Tocilizumab (ACTEMRA) in Systemic Sclerosis Interstitial Lung Disease

Criteria for Use

August 2025

VA Pharmacy Benefits Management Services and National Formulary Committee

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. THE CLINICIAN SHOULD USE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.

The Product Information should be consulted for detailed prescribing information.

Exclusion Criteria

If ANY of the following are selected, the patient will NOT meet criteria for tocilizumab.

- ☐ Uncontrolled active infection (however, tocilizumab may be started/restarted once treatment for the infection is initiated).
- ☐ Untreated latent or active tuberculosis infection.
- ☐ Hepatitis B surface antigen (HBsAg)-positive and not on antiviral prophylaxis.^1 Tocilizumab may be initiated after starting antiviral prophylaxis.
- ☐ Untreated HIV infection. Treated, well-controlled, asymptomatic HIV-positive patients can be treated with tocilizumab.
- ☐ Congenital or acquired immunodeficiency.
- ☐ Concomitant live or live-attenuated vaccines or administration of inactivated, live, or live-attenuated vaccines less than 2 weeks before initiation of tocilizumab.^2
- ☐ Concomitant immunosuppressive biologic, immunosuppressive targeted synthetic drug (e.g., tofacitinib or other JAK inhibitors), cyclophosphamide, or alkylating agents.^3
- ☐ Active hepatic disease or hepatic impairment
- ☐ Baseline absolute neutrophil count (ANC) < 2000/mm^3 unless associated with Duffy-null Associated Neutrophil Count
- ☐ Baseline platelet count <100,000/mm^3
- ☐ Baseline ALT and/or AST > 1.5x the upper limit of normal (ULN)

Inclusion Criteria

All the following criteria must be selected to meet criteria.

- ☐ Documented active^4 systemic sclerosis (SSc) with laboratory,^5 radiographic, histologic, or other clinical evidence of an inflammatory component.
- ☐ Diagnosis of SSc-interstitial lung disease (ILD), preferably confirmed by multidisciplinary discussion (e.g., rheumatologist, pulmonologist, radiologist, pathologist) and preferably without WHO functional class 2 to 4 pulmonary arterial hypertension.^5

- ☐ SSc duration of not more than 5 years from onset of the first non-Raynaud phenomenon manifestation. (Not SSc-ILD duration.)
- ☐ Prescribed and monitored by a VA/VA Community Care rheumatologist, pulmonologist, or locally designated expert.
- ☐ Offered all age-appropriate vaccinations prior to initiating therapy.
- ☐ Completed tuberculosis (TB) test using tuberculin skin test or interferon-gamma release assay [IGRA].
- ☐ Completed hepatitis B screening (HBsAg, total antibody to hepatitis B core antigen [anti-HBc], and antibody to hepatitis B surface antigen [anti-HBs]).
- ☐ Current or past completion of hepatitis C screening. Tocilizumab may be initiated while waiting for test results.

Additional Inclusion Criteria

ONE of the following must be met:

- ☐ Progression^6 of clinically evident SSc-ILD during **mycophenolate** therapy or mycophenolate is not tolerated or is medically inadvisable.
- ☐ Progression^6 of clinically evident SSc-ILD during **cyclophosphamide** therapy or cyclophosphamide is not tolerated or is medically inadvisable.
- ☐ Rapid clinical progression^6 of SSc-ILD even without any prior **mycophenolate** or **cyclophosphamide** therapy.
- ☐ Subclinical SSc-ILD. No prior mycophenolate or cyclophosphamide is required. The objective of early tocilizumab therapy is to slow or prevent progression of ILD.

Additional Inclusion Criteria

Select if applicable.

- ☐ If HBsAg-negative but anti-HBc-positive and patient's practitioner deems (e-)consult is indicated: A GI/liver or infectious diseases expert has been consulted for advice on whether to start antiviral prophylaxis or to preemptively monitor for HBV reactivation.
- ☐ For females who can become pregnant: Counseling provided on potential risks vs benefits of treatment and the use of effective contraception.
- ☐ For females who are breastfeeding/providing breastmilk to an infant: Counseling provided on potential risks vs benefits of treatment.

Footnotes

[1] Antiviral prophylaxis for HBV: Agents with high genetic barrier to resistance such as entecavir or tenofovir should be used.

[2] When possible, vaccinations should be updated before the patient initiates tocilizumab. Unless contraindicated, recombinant zoster (SHINGRIX) vaccine should be completed or at least initiated by the end of the first year of treatment with tocilizumab, preferably when dosage is low, disease is stable, or at other times when a robust immune response to vaccination can be expected.

[3] Tocilizumab may be used in combination with methotrexate, other nonbiologic disease-modifying antirheumatic drugs (DMARDs), mycophenolate, hydroxychloroquine, or glucocorticoids. In general, concomitant use of potent immunosuppressives with tocilizumab should be avoided.

[4] The criteria do not restrict use of tocilizumab by SSc subtype, consistent with the FDA-approved indication. Patients with either diffuse cutaneous or limited cutaneous SSc are eligible as long as the other criteria are met. These criteria attempt to identify a subset of patients with very early, active SSc with an inflammatory component and mild SSc-ILD, similar to the type of patients included in the phase 3 focuSSced trial. IL-6 may be a key cytokine mediator of inflammation in early stages of SSc. There is no evidence that tocilizumab is effective for later SSc/SSc-ILD, when IL-6 may be less important in pathogenesis of the disease. Active disease can be defined as at least one of the following: (1) disease duration 18 months or less; (2) worsening of the severity or extent of skin / body involvement; or (3) at least one tendon friction rub. Examples of laboratory evidence: one or more elevated acute phase reactants (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], or platelet count above upper limit of normal of local laboratory reference range).

[5] For patients with pulmonary arterial hypertension (PAH), World Health Organization (WHO) functional class 1 is preferred.
Class 1 = Without limitation of physical activity; no symptoms of PAH with exercise or at rest.
Class 2 = Slight limitation; ordinary activities cause some symptoms.
Class 3 = Marked limitation; less than ordinary activity causes symptoms.
Class 4 = Severe limitation; any activity causes symptoms; overt right heart failure.

[6] SSc-ILD progression is defined as either ≥10% absolute decrease from baseline in percent predicted forced vital capacity (FVC) OR ≥15% absolute decrease from baseline in percent predicted diffusing capacity of the lung for carbon monoxide (DLCO) OR progression on high-resolution computed tomography (HRCT). (This is not intended to encourage very frequent HRCT scanning.)

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