BlueCross BlueShield Federal Employee Program

ACTEMRA (tocilizumab)
TOFIDENCE* (tocilizumab-bavi)
TYENNE (tocilizumab-aazg)

*These medications are currently pending tier determination and may not be available at this time

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Actemra and its biosimilars are agents in the class of drugs known as biologic disease modifiers. Biologic disease modifiers are genetically engineered drugs that are used to modify imbalances of the immune system in autoimmune disease. Some of these agents block, or modify, the activity of selected cells in the immune system, while others (including Actemra and its biosimilars) work by blocking certain messenger proteins, known as cytokines, that send signals between those cells. Tocilizumab works by blocking a cytokine known as interleukin 6, or IL-6, which is believed to be an inflammation mediator in certain inflammatory diseases such as rheumatoid arthritis (RA). Inhibition of IL-6 receptors by tocilizumab leads to a reduction in cytokine and acute phase reactant production (1).

The use of Actemra or its biosimilars for the treatment of COVID-19 should be billed under the medical benefit.

Regulatory Status

FDA-approved indications: Actemra and its biosimilars are interleukin-6 (IL-6) receptor antagonists indicated for treatment of: (2-4)

1. Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs).
2. Adult patients with giant cell arteritis
3. Slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD)
4. Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis.
5. Patients 2 years of age and older with active systemic juvenile idiopathic arthritis.
6. Adults and pediatric patients 2 years of age and older with chimeric antigen receptor (CAR) T cell-induced severe or life-threatening cytokine release syndrome.

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7. Hospitalized adult patients with coronavirus disease 2019 (COVID-19) who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).

Off-Label Uses: (5-7)
Per the NCCN compendium, Actemra and its biosimilars have been found to be effective in the following disease states:

1. Unicentric Castleman's Disease: Second-line therapy as a single agent for relapsed or refractory unicentric CD for patients who are human immunodeficiency virus-negative and human herpesvirus-8-negative at a dose of 8mg/kg every 2 weeks
2. Multicentric Castleman's Disease: Subsequent therapy as a single agent for multicentric CD that has progressed following treatment of relapsed/refractory or progressive disease at a dose of 8mg/kg every 2 weeks

Actemra and its biosimilars should not be administered in patients with an active infection, including localized infections. Serious infections leading to hospitalization or death including tuberculosis (TB), bacterial, invasive fungal, viral, and other opportunistic infections have occurred in patients receiving Actemra and its biosimilars. If a serious infection develops, interrupt Actemra and its biosimilars until the infection is controlled. Patients have presented with disseminated rather than localized disease and were often taking concomitant immunosuppressants such as methotrexate or corticosteroids which in addition to rheumatoid arthritis may predispose them to infections (2-4).

Patients should be tested for latent TB infection prior to initiating Actemra and its biosimilars. Anti-tuberculosis therapy should also be considered prior to initiation of Actemra and its biosimilars in patients with a past history of latent or active tuberculosis in whom an adequate course of treatment cannot be confirmed, and for patients with a negative test for latent tuberculosis but having risk factors for tuberculosis infection. Patients should be closely monitored for the development of signs and symptoms of tuberculosis including patients who tested negative for latent tuberculosis infection prior to initiating therapy (2-4).

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Gastrointestinal (GI) perforation may occur, primarily as complications of diverticulitis in RA patients. Actemra and its biosimilars should be used with caution in patients who may be at increased risk for gastrointestinal perforation (2-4).

Laboratory monitoring is recommended prior to and monitored every 4 to 8 weeks due to potential consequences of treatment-related changes in neutrophils, platelets, lipids, and liver function tests (2-4).

Treatment with Actemra and its biosimilars was associated with a higher incidence of neutropenia. Initiation of Actemra and its biosimilars is not recommended in patients with an absolute neutrophil count (ANC) below 2000 per mm3. Treatment must be withheld if the ANC is 500-1000 cells per mm^3 and resumed at a decreased dose when the ANC is >1000 mm^3. Treatment must be discontinued if the ANC is less than 500 cells per mm^3 (2-4).

Treatment with Actemra and its biosimilars was associated with a reduction in platelet counts. Treatment is not recommended in patients with a platelet count below 100,000 per mm^3 (2-4).

Treatment with Actemra and its biosimilars was associated with a higher incidence of transaminase elevations. Increased frequency and magnitude of these elevations was observed when potentially hepatotoxic drugs (e.g., methotrexate) were used in combination with Actemra or its biosimilars (2-4).

Treatment with Actemra and its biosimilars was associated with increases in lipid parameters such as total cholesterol, triglycerides, LDL cholesterol, and/or HDL cholesterol. Patients should be managed according to clinical guidelines [e.g., National Cholesterol Educational Program (NCEP)] for the management of hyperlipidemia (2-4).

Actemra and its biosimilars have not been studied and its use should be avoided in combination with biological DMARDs such as TNF antagonists, IL-1R antagonists, anti-CD20 monoclonal

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antibodies and selective co-stimulation modulators because of the possibility of increased immunosuppression and increased risk of infection. Actemra and its biosimilars may be used as monotherapy or concomitantly with methotrexate or other non-biological DMARDs such as hydroxychloroquine, leflunomide, azathioprine, and cyclosporine (2-4).

Treatment with Actemra and its biosimilars is not recommended in patients with active hepatic disease or hepatic impairment, including patients with positive hepatitis B virus (HBV) and hepatitis C virus (HCV) (2-4).

Safety and effectiveness of Actemra and its biosimilars in pediatric patients with conditions other than PJIA, SJIA, or cytokine release syndrome have not been established. Children under the age of two have not been studied (2-4).

Doses exceeding 800 mg per infusion of Actemra or its biosimilars are not recommended in RA or CRS patients (2-4).

Summary Actemra (tocilizumab) and its biosimlars are interleukin-6 (IL-6) receptor antagonists indicated for the treatment of adult onset rheumatoid (RA) arthritis, polyarticular juvenile idiopathic arthritis (PJIA), systemic juvenile idiopathic arthritis (SJIA), giant cell arteritis, cytokine release syndrome (CRS), and systemic sclerosis-associated interstitial lung disease (SSc-ILD). Additionally, Actemra and its biosimilars have shown efficacy in the off-label treatment of unicentric and multicentric castleman's disease. Laboratory monitoring is recommended prior to and monitored every 4 to 8 weeks due to potential consequences of treatment-related changes in neutrophils, platelets, lipids, and liver function tests. Actemra and its biosimilars should not be administered in patients with an active infection, including localized infections. Treatment with Actemra and its biosimilars is not recommended in patients with active hepatic disease or hepatic impairment. Actemra and its biosimilars may be used as monotherapy or concomitantly with methotrexate or other non-biological DMARDs. Actemra and its biosimilars have not been studied in combination with biological DMARs and their use should be avoided in combination with biological DMARDs. Safety and effectiveness of Actemra and its biosimilars in pediatric patients

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with conditions other than PJIA, SJIA, or cytokine release syndrome have not been established. Patients under the age of 2 have not been studied (1-4).

The use of Actemra or its biosimilars for the treatment of COVID-19 should be billed under the medical benefit.

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Actemra and its biosimilars while maintaining optimal therapeutic outcomes.

References

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