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SPECIALTY GUIDELINE MANAGEMENT

ACTEMRA (tocilizumab) TOFIDENCE (tocilizumab-bavi)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications

1. Adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs).
2. Patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis.
3. Patients 2 years of age and older with active systemic juvenile idiopathic arthritis (SJIA).
4. Adult patients with giant cell arteritis (GCA).
5. Adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) for slowing the rate of decline in pulmonary function.
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 (CRS).
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).

B. Compendial Uses

1. Unicentric Castleman disease
2. Multicentric Castleman disease
3. Oligoarticular juvenile idiopathic arthritis
4. Immune checkpoint inhibitor-related toxicities - inflammatory arthritis
5. Acute graft versus host disease
6. Cytokine release syndrome (other than severe or life-threatening CAR T cell-induced CRS)

Note: The criteria outlined in this policy is only applicable to coverage in the outpatient setting. Hospitalized members receiving treatment for COVID-19 will be managed according to the member's inpatient benefit.

All other indications are considered experimental/investigational and not medically necessary.

II. DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:

A. Rheumatoid arthritis (RA)

1. Initial requests:
 - i. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

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- ii. Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).
 - 2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.
- B. Articular juvenile idiopathic arthritis
 - 1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy.
 - 2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.
- C. Systemic juvenile idiopathic arthritis (sJIA)
 - 1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy.
 - 2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.
- D. Cytokine release syndrome, immune checkpoint inhibitor-related toxicity, and acute graft versus host disease: For initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
- E. Giant cell arteritis (GCA): For continuation requests: Chart notes or medical record documentation supporting positive clinical response.
- F. Systemic sclerosis-associated interstitial lung disease (SSc-ILD): For initial requests: Result of a chest high-resolution computed tomography (HRCT) study.

III. PRESCRIBER SPECIALTIES

This medication must be prescribed by or in consultation with one of the following:

- A. Rheumatoid arthritis, articular juvenile idiopathic arthritis, systemic juvenile idiopathic arthritis, and giant cell arteritis: rheumatologist
- B. Systemic sclerosis-associated interstitial lung disease: rheumatologist or pulmonologist
- C. Immune checkpoint inhibitor-related toxicity: oncologist, hematologist, or rheumatologist
- D. Cytokine release syndrome, unicentric Castleman disease, multicentric Castleman disease, and acute graft versus host disease: oncologist or hematologist

IV. CRITERIA FOR INITIAL APPROVAL

A. Rheumatoid arthritis (RA)

- 1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.
- 2. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active RA when both of the following criteria are met:
 - i. Member meets either of the following criteria:
 - a. Member has been tested for either of the following biomarkers and the test was positive:

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1. Rheumatoid factor (RF)
2. Anti-cyclic citrullinated peptide (anti-CCP)
- b. Member has been tested for ALL of the following biomarkers:
 1. RF
 2. Anti-CCP
 3. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)
- ii. Member meets either of the following criteria:
 - a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week).
 - b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Articular juvenile idiopathic arthritis

1. Authorization of 12 months may be granted for members 2 years of age or older who have previously received a biologic or targeted synthetic drug (e.g., Xeljanz) indicated for active articular juvenile idiopathic arthritis.
2. Authorization of 12 months may be granted for members 2 years of age or older for treatment of active articular juvenile idiopathic arthritis when any of the following criteria is met:
 - i. Member has had an inadequate response to methotrexate or another conventional synthetic drug (e.g., leflunomide, sulfasalazine, hydroxychloroquine) administered at an adequate dose and duration.
 - ii. Member has had an inadequate response to a trial of scheduled non-steroidal anti-inflammatory drugs (NSAIDs) and/or intra-articular glucocorticoids (e.g., triamcinolone hexacetonide) and one of the following risk factors for poor outcome:
 - a. Involvement of ankle, wrist, hip, sacroiliac joint, and/or temporomandibular joint (TMJ)
 - b. Presence of erosive disease or enthesitis
 - c. Delay in diagnosis
 - d. Elevated levels of inflammation markers
 - e. Symmetric disease
 - iii. Member has risk factors for disease severity and potentially a more refractory disease course (see Appendix B) and the member also meets one of the following:
 - a. High-risk joints are involved (e.g., cervical spine, wrist, or hip).
 - b. High disease activity.
 - c. Is judged to be at high risk for disabling joint disease.

C. Systemic juvenile idiopathic arthritis (sJIA)

1. Authorization of 12 months may be granted for members 2 years of age or older who have previously received a biologic indicated for active sJIA.
2. Authorization of 12 months may be granted for members 2 years of age or older for treatment of active sJIA when both of the following criteria are met:
 - i. Member has active systemic features (e.g., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, serositis).
 - ii. Member has had an inadequate response to non-steroidal anti-inflammatory drugs (NSAIDs) or systemic glucocorticoids.

D. Giant cell arteritis (GCA)

Authorization of 12 months may be granted for adult members for treatment of giant cell arteritis when the member's diagnosis was confirmed by the following:

1. Temporal artery biopsy or cross-sectional imaging; or
2. Acute-phase reactant elevation (i.e., high erythrocyte sedimentation rate [ESR] and/or high serum C-reactive protein [CRP]).

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E. Systemic sclerosis-associated interstitial lung disease (SSc-ILD)

Authorization of 12 months may be granted for adult members for treatment of sclerosis-associated interstitial lung disease when the diagnosis was confirmed by a high-resolution computed tomography (HRCT) study of the chest.

F. Cytokine release syndrome

1. Authorization of 1 month may be granted for members 2 years of age or older for treatment of chimeric antigen receptor (CAR) T cell-induced cytokine release syndrome (CRS).
2. Authorization of 1 month may be granted for treatment of cytokine release syndrome in members with refractory CRS related to blinatumomab therapy.

G. Unicentric Castleman disease

Authorization of 12 months may be granted for treatment of unicentric Castleman disease when all of the following are met:

1. The member is HIV-negative.
2. The member is human herpesvirus-8-negative.
3. The requested medication will be used as a single agent.
4. The disease has progressed following treatment of relapsed/refractory disease.

H. Multicentric Castleman disease

Authorization of 12 months may be granted for treatment of multicentric Castleman disease when both of the following are met:

1. The requested medication will be used as a single agent.
2. The disease has progressed following treatment of relapsed/refractory or progressive disease.

I. Immune checkpoint inhibitor-related toxicity

Authorization of 12 months may be granted for treatment of immune checkpoint inhibitor-related toxicity when then member has severe immunotherapy-related inflammatory arthritis and meets either of the following:

1. Member has had an inadequate response to corticosteroids or a conventional synthetic drug (e.g., methotrexate, sulfasalazine, leflunomide, hydroxychloroquine).
2. Member has an intolerance or contraindication to corticosteroids and a conventional synthetic drug.

J. Acute graft versus host disease

Authorization of 12 months may be granted for treatment of acute graft versus host disease when either of the following criteria is met:

1. Member has experienced an inadequate response to systemic corticosteroids.
2. Member has an intolerance or contraindication to corticosteroids.

V. CONTINUATION OF THERAPY

A. Rheumatoid arthritis (RA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active RA and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B. Articular juvenile idiopathic arthritis

Authorization of 12 months may be granted for all members 2 years of age or older (including new members) who are using the requested medication for active articular juvenile idiopathic arthritis and who

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achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
2. Number of joints with limitation of movement
3. Functional ability

C. Systemic juvenile idiopathic arthritis (sJIA)

Authorization of 12 months may be granted for all members 2 years of age or older (including new members) who are using the requested medication for sJIA and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
2. Number of joints with limitation of movement
3. Functional ability
4. Systemic features (e.g., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, serositis)

D. Giant cell arteritis (GCA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for GCA and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Headaches
2. Scalp tenderness
3. Tenderness and/or thickening of superficial temporal arteries
4. Constitutional symptoms (e.g., weight loss, fever, fatigue, night sweats)
5. Jaw and/or tongue claudication
6. Acute visual symptoms (e.g., amaurosis fugax, acute visual loss, diplopia)
7. Symptoms of polymyalgia rheumatica (e.g., shoulder and/or hip girdle pain)
8. Limb claudication

E. Systemic sclerosis-associated interstitial lung disease (SSc-ILD)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for SSc-ILD when the member is currently receiving treatment with Actemra.

F. Immune checkpoint inhibitor-related toxicity

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for immunotherapy-related inflammatory arthritis and who achieve or maintain a positive clinical response with the requested medication as evidenced by low disease activity or improvement in signs and symptoms of the condition.

G. Cytokine release syndrome and acute graft versus host disease

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

H. All other diagnoses

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section IV when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

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For all indications: Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

*If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug for the same indication.

VII. DOSAGE AND ADMINISTRATION

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

VIII. APPENDICES

Appendix A: Examples of clinical reasons to avoid pharmacologic treatment with methotrexate¹⁹

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease, or other chronic liver disease
2. Drug interaction
3. Risk of treatment-related toxicity
4. Pregnancy or currently planning pregnancy
5. Breastfeeding
6. Significant comorbidity prohibits use of systemic agents (e.g., liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
7. Hypersensitivity
8. History of intolerance or adverse event

Appendix B: Risk factors for articular juvenile idiopathic arthritis¹⁸

1. Positive rheumatoid factor
2. Positive anti-cyclic citrullinated peptide antibodies
3. Pre-existing joint damage

IX. REFERENCES

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