or hospital admission notes.

Refer to the product package insert for dosing, administration and safety guidelines.

For Medicare Plan members, reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

If there is no NCD or LCD present, reference the CareSource Policy for coverage.

CONDITIONS OF COVERAGE

HCPCS
J0135 Adalimumab **(Humira)**
J0717 Certolizumab pegol **(Cimzia)**
J1438 Etanercept **(Enbrel)**
J3590, C9399 Golimumab SC **(Simponi)**
J1602 Golimumab IV **(Simponi Aria)**
J1745 Infliximab **(Remicade)**
J3357 Ustekinumab **(Stelara)**
J8499 Apremilast **(Oztela)**
J3590, C9026 Vedolizumab **(Entyvio)**
J0638 Canakinumab **(Ilaris)**
J8499 Tofacitinib **(Xeljanz)**

CPT

PLACE OF SERVICE
Office, Outpatient, Home
****Preferred place of service is in the home.**
This medication can be self-administered and can be billed through the pharmacy benefit.
Note: CareSource supports administering inject able medications in various setting, as long as those services are furnished in the most appropriate and cost effective setting that are supportive of the patient's medical condition and unique needs and condition. The decision on the most appropriate setting for administration is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of the specific medication.

AUTHORIZATION PERIOD
Approved initial authorizations are valid for 12 months. Continued treatment may be considered when the member has shown biological response to treatment. A reauthorization will be placed if there is evidence of patient taking the medication within the last 60 days. **ALL** authorizations are subject to continued eligibility.

E. RELATED POLICIES/RULES

F. REVIEW/REVISION HISTORY

Date Issued:	06/22/2011
Date Reviewed:	06/22/2011, 12/22/2012, 12/22/2013, 10/22/2014, 02/22/2015, 04/21/2015
Date Revised:	12/22/2012 12/22/2013 – Added detail to criteria, increased % body involvement, changed agents to fail 10/22/2104 – Add indication Psoriatic Arthritis & Crohn's Disease 02/22/2015 – Combine TNF and Stelara policies; revised diagnoses for Certolizumab, Infliximab & Adalimumab, added Apremilast and changed duration of initial authorization for all

4/21/2015 – Add Ilaris & criteria, Entyvio & criteria, Xeljanz & criteria, trial length added for UC and Crohn's
07/09/2015 – Additional background information and criteria changes

G. REFERENCES

1. Stelara [package insert]. Horsham, PA: Janssen Biotech Inc; Revised March 2014.
2. US Food and Drug Administration Drug Safety Data. http://www.accessdata.fda.gov/drugsatfda_docs/label/2014/125261s114lbl.pdf (October 14, 2014)
3. Menter A, Gottlieb A, Feldman SR, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. J Am Acad Dermatol. 2008 May;58(5):826-50.
4. Hsu S, Papp KA, Lebwohl MG, et al. Consensus guidelines for the management of plaque psoriasis. Arch Dermatol. 2012 Jan;148(1):95-102.
5. Gottlieb A, Korman NJ, Gordon KB, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 2. Psoriatic arthritis: overview and guidelines of care for treatment with an emphasis on the biologics. J Am Acad Dermatol. 2008 May;58(5):851-64.
6. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: section 4. Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. J Am Acad Dermatol. 2009 Sep;61(3):451-85. Epub 2009 Jun 3
7. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis Section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: Case-based presentations and evidence-based conclusions. J Am Acad Dermatol. 2011 Feb 7. [Epub ahead of print]
8. MCG 19th edition, 2015.
9. Xeljanz [prescribing information]. New York, NY: Pfizer; May 2014.
10. Ilaris [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation. Revised October 2014.
11. Entyvio [package insert]. Deerfield, IL: Takeda Pharmaceuticals America, Inc.; May 2014
12. Feagan, BG, Rutgeerts, P, Sands, BE, et al. Vedolizumab as induction and maintenance therapy for ulcerative colitis. The New England journal of medicine. 2013 Aug 22;369(8):699-710. PMID: 23964932
13. Sands, BE, Feagan, BG, Rutgeerts, P, et al. Effects of Vedolizumab Induction Therapy for Patients With Crohn's Disease in Whom Tumor Necrosis Factor Antagonist Treatment Had Failed. Gastroenterology. 2014 May 21. PMID: 24859203
14. Sandborn, WJ, Feagan, BG, Rutgeerts, P, et al. Vedolizumab as induction and maintenance therapy for Crohn's disease. The New England journal of medicine. 2013 Aug 22;369(8):711-21. PMID: 23964933
15. DeWitt EM, Kimura Y, Beukelman T, et al; Juvenile Idiopathic Arthritis Disease-specific Research Committee of Childhood Arthritis Rheumatology and Research Alliance. Consensus treatment plans for new-onset systemic juvenile idiopathic arthritis. Arthritis Care Res (Hoboken). 2012 Jul;64(7):1001-10. doi: 10.1002/acr.21625. PubMed PMID: 22290637; PubMed Central PMCID: PMC3368104
16. National Institutes of Health, Clinicaltrials.gov. [cited 9/16/2014]; Available from: http://www.clincaltrials.gov
17. Lachmann, HJ, Kone-Paut, I, Kuemmerle-Deschner, JB, et al. Use of canakinumab in the cryopyrin-associated periodic syndrome. N Engl J Med. 2009 Jun 4;360(23):2416-25. PMID 19494217
18. Medscape; Juvenile Idiopathic Arthritis Treatment & Management Author: David D Sherry, MD; Chief Editor: Lawrence K Jung, MD
19. Humira [prescribing information]. North Chicago, IL; AbbVie Inc.: Revised December 2014.

20. Cimzia [prescribing information]. Smyrna, GA; UCB, Inc.: Revised October 2013.
21. Enbrel [prescribing information]. Thousand Oaks, CA; Immunex Corporation: Revised September 2013.
22. Simponi [prescribing information]. Horsham, PA; Janssen Biotech, Inc.: Revised January 2014.
23. Simponi Aria [prescribing information]. Horsham, PA; Janssen Biotech, Inc.: Approved December 2014.
24. Remicade [prescribing information]. Horsham, PA; Janssen Biotech, Inc.: Revised January 2015.
25. Otezla [prescribing information]. Summit, NJ; Celgene Corporation: Revised December 2014.
26. Higgins J, Green S, editors. Cochrane handbook for systematic reviews of interventions, Version 5.1.0 [updated March 2011]. The Cochrane Collaboration. Available from: URL:www.cochrane-handbook.org
27. Sakane T, Takeno M, Suzuki N, Inaba G. Behçet's disease. N Engl J Med 1999; 341:1284.
28. Reed JB, Morse LS, Schwab IR. High-dose intravenous pulse methylprednisolone hemisuccinate in acute Behçet retinitis. Am J Ophthalmol 1998; 125:409.
29. Huppertz HI, Tschammler A, Horwitz AE, Schwab KO. Intraarticular corticosteroids for chronic arthritis in children: efficacy and effects on cartilage and growth. J Pediatr 1995; 127:317.
30. Lanni S, Bertamino M, Consolaro A, et al. Outcome and predicting factors of single and multiple intra-articular corticosteroid injections in children with juvenile idiopathic arthritis. Rheumatology (Oxford) 2011; 50:1627.
31. Lichtenstein GR, Hanauer SB, Sandborn WJ, Practice Parameters Committee of American College of Gastroenterology. Management of Crohn's disease in adults. American Journal of Gastroenterology 2009;104(2):465-83; quiz 464, 484. DOI: 10.1038/ajg.2008.168. (Reaffirmed 2014 Oct)
32. Singh, J., et.al.,(2012). 2012 Update of the 2008 American College of Rheumatology Recommendations for the Use of Disease-Modifying Antirheumatic Drugs and Biologic Agents in the Treatment of Rheumatoid Arthritis. Arthritis Care & Research, 64(5), 625-639.
33. Tysabri [package insert]. Cambridge, MA: Biogen Idec Inc.; December 2013.
34. Terdiman JP, Gruss CB, Heidelbaugh JJ, Sultan S, Falck-Ytter YT; AGA Institute Clinical Practice and Quality Management Committee. American Gastroenterological Association Institute guideline on the use of thiopurines, methotrexate, and anti-TNF-α biologic drugs for the induction and maintenance of remission in inflammatory Crohn's disease. *Gastroenterology.* 2013 Dec;145(6):1459-63.
35. van der Heijde D, Dijkmans B, Geusens P, et al. Efficacy and safety of infliximab in patients with ankylosing spondylitis. Results of a randomized placebo-controlled trial (ASSERT) Arthritis Rheum. 2005;52:582–91.

This guideline contains custom content that has been modified from the standard care guidelines and has not been reviewed or approved by MCG Health, LLC.

The medical Policy Statement detailed above has received due consideration as defined in the Medical Policy Statement Policy and is approved.

Independent Medical Review - 2011