golimumab (Simponi Aria®, Simponi®)

Policy # 00223
Original Effective Date: 07/22/2009
Current Effective Date: 10/19/2016

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Simponi Aria®‡

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Rheumatoid Arthritis
Based on review of available data, the Company may consider the use of intravenous (IV) golimumab (Simponi Aria) for the treatment of rheumatoid arthritis (RA) to be eligible for coverage.

Patient Selection Criteria
Coverage eligibility for the use of intravenous (IV) golimumab (Simponi Aria) for the treatment of rheumatoid arthritis (RA) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; and
- Patient has moderately to severely active rheumatoid arthritis (RA); and
- Intravenous (IV) golimumab (Simponi Aria) is used in combination with methotrexate (MTX) unless there is a contraindication to taking methotrexate (MTX) or a history of methotrexate (MTX) intolerance; and
- Patient has failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDs); and
  (Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)
- Patient has a negative purified protein derivative (PPD) test prior to treatment.

Note: The FDA approved prescribing information recommends:

- Simponi Aria should not be prescribed with other biologic products approved to treat conditions such as rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), or ulcerative colitis (UC) (including, but not limited to tumor necrosis factor (TNF) blockers, anakinra, and abatacept).

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of intravenous (IV) golimumab (Simponi Aria) when patient selection criteria are not met to be investigational* (except in the absence of a failure to one or more disease modifying anti-rheumatic drugs [DMARDS] which is considered not medically necessary**).
Based on review of available data, the Company considers the use of intravenous (IV) golimumab (Simponi Aria) for indications other than those listed above to be investigational.*

**When Services Are Considered Not Medically Necessary**
Based on review of available data, the Company considers the use of intravenous (IV) golimumab (Simponi Aria) in the absence of a treatment failure to one or more disease modifying anti-rheumatic drugs to be **not medically necessary**

**Simponi®‡**

**When Services May Be Eligible for Coverage**
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

**Rheumatoid Arthritis**
Based on review of available data, the Company may consider the use of subcutaneous (SC) golimumab (Simponi) for the treatment of rheumatoid arthritis (RA) to be eligible for coverage.

**Patient Selection Criteria**
Coverage eligibility for the use of subcutaneous (SC) golimumab (Simponi) for the treatment of rheumatoid arthritis (RA) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; and
- Patient has moderately to severely active rheumatoid arthritis (RA); and
- Subcutaneous (SC) golimumab (Simponi) is used in combination with methotrexate (MTX) unless there is a contraindication to taking methotrexate (MTX) or a history of methotrexate (MTX) intolerance; and
- Patient has failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDs); and
  (Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary if not met.)
- Patient has failed treatment with adalimumab (Humira®)† AND etanercept (Enbrel®)‡ after at least two months of therapy with each product (unless there is clinical evidence or patient history that suggests that the these products will be ineffective or cause an adverse reaction to the patient); and
  (Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary if not met.)
- Patient has a negative purified protein derivative (PPD) test prior to treatment.

**Psoriatic Arthritis**
Based on review of available data, the Company may consider the use of subcutaneous (SC) golimumab (Simponi) for the treatment of psoriatic arthritis (PsA) to be eligible for coverage.
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Patient Selection Criteria
Coverage eligibility for the use of subcutaneous (SC) golimumab (Simponi) for the treatment of psoriatic arthritis (PsA) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; and
- Patient has active psoriatic arthritis (PsA); and
- Subcutaneous (SC) golimumab (Simponi) is used alone or in combination with methotrexate (MTX); and
- Patient has failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDs); and
  (Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)
- Patient has failed treatment with adalimumab (Humira) AND etanercept (Enbrel) after at least two months of therapy with each product (unless there is clinical evidence or patient history that suggests that the these products will be ineffective or cause an adverse reaction to the patient); and
  (Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)
- Patient has a negative purified protein derivative (PPD) test prior to treatment.

Ankylosing Spondylitis
Based on review of available data, the Company may consider the use of subcutaneous (SC) golimumab (Simponi) for the treatment of ankylosing spondylitis (AS) to be eligible for coverage.

Patient Selection Criteria
Coverage eligibility for the use of subcutaneous (SC) golimumab (Simponi) for the treatment of active ankylosing spondylitis (AS) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; and
- Patient has active ankylosing spondylitis (AS); and
- Patient has failed treatment with non steroidal anti-inflammatory drugs (NSAIDs) or has documented contraindications to non steroidal anti-inflammatory drug (NSAID) usage; and
  (Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)
- Patient has failed treatment with adalimumab (Humira) AND etanercept (Enbrel) after at least two months of therapy with each product (unless there is clinical evidence or patient history that suggests that the these products will be ineffective or cause an adverse reaction to the patient); and
  (Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)
- Patient has a negative purified protein derivative (PPD) test prior to treatment.

Ulcerative Colitis
Based on review of available data, the Company may consider the use of subcutaneous (SC) golimumab (Simponi) for the treatment of ulcerative colitis (UC) to be eligible for coverage.
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**Patient Selection Criteria**

Coverage eligibility for the use of subcutaneous (SC) golimumab (Simponi) for the treatment of ulcerative colitis (UC) will be considered when all of the following criteria are met:

- Patient is 18 years of age or older; and
- Patient has moderately to severely active ulcerative colitis (UC); and
- Patient has demonstrated corticosteroid dependence OR has failed treatment with oral aminosalicylates, oral corticosteroids, azathioprine, or 6-mercaptopurine; and
- Patient has failed treatment with adalimumab (Humira) after at least two months of therapy (unless there is clinical evidence or patient history that suggests that the this product will be ineffective or cause an adverse reaction to the patient); and
  (Note: This specific patient criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)
- Patient has a negative purified protein derivative (PPD) test prior to treatment.

**Note:** The FDA approved prescribing information recommends:

- Simponi should not be prescribed with other biologic products approved to treat rheumatoid (RA) arthritis, psoriatic arthritis (PsA), ankylosing spondylitis (AS), or ulcerative colitis (UC) (including, but not limited to tumor necrosis factor (TNF) blockers, anakinra, and abatacept).

**When Services Are Considered Investigational**

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of subcutaneous (SC) golimumab (Simponi) when patient selection criteria are not met to be investigational* (with the exception of those denoted above as not medically necessary**).

Based on review of available data, the Company considers the use of subcutaneous (SC) golimumab (Simponi) for indications other than those listed above to be investigational.*

**When Services Are Considered Not Medically Necessary**

Based on review of available data, the Company considers the use of subcutaneous (SC) golimumab (Simponi) when any of the following criteria for their respective disease listed below (and denoted in the patient selection criteria above) are not met to be not medically necessary**:  

- For rheumatoid arthritis (RA) and psoriatic arthritis (PsA):
  - Patient has failed treatment with one or more disease-modifying anti-rheumatic drugs (DMARDs)
  - Patient has failed treatment with adalimumab (Humira) AND etanercept (Enbrel) after at least two months of therapy with each product
- For ankylosing spondylitis (AS):
  - Patient has failed treatment with non steroidal anti-inflammatory drugs (NSAIDs) or has documented contraindications to non steroidal anti-inflammatory drug (NSAID) usage
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- Patient has failed treatment with adalimumab (Humira) AND etanercept (Enbrel) after at least two months of therapy with each product
- For ulcerative colitis (UC):
  - Patient has failed treatment with adalimumab (Humira) after at least two months of therapy

**Background/Overview**

Simponi is a TNF blocker approved for the treatment of RA, PsA, AS, and UC. A new IV formulation, with the name of Simponi Aria has been approved for use in patients with RA. Tumor necrosis factor is a naturally occurring cytokine that is involved with the inflammatory and immune responses. Excessive activation of immune effector cells and overproduction of TNF can cause severe inflammation and tissue damage. Inhibition of TNF activity in certain inflammatory diseases may alleviate symptoms and prevent disease progression.

Simponi is a human IgG1κ monoclonal antibody specific for human TNF-α that binds to both the soluble and transmembrane bioactive forms of human TNF-α. This interaction prevents the binding of TNF-α to its receptors, thereby inhibiting the biological activity of TNF-α (a cytokine protein). Elevated TNF-α levels in the blood, synovium and joints have been implicated in the pathophysiology of several chronic inflammatory diseases such as RA, PsA and AS. Tumor necrosis factor-α is an important mediator of the articular inflammation that is characteristic of these diseases.

Simponi is the first anti-TNF agent administered SC and dosed once a month for the treatment of RA, PsA and AS and has a loading period for UC followed by a monthly dose. The Simponi drug product is a sterile solution of the golimumab antibody supplied as either a single dose prefilled syringe (with a passive needle safety guard) or a single dose prefilled autoinjector. Simponi does not contain preservatives. The solution is clear to slightly opalescent, colorless to light yellow with a pH of approximately 5.5. Simponi is provided in one strength:

- 50mg of the golimumab antibody in 0.5mL of solution. Each 0.5mL of Simponi contains 50mg of the golimumab antibody, 0.44mg of L-histidine and L-histidine monohydrochloride monohydrate, 20.5mg of sorbitol, 0.08mg of polysorbate 80 and water for injection.

**Disease-Modifying Anti-Rheumatic Drugs**

Disease-modifying anti-rheumatic drugs are used as a second line defense for the treatment of RA, AS, PsA and lupus. These drugs slow the disease process by modifying the immune system:

- MTX
- Cyclosporine
- Sulfasalazine
- Mercaptopurine
- Gold Compounds

For patients with RA, Simponi should be given in combination with MTX and for patients with PsA or AS, Simponi may be given with or without MTX or other non-biologic DMARDs. For patients with RA, PsA, UC or AS, corticosteroids, non-biologic DMARDs, and/or NSAIDs may be continued during treatment with Simponi.
Rheumatoid Arthritis
Simponi and Simponi Aria, in combination with MTX, have been shown to improve RA signs and symptoms according to the American College of Rheumatology (ACR) responses, including tender and swollen joint count, pain, physician and patient global assessment scores, as well as disability index (HAQ-DI), and acute markers of inflammation, compared to MTX alone. Simponi + MTX efficacy in these parameters has been observed in MTX-naïve, MTX inadequate responders and patients previously treated with ≥ anti-TNF agent. Simponi dosing for RA is 50mg SC once per month. Simponi Aria dosing is 2mg/kg IV infusion at weeks 0 and 4, then every 8 weeks.

Psoriatic Arthritis
Available data from a Phase III clinical trial (GO-REVEAL) including patients with active PsA who had an inadequate response to NSAIDs or DMARDs suggests that Simponi provides dramatic improvement in both arthritis and psoriasis symptoms. Substantial efficacy of Simponi in patients with PsA has been observed using a dose of 50mg once monthly, with or without concomitant MTX, significantly reduced clinical signs and symptoms of PsA.

Ankylosing Spondylitis
Available data from a Phase III clinical trial (GO-RAISE) including adult patients with active AS despite current or previous NSAID or DMARD therapy suggests that Simponi provides dramatic improvement in spondylitis symptoms, including total back pain and morning stiffness as well as improvement in patient's global assessment of disease activity and physical function according to the Bath Ankylosing Spondylitis Functional Index (BASFI). Substantial efficacy of Simponi in patients with AS has been observed using a dose of 50mg once monthly. Results of this study indicate that Simponi significantly reduced clinical signs and symptoms of AS. Simponi dosing for AS is 50mg SC once per month.

Ulcerative Colitis
Available data from Phase III trials (UC-1 and UC-2) in adult patients with moderately to severely active UC show that a greater proportion of patients achieved clinical response, clinical remission and had improvement of endoscopic appearance of the mucosa. Simponi dosing for UC is 200mg SC at week 0, followed by 100mg at week 2, and then 100mg every 4 weeks.

FDA or Other Governmental Regulatory Approval
U.S. Food and Drug Administration (FDA)
Simponi is a TNF blocker indicated for the treatment of adult patients with:
- Moderately to severely active RA, in combination with MTX. (Both Simponi Aria and Simponi)
- Active PsA, alone or in combination with MTX.
- Active AS.
- Moderately to severely active UC.

WARNING RISK OF SERIOUS INFECTIONS
Patients treated with Simponi are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as MTX or corticosteroids.
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Simponi should be discontinued if a patient develops a serious infection.

Reported infections include:
- Active tuberculosis, including reactivation of latent tuberculosis. Patients with tuberculosis have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent tuberculosis before Simponi use and during therapy. Treatment for latent infection should be initiated prior to Simponi use.
- Invasive fungal infections, including histoplasmosis, coccidioidomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Empiric antifungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.
- Bacterial, viral, and other infections due to opportunistic pathogens.

The risks and benefits of treatment with Simponi should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with Simponi, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

**Rationale/Source**
This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, Blue Cross and Blue Shield Association technology assessment program (TEC) and other non-affiliated technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Golimumab is a human anti-TNF monoclonal antibody that acts principally by targeting and neutralizing TNF to prevent inflammation and destruction of cartilage and bone. Large, randomized, double-blind trials in patients with RA who were MTX-naïve (GO-BEFORE) or -experienced (GO-FORWARD) have shown that golimumab 50 or 100mg every 4 weeks, in combination with MTX, was more effective than MTX alone for improving signs and symptoms of arthritis at weeks 14 and/or 24, according to ACR criteria. In patients with active RA despite previous treatment with anti-TNF agents (GO-AFTER), golimumab 50 or 100mg every 4 weeks was more effective than placebo for improving ACR responses at weeks 14 and 24; most patients in the study received concomitant MTX. In patients with PsA in the GO-REVEAL study, significantly more golimumab than placebo recipients achieved a > or = 20% improvement in ACR criteria at week 14. Golimumab was also superior to placebo for improving the signs and symptoms of AS in the GO-RAISE study; significantly more golimumab than placebo recipients achieved a > or = 20% improvement in the Assessment in Ankylosing Spondylitis (ASAS) criteria at week 14. In the 5 phase III trials in patients with RA, PsA or AS, there was no clear evidence of improved ACR or ASAS responses with the 100mg dosage compared with the 50mg dosage of golimumab. The tolerability profile of golimumab was generally consistent with that of other anti-TNF agents. Ulcerative colitis was studied in two trials, the UC-1 and UC-2
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trials. In the UC-1 trial, a greater proportion of patients achieved clinical response, clinical remission and had improvement of endoscopic appearance of the mucosa. In UC-2, a greater proportion of patients maintained clinical response through week 54.

References
2. FDA Simponi Formulary Dossier

Policy History
Original Effective Date:  07/22/2009
Current Effective Date:  10/19/2016
07/02/2009 Medical Director review
07/22/2009 Medical Policy Committee approval. New policy.
07/01/2010 Medical Director approval
07/21/2010 Medical Policy Implementation Committee approval. Changed the recommendation in the coverage section to read, “prior to receiving treatment with golimumab, all patients have a negative cancer history” instead of a “negative cancer screening”.
07/07/2011 Medical Policy Committee review
11/03/2011 Medical Policy Committee review
11/16/2011 Medical Policy Implementation Committee approval. Added criteria for rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis stating that patients must have failed treatment with adalimumab (Humira) or etanercept (Enbrel) before using golimumab (Simponi) after two months of use. Noted that the reason for denial will be not medically necessary if this criterion is not met. The not medically necessary denial statement is also incorporated into the Investigational and Not Medically Necessary coverage sections.
02/07/2013 Medical Policy Committee review
02/20/2013 Medical Policy Implementation Committee approval. Cancer criteria removed from policy.
06/06/2013 Medical Policy Committee review
06/25/2013 Medical Policy Implementation Committee approval. Added a new indication for Ulcerative colitis with similar criteria as other similar drugs. Reworded the investigational and not medically necessary denial statement.
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necessary sections. Relocated PPD to each indication instead of a note. Updated some background info.

10/10/2013  Medical Policy Committee review
10/16/2013  Medical Policy Implementation Committee approval. Added “Simponi Aria” to the title. Modified the title since there is a new formulation of the drug that has been approved. Added new product: Simponi Aria and gave similar criteria as infused products with indication of Rheumatoid Arthritis. Changed the requirement for subcutaneous Simponi to trying both Humira AND Enbrel first for Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis. Modified the not medically necessary section to reflect changes

07/16/2014  Coding updates due to new code for 2014, J1602- Golimumab being added for review.
10/02/2014  Medical Policy Committee review
08/03/2015  Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
10/08/2015  Medical Policy Committee review
10/21/2015  Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/06/2016  Medical Policy Committee review
10/19/2016  Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017  Coding update: Removing ICD-9 Diagnosis Codes

Next Scheduled Review Date: 10/2017

Coding
The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®), copyright 2015 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

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| M05.89-M05.9 | M06.00-M06.079 | M06.08-M06.09 | M06.1 |
| M06.20-M06.279 | M06.28-M06.30 | M06.311-M06.379 | M06.38-M06.39 |
| M06.80-M06.879 | M06.88-M06.9 | M08.00-M08.079 | M08.08-M08.1 |
| M08.20-M08.279 | M08.28-M08.29 | M08.3 | M08.40-M08.479 |
| M08.48 | M08.80-M08.879 | M08.88-M08.89 | M08.90-M08.979 |
| M08.98-M08.99 | M45.0-M45.9 | M48.8X1-M48.8X9 |

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:
A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
   1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
   2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
   3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:
A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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