MEDICAL POLICY STATEMENT		
Original Effective Date	**Next Annual Review Date**	**Last Review / Revision Date**
02/22/2011	**02/22/2016**	**08/11/2015**
Policy Name		**Policy Number**
Autoimmune Diseases: Biologic Therapies		**SRx-0042**

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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

Autoimmune Disorders: Biologic 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**
- Intereukin-1 Antagonist
  - **Anakira (Kineret)**
- T-cell Activation Inhibitor
  - **Abatacept (Orencia)**
- Interleukin 6 (IL-6) receptor
  - **Tocilizumab (Actemra)**

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.

IL-6 is a pleiotropic pro-inflammatory cytokine produced by a variety of cell types including T- and B-cells, lymphocytes, monocytes and fibroblasts. IL-6 has been shown to be involved in diverse physiological processes such as T-cell activation, induction of immunoglobulin secretion, initiation of hepatic acute phase protein synthesis, and stimulation of hematopoietic precursor cell proliferation and differentiation. IL-6 is also produced by synovial and endothelial cells leading to local production of IL-6 in joints affected by inflammatory processes such as rheumatoid arthritis.

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.

IL-1 production is induced in response to inflammatory stimuli and mediates various physiologic responses including inflammatory and immunological responses. IL-1 has a broad range of

activities including cartilage degradation by its induction of the rapid loss of proteoglycans, as well as stimulation of bone resorption. The levels of the naturally occurring IL-1Ra in synovium and synovial fluid from RA patients are not sufficient to compete with the elevated amount of locally produced IL-1.

Inhibiting T cell (T lymphocyte) activation by binding to CD80 and CD86, blocks the interaction with CD28. This interaction provides a costimulatory signal necessary for full activation of T lymphocytes. Activated T lymphocytes are implicated in the pathogenesis of RA and are found in the synovium of patients with RA.

C. DEFINITIONS

N/A

D. POLICY

CareSource will approve the use of the following medications and consider them use as **medically necessary** when the following criteria have been met:

I. **Infliximab (Remicade)** 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 with moderate to severe active RA
2. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
3. Prescribed by a rheumatologist
4. 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

B. **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 a rheumatologist
3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
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 **one (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 **one (1) or more** of the following:
   5.1 Axial (spinal) disease
   5.2 Peripheral arthritis without axial involvement, and failure of **three (3) or more** months of therapy with sulfasalazine or methotrexate

5.3 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

C. **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 a rheumatologist or dermatologist
   3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
   4. Moderate to severe active psoriatic arthritis, as indicated by **one (1) or more** of the following:
      4.1 Predominately axial disease (ie, sacroiliitis or spondylitis), as indicated by **one (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

D. **Behcet disease and uveitis**, as indicated by **ALL** of the following:
   1. Loss of visual acuity or evidence of retinal involvement
   2. Prescribed by an ophthalmologist that is a uveitis specialist or ocular immunologist
   3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
   4. Failure to respond to corticosteroids or other immunosuppressant's after a 4-week trial

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. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
   3. Prescribed by 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. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
   3. Prescribed by 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 **one (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 **one (1) or more** of the following:
   5.1 Axial (spinal) disease
   5.2 Peripheral arthritis without axial involvement, and failure of 3 or more months of therapy with sulfasalazine or methotrexate
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 a rheumatologist
3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
4. Joint involvement and treatment scenario includes **one (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 a rheumatologist or dermatologist
3. Moderate to severe active psoriatic arthritis, as indicated by **one (1) or more** of the following:
   3.1 Predominantly axial disease (ie, sacroiliitis or spondylitis), as indicated by **one (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 a least a 8-week trial of methotrexate and a trial of a NSAID

III. **Adalimumab (Humira)** 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 with moderately to severely active RA
2. Prescribed by a rheumatologist
3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
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. Prescribed by a rheumatologist
3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
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 **one (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
   4.4 Disease activity and treatment scenario, as indicated by **one (1) or more** of the following:
      a. Axial (spinal) disease
      b. Peripheral arthritis without axial involvement, and failure of 3 or more months of therapy with sulfasalazine or methotrexate
5. 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.

C. **Juvenile Idiopathic Arthritis (JIA**) when **ALL** of the following are met:
1. Individual is 2 years of age or older with moderately to severely active JIA
2. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
3. Prescribed by a rheumatologist
4. Treatment needed for disease severity, as indicated by **one (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
   4.4 Uveitis, and inadequate response to **ALL** of the following:
      a. Systemic corticosteroids
      b. Systemic immunosuppressant (eg, azathioprine or methotrexate)
      c. Topical ophthalmic corticosteroids

D. **Psoriatic Arthritis (PsA)** when **ALL** of the following are met:
1. Individual is 18 years of age or older with active PsA
2. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
3. Prescribed by a rheumatologist or dermatologist
4. Moderate to severe active psoriatic arthritis, as indicated by **one (1) or more** of the following:
   4.1 Predominantly axial disease (ie, sacroiliitis or spondylitis), as indicated by **one (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

E. **Uveitis** (noninfectious, chronic) when **ALL** of the following are met:
1. Prescribed by an ophthalmologist that is a uveitis specialist or ocular immunologist
2. Inadequate response to at least one of the following of the following after a 4-week trial:
2.1 Corticosteroids
2.2 Systemic immunosuppressants (eg, azathioprine)
3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
4. Loss of visual acuity or evidence of retinal involvement

IV. **Certolizumab Pegol (Cimzia)** 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 with moderately to severely active RA
2. Prescribed by a rheumatologist
3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
4. Individual has failed to respond to 12 weeks to t**wo (2) or more** non-biologic DMARDs

B. **Psoriatic Arthritis (PsA),** when ALL of the following are met:
1. Age 18 years or older with moderate to severe active psoriatic arthritis
2. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
3. Prescribed by a rheumatologist or dermatologist
4. Moderate to severe active psoriatic arthritis, as indicated by **one (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

V. **Golimumab (Simponi)** 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 a rheumatologist
3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
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

B. **Ankylosing Spondylitis (AS)** when **ALL** of the following are met:
1. Individual is 18 years of age or older
2. Prescribed by a rheumatologist
3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
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 **one (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
   4.4 Disease activity and treatment scenario, as indicated by **one (1) or more** of the following:
      a. Axial (spinal) disease
      b. Peripheral arthritis without axial involvement, and failure of 3 or more months of therapy with sulfasalazine or methotrexate
   4.5 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

C. **Psoriatic Arthritis (PsA)** when **ALL** of the following are met:
1. Individual is 18 years of age or older
2. Prescribed by a rheumatologist or dermatologist
3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
4. Moderate to severe active psoriatic arthritis, as indicated by **one (1) or more** of the following:
   4.1 Predominantly axial disease (ie, sacroiliitis or spondylitis), as indicated by **one (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

VI. **Ustekinumab (Stelara)** is considered **medically necessary** when criteria are met for the following indication:
   A. **Active Psoriatic Arthritis (PsA)** when **ALL** of the following are met:
      1. Age 18 years or older
      2. Prescribed by a rheumatologist or dermatologist
      3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
      4. Moderate to severe active psoriatic arthritis, as indicated by **one (1) or more** of the following:
         4.1 Predominantly axial disease (ie, sacroiliitis or spondylitis), as indicated by **one (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 two (2)** months duration, and unresponsive to trail 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

VII. **Apremilast (Otezla)** is considered **medically necessary** for individuals when criteria are met for the following indication:
   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 **one (1) or more** of the following:
         3.1 Predominantly axial disease (ie, sacroiliitis or spondylitis), as indicated by **one (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

VIII. **Tofacitinib (Xeljanz)** is considered **medically necessary** for individuals when criteria are met for the following indication:
   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 a rheumatologist
      3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
      4. Individual has failed to respond to 12 weeks of to **two (2) or more** non-biologic DMARDs

IX. **Tocilizumab (Actemra)** is considered **medically necessary** for individuals when criteria are met for **ANY** of the following indications:
   A. **Rheumatoid Arthritis** when **ALL** of the following are met:
      1. Documented diagnosis of moderate to severe active rheumatoid arthritis
      2. Age 18 years or older
      3. Prescribed by a rheumatologist
      4. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
   B. **Juvenile Idiopathic Arthritis** when **ALL** of the following are met:
      1. Documented diagnosis of active systemic juvenile idiopathic arthritis or polyarticular juvenile idiopathic arthritis
      2. Age 2 years or older
      3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
      4. Prescribed by a rheumatologist
      5. Inadequate response to treatment with tumor necrosis factor-alpha inhibitor AND disease-modifying anti-rheumatic drug after 12-week trial
      6. Joint involvement and treatment scenario includes **one (1) or more** of the following:
         6.1 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
         6.2 Five or more joints involved and inadequate response to methotrexate

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) when **ALL** of the following are met:
      1. Age 4 years or older
      2. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
      3. Prescribed by a rheumatologist
      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, when **ALL** of the following are met:
      1. Individual is two (2) years of age or older
      2. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
      3. Prescribed by a rheumatologist

4. Systemic juvenile idiopathic arthritis, as indicated by arthritis involving **two (2) or more** joints **AND one (1) or more** of the following:
   4.1 Evanescent erythematous rash
   4.2 Fever for at least **two (2)** weeks
   4.3 Generalized lymphadenopathy
   4.4 Hepatomegaly or splenomegaly
   4.5 Pericarditis, pleuritic, or peritonitis
5. Inadequate response to **ALL** of the following:
   5.1 Glucocorticosteroid injection
   5.2 Methotrexate
   5.3 NSAIDs after a 12-week trial
   5.4 Tumor necrosis factor-alpha inhibitor (eg, adalimumab (Humira)) after a 12 -week trial

XI. **Anakinra (Kineret)** is considered medically necessary for individuals when criteria are met for **ANY** of the following indications:
   A. **Rheumatoid arthritis**, as indicated by **ALL** of the following:
      1. Age 18 years or older
      2. Documented diagnosis of moderate to severe active rheumatoid arthritis
      3. Prescribed by a rheumatologist
      4. No concurrent treatment with anti-tumor necrosis factor drug
      5. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
      6. Individual has failed to respond to at least 12 weeks of **two (2) or more** non-biologic DMARDs
      7. Individual has failed to respond to at least 12 weeks trial with Tumor Necrosis Factor Inhibitors
   B. **Cryopyrin-associated periodic syndrome (CAPS),** as indicated by **ALL** of the following:
      1. Diagnosis of Neonatal-Onset Multisystem Inflammatory Disease (NOMID)
      2. There is laboratory evidence of a genetic mutation in the Cold-Induced Auto-inflammatory Syndrome 1 (CIAS1 – sometimes referred to as the NLRP3)
      3. Prescribed by a rheumatologist or under recommendation of rheumatologist or CAPS specialist
      4. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy

XII. **Abatacept (Orencia)** CareSource will approve the use of abatacept (Orencia), and considers its use as medically necessary when **ALL** of the following criteria have been met for:
   A. **Rheumatoid Arthritis**, as indicated by **ALL** of the following:
      1. Documented diagnosis of moderate to severe active rheumatoid arthritis
      2. Age 18 years or older
      3. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
      4. Prescribed by a rheumatologist.
      5. Inadequate response to **three (3) or more** months of treatment with a DMARD (disease- modifying anti-rheumatic drug), including **one (1) or more** of the following:
         5.1 methotrexate (e.g., Rheumatrex)

5.2 leflunomide
5.3 sulfasalazine (Azulfidine)

6. Individual has failed to respond to at least 12 weeks trial with Tumor Necrosis Factor Inhibitors

B. **Juvenile Idiopathic Arthritis**, as indicated by **ALL** of the following:
1. Documented diagnosis of moderate to severe juvenile idiopathic arthritis
2. Prescribed by a rheumatologist
3. Age 6 years or older
4. Documented negative TB test (ie, tuberculosis skin test (PPD), an interferon-release assay (IGRA), or a chest x-ray) within 6 months of initiating a biologic therapy OR yearly for members with risk factors that are requesting continuation of therapy
5. Joint involvement of five (5) joints or more
6. Inadequate response to **three (3) or more** months of treatment with a DMARD (disease- modifying anti-rheumatic drug), including **one (1) or more** of the following:
6.1 methotrexate (e.g., Rheumatrex)
6.2 leflunomide
7. Inadequate response to 12 weeks of one or more tumor necrosis factor (TNF) antagonists: e.g. adalimumab (Humira), etanercept (Enbrel), infliximab (Remicade)

ALL other uses of Adalimumab, Certolizumab pegol, Etanercept, Golimumab, Infliximab, Apremilast, Ustekinumab, Tofacitinib, Canakinumab, Anakinra, Tocilizumab, Abatacept 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)**
J0638 Canakinumab **(Ilaris)**
J8499 Tofacitinib **(Xeljanz)**
J3262 Tocilizumab **(Actemra)**

J3490 Anakinra **(Kineret)**
J0129 Abatacept **(Orencia)**

CPT

Step Therapy
Under some plans, including plans that use an open or closed formulary, some of the medications in this policy may be subject to step-therapy. Refer to the CareSource formulary tool or PDL for further guidance.

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

- SRx-0041 Inflammatory Bowel Disease: Biologic Therapies
- SRx-0043 Psoriasis: Biologic Therapies

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,, Xeljanz & criteria, 06/2/2015-Changed trial criteria for RA 08/11/2015- Removed Crohn's, IBD and Psoriasis Criteria and references from policy, added detail to TB criteria, retitled policy name; added related policies

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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