

**Regence BlueCross BlueShield of Oregon • Regence BlueShield
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Medication Policy Manual

Policy No: dru183

Topic: Simponi[®], golimumab

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Next Review Date: July 2010

IMPORTANT REMINDER

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Golimumab (Simponi[®]) binds to and inhibits the activity of tumor necrosis factor (TNF), a chemical in the body that causes inflammation. It is used to treat diseases that may be caused or worsened by an overactive immune system, such as rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis.

Policy/Criteria

- I. Most contracts require prior authorization approval of golimumab prior to coverage. Golimumab may be considered medically necessary in patients when criteria A, B, or C, below are met.

A. Psoriatic arthritis when:

1. There is a diagnosis that has been established by a rheumatologist or a dermatologist.

AND

2. Etanercept (Enbrel[®]) and adalimumab (Humira[®]) are not effective after at least a 12-week treatment course of each except if not tolerated due to documented clinical side effects.

OR

B. Ankylosing spondylitis when:

1. There is a diagnosis that has been established by a rheumatologist.

AND

2. Etanercept (Enbrel[®]) and adalimumab (Humira[®]) are not effective after at least a 12-week treatment course of each except if not tolerated due to documented clinical side effects.

OR

C. Rheumatoid arthritis (RA) when:

1. There is a diagnosis that has been established by a rheumatologist (or by the criteria in Appendix 1).

AND

2. Methotrexate is ineffective alone after at least a 6 to 12 week treatment course based on documentation which includes one or more of the assessment components listed in Appendix 2 except if methotrexate is contraindicated or not tolerated based on clinical documentation.

AND

3. Etanercept (Enbrel[®]) and adalimumab (Humira[®]) are not effective after at least a 12-week treatment course of each except if not tolerated due to documented clinical side effects.

AND

4. Golimumab is administered with an oral DMARD (such as methotrexate).

Note: Golimumab may be covered when administered without a concomitant oral DMARD when etanercept, adalimumab, and abatacept each have been ineffective, contraindicated, or not tolerated, as these medications have been proven to be effective when given without the concomitant administration of an oral DMARD.

II. Administration, Quantity Limitations, and Authorization Period

- A. Regence considers golimumab to be a self-administered medication.
- B. When prior authorization is approved, golimumab may be authorized in quantities of 50 mg per month.
- C. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

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

- A. Crohn's disease
- B. Ulcerative Colitis
- C. Uveitis

Position Summary

Treatment of rheumatic disorders (rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, ankylosing spondylitis) ^[1-18]

- There are many treatments for rheumatic disorders that are effective, have known long-term safety profiles, and are recommended by national treatment guidelines.
- Nonmedical therapies, such as prescribed exercise therapy, physical therapy and weight loss, are important components in any treatment plan for patients suffering from a rheumatic disorder.
- When a systemic medication therapy is needed to manage one of the rheumatic disorders, oral therapies are usually the best value.
 - * Medications to control inflammation, such as nonsteroidal antiinflammatory medications (e.g., ibuprofen, indomethacin, and naproxen) and glucocorticoids (oral and injected into the joint) are effective for the management of symptoms, particularly during the early stages of disease.
 - * Orally administered disease-modifying antirheumatic drugs (DMARDs), including methotrexate (MTX), hydroxychloroquine, leflunomide, and sulfasalazine, are effective for decreasing symptoms and slowing disease progression, have a proven track record, and have been the standard of care for many years.
 - * Oral therapies have known potential risks. The management of these risks is well established.
- Methotrexate is considered effective in the treatment of RA and the standard reference DMARD to which newer DMARDs (etanercept, anakinra, adalimumab, and leflunomide) are compared for efficacy.
- When non-medical therapies and oral medications are inadequate, the biologic medications (e.g., adalimumab, etanercept, infliximab, or abatacept) may be appropriate. Certolizumab and rituximab have been studied in rheumatoid arthritis, but their role in therapy remains uncertain at this time.
- No studies have shown that any of biologic medications is more effective than another in the treatment of rheumatic disorders, with the exception of indirect evidence that anakinra may be less effective than other alternatives.

- * The biologic agents can decrease symptoms, help preserve joint functioning, and slow the progression of rheumatic disease.
- * There have been no reliable, direct-comparative trials that have demonstrated a difference in clinical effect or safety of one agent over another.
- * Individual responses and tolerability are unpredictable and may vary between patients.
- * Because responses vary, if one of the biologic agents provides an inadequate response, another biologic medication may yet be effective.
- * In RA, the best response is seen when methotrexate is used concomitantly with any of the biologics. Infliximab has been shown to be effective only when used with methotrexate. Treatment options other than infliximab should be considered for patients who cannot take methotrexate.

Efficacy of biologic agents in rheumatic conditions ^[1-18]

The benefit of medications can be indirectly compared by calculating their number needed to treat (NNT). The number needed to treat is a measure of the chances of a patient achieving a benefit (how many patients need to be treated before a benefit is achieved over a certain period of time). The lower the number needed to treat, the more likely the medication will have benefit.

Table 1 summarizes the chances that certain biologic rheumatologic medications will improve joint pain and stiffness in rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis:

Table 1: Chances of improving joint pain and stiffness by at least 20% after three to six months of treatment with biologic medications (compared to no treatment).

| Biologic Medications (when used with methotrexate) | Rheumatoid Arthritis | Psoriatic Arthritis | Ankylosing Spondylitis |
|--|--|---|---|
| adalimumab (Humira) etanercept (Enbrel) infliximab (Remicade) certolizumab (Cimzia) | About 1 in 3 likely to benefit ^a NNT = 3 (Range 2-4) | About 1 in 3 likely to benefit ^a NNT = 3 N/A | About 1 in 4 likely to benefit ^a NNT = 4 (Range 3-4) N/A |
| golimumab (Simponi) | About 1 in 5 likely to benefit NNT = 5 | About 1 in 3 likely to benefit NNT = 3 | About 1 in 3 likely to benefit NNT = 3 |
| abatacept (Orencia) | About 1 in 4 likely to benefit ^a NNT = 4 (Range 3-4) | N/A | N/A |
| anakinra (Kineret) | About 1 in 7 likely to benefit ^a NNT = 7 | N/A | N/A |
| rituximab (Rituxan) | Uncertain ^b | N/A | N/A |

^a Benefit = at least 20% improvement in joint pain and stiffness after six months of treatment.

^b The trials for these medications had flaws that make estimating their efficacy uncertain. These flaws included large numbers of patients not completing the clinical trials, not all patients counted in the final results, and uncertainty about whether patients and caregivers were truly unaware of the assigned treatments.

- There is reliable evidence that etanercept, adalimumab, and abatacept (when given with methotrexate) are effective in the management of patients with polyarticular juvenile idiopathic arthritis (JIA). The design of the clinical studies prevents calculation of “number-needed-to-treat” (NNT) for this use. ^[1-18]

Clinical Efficacy of golimumab in rheumatic diseases

- There is one published and two unpublished randomized, placebo-controlled trials that evaluate the effectiveness of golimumab in patients with rheumatoid arthritis.
 - * There is insufficient information available to evaluate the validity of the two unpublished trials. ^[3,4]
 - * In the one published trial, 444 patients were randomized to receive golimumab 50 mg or 100 mg subcutaneously given every 4 weeks along with weekly methotrexate, golimumab 100 mg given 4 weeks alone, or placebo given every 4 weeks with methotrexate. ^[2]
 - + At the end of 24 weeks (6 months), 55% and 56 % of patients receiving golimumab 50 mg or 100 mg (respectively) plus methotrexate experienced a 20% improvement in symptoms compared with 33% of patients receiving placebo plus methotrexate.
 - + Patients receiving golimumab 100 mg alone did not differ significantly from patients receiving methotrexate alone.
 - * Golimumab has been shown to have the best efficacy when administered with methotrexate for the treatment of moderate to severe rheumatoid arthritis.
- There is reliable evidence that golimumab improves symptoms in patients with psoriatic arthritis. ^[5]
 - * In a trial of 405 patients, 45% to 51% of patients taking golimumab (with or without methotrexate) achieved a 20% reduction in the symptoms of arthritis compared to only 9% of patients taking a placebo.

- * 40% to 58% of patients taking golimumab experienced a 75% improvement in symptoms of psoriasis compared with only 2.5% of patients taking placebo.

- There is reliable evidence that golimumab improves symptoms in patients with ankylosing spondylitis. ^[6]
 - * In a trial of 356 patients, about 60% of patients taking golimumab achieved a 20% reduction in the symptoms of ankylosing spondylitis compared to only 22% of patients taking a placebo.

Safety

- Commonly seen side effects of golimumab include upper respiratory tract infections and nasopharyngitis. ^[1]

- Rare, but serious side effects include serious infections (fungal infections, tuberculosis), reactivation of hepatitis B, some forms of cancer (such as lymphoma), heart failure, and disorders of the brain and central nervous system. ^[1]

Dosing

- The FDA approved dosing for golimumab for all indications is 50 mg administered by subcutaneous injection once a month. ^[1]

- Higher doses do not appear to result in improved efficacy. ^[1-6]

Appendix 1: American College of Rheumatology (ACR) Classification Criteria for Establishing the Diagnosis of Rheumatoid Arthritis (RA) ^[18]

Diagnosis of RA requires the presence of at least 4 of 7 criteria below:

| | |
|----|--|
| 1. | Morning stiffness in and around joints lasting more than 1 hour. |
| 2. | Arthritis in at least 1 area in a wrist or proximal interphalangeal (PIP) joint (hands or fingers) for > 6 weeks. |
| 3. | Simultaneous swelling or fluid accumulation in 3 or more joints for > 6 weeks. |
| 4. | Symmetric (bilateral joint) involvement for > 6 weeks. |
| 5. | Presence of rheumatoid nodules. |
| 6. | Positive serum rheumatoid factor. |
| 7. | Radiographic changes typical of RA (erosion or unequivocal bony decalcification in or adjacent to the involved joint) on hand and wrist present. |

Appendix 2: American College of Rheumatology (ACR) Assessment Components for Improvement in Rheumatoid Arthritis (RA) ^[19]

| | |
|---|--|
| - | Tender joint count. |
| - | Swollen joint count. |
| - | Patient's assessment of pain. |
| - | Patient's global assessment of disease activity. |
| - | Physician's global assessment of disease activity. |
| - | Patient's assessment of physical function. |
| - | Acute phase-reactant measures (erythrocyte sedimentation rate or C-reactive protein levels). |

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| Cross References |
|---|
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| Humira [®] , adalimumab dru081 |
| Remicade [®] , infliximab dru036 |
| Kineret [®] , anakinra dru049 |
| Tysabri [®] , natalizumab dru111 |
| Orencia [®] , abatacept dru129 |
| Cimiza [®] , certolizumab pegol dru160 |

| Codes | Number | Description |
|--------------|---------------|------------------------|
| HCPCS | J3590 | Unclassified biologics |