PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Tocilizumab Intravenous Products Prior Authorization Policy
- Actemra® (tocilizumab intravenous infusion – Genentech/Roche)
- Tofidence™ (tocilizumab-bavi intravenous infusion – Biogen)
- Tyenne® (tocilizumab-aazg intravenous infusion – Fresenius Kabi)

REVIEW DATE: 04/24/2024; selected revision 06/06/2024, 09/11/2024

OVERVIEW

Tocilizumab intravenous infusion, an interleukin-6 (IL-6) receptor inhibitor, is indicated for the following conditions:[1]

- **Coronavirus Disease 2019 (COVID-19)**, in hospitalized adults who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).
- **Cytokine release syndrome**, in patients ≥ 2 years of age with severe or life-threatening disease associated with chimeric antigen receptor (CAR) T-cell therapy.
- **Giant cell arteritis** in adults.
- **Polyarticular juvenile idiopathic arthritis**, for the treatment of active disease in patients ≥ 2 years of age.
- **Rheumatoid arthritis**, for treatment of adults with moderate to severe active disease who have had an inadequate response to one or more disease modifying antirheumatic drugs (DMARDs).
- **Systemic juvenile idiopathic arthritis**, for the treatment of active disease in patients ≥ 2 years of age.

Guidelines/Clinical Efficacy

IL-6 blockers are mentioned in multiple guidelines for treatment of inflammatory conditions. Clinical data also support use of tocilizumab in other conditions.

- **Cytokine Release Syndrome:** The National Comprehensive Cancer Network (NCCN) clinical practice guidelines for Management of Immunotherapy-Related Toxicities (version 1.2024 – December 7, 2023) give specific recommendations for use of tocilizumab in the management of inflammatory arthritis, cytokine release syndrome, and CAR T-cell-related toxicities.[6]
  - For cytokine release syndrome and CAR T-cell-related toxicities, tocilizumab is recommended for all grades of disease.
  - For immune checkpoint inhibitor-related inflammatory arthritis, infliximab and tocilizumab are among the alternatives that may be considered for severe arthritis not responding to steroids.
- **Giant Cell Arteritis and Polymyalgia Rheumatica:** Recommendations from the European League Against Rheumatism (EULAR) [2023] state the diagnosis of giant cell arteritis may be made without biopsy if there is a high suspicion of giant cell arteritis and a positive imaging test.[25] In the pivotal trial evaluating tocilizumab subcutaneous for giant cell arteritis (n = 251), patients were treated with corticosteroids in an open-label fashion (20 mg to 60 mg/day) during the screening period prior to treatment with tocilizumab subcutaneous.[31,32] Sustained remission at Week 52 was achieved in 56% of patients who received tocilizumab subcutaneous every week + 26-week prednisone taper and 53% of patients who received Actemra every other week + 26-week prednisone taper vs. in 14% of patients in the 26-week prednisone taper and 18% of patients in the 52-week prednisone taper.
- **Polyarticular Juvenile Idiopathic Arthritis:** Guidelines for the treatment of juvenile idiopathic arthritis from the American College of Rheumatology (ACR) [2021] address oligoarthritis and

temporomandibular joint (TMJ) arthritis.[31] For oligoarthritis, a biologic is recommended following a trial of a conventional synthetic DMARD. In patients with TMJ arthritis, scheduled nonsteroidal anti-inflammatory drugs (NSAIDs) and/or intra-articular glucocorticoids are recommended first-line. A biologic is a therapeutic option if there is an inadequate response or intolerance. Additionally, rapid escalation to a biologic ± conventional synthetic DMARD (methotrexate preferred) is often appropriate given the impact and destructive nature of TMJ arthritis. In these guidelines, there is not a preferred biologic that should be initiated for JIA. ACR/Arthritis Foundation has guidelines for the treatment of juvenile idiopathic arthritis (2019) specific to juvenile non-systemic polyarthritis, sacroiliitis, and enthesitis.[7] For patients without risk factors, initial therapy with a DMARD is conditionally recommended over a biologic (including tocilizumab). Biologics (e.g., Actemra) are conditionally recommended as initial treatment when combined with a DMARD over biologic monotherapy.

- **Rheumatoid Arthritis:** Guidelines from ACR (2021) recommend addition of a biologic or a targeted synthetic DMARD for a patient taking the maximum tolerated dose of methotrexate who is not at target.[9]
- **Systemic Juvenile Idiopathic Arthritis:** Guidelines for the treatment of JIA from the ACR (2021) address systemic juvenile idiopathic arthritis (SJIA).[8] A brief trial of NSAIDs and/or an interleukin (IL)-1 or IL-6 inhibitor are recommended as initial monotherapy for patients with SJIA without macrophage activation syndrome. In a patient who presents with macrophage activation syndrome, an IL-1 or IL-6 blocker and/or systemic glucocorticoids are recommended.
- **Castleman's Disease:** The NCCN clinical practice guidelines for Castleman Disease (version 1.2024 – January 18, 2024) mention tocilizumab as a second-line therapy for relapsed or refractory unicentric Castleman disease in patients who are negative for the human immunodeficiency virus and human herpesvirus-8.[10] For multicentric Castleman's disease, the guidelines list tocilizumab as a subsequent therapy for relapsed, refractory, or progressive disease.
- **COVID-19 (Coronavirus Disease 2019):** By inhibiting IL-6, tocilizumab is speculated to be associated with better clinical outcomes in COVID-19, such as decreased systemic inflammation, improved survival rate, better hemodynamics, and improvement of respiratory distress.[24]
- **Still's Disease:** Still's disease presents in adults with features similar to those of SJIA.[11] Tocilizumab IV has been effective in reducing fever, symptoms, and markers of inflammation in patients who were refractory to treatment with prednisone, methotrexate, Kineret, and/or a tumor necrosis factor inhibitor.[11-20]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of tocilizumab intravenous products. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of a patient treated with Actemra intravenous as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Actemra intravenous to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Tocilizumab intravenous products is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **COVID-19 (Coronavirus Disease 2019) – Hospitalized Patient.** For a patient who is hospitalized, forward all requests to the Medical Director. For a non-hospitalized patient, do not approve (refer to Conditions Not Recommended for Approval – COVID-19 – Non-Hospitalized Patient). Tocilizumab intravenous is indicated for COVID-19 only in hospitalized adults who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).[1] For COVID-19, the dose is 8 mg/kg (to a maximum of 800 mg) given as a single intravenous infusion. A second dose may be administered at least 8 hours after the initial infusion if clinical signs or symptoms worsen or do not improve after the first dose.
   Note: This includes requests for cytokine release syndrome in a patient hospitalized with COVID-19.

2. **Cytokine Release Syndrome Associated with Chimeric Antigen Receptor (CAR) T-Cell Therapy.** Approve for 1 week (which is adequate duration to receive four doses) if prescribed for a patient who has been or will be treated with a CAR T-cell therapy.
   Note: Examples of CAR T-cell therapy include Abecma (idecabtagene vicleucel intravenous infusion), Breyanzi (lisocabtagene maraleucel intravenous infusion), Kymriah (tisagenlecleucel intravenous infusion), Tecartus (brexucabtagene intravenous infusion), and Yescarta (axicabtagene ciloleucel intravenous infusion).

3. **Giant Cell Arteritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient has tried one systemic corticosteroid; AND
       Note: An example of a systemic corticosteroid is prednisone.
     - **iii.** The medication is prescribed by or in consultation with a rheumatologist.
   - **B)** Patient is Currently Receiving a Tocilizumab Subcutaneous or Intravenous Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):
     - **i.** Patient has been established on therapy for at least 6 months; AND
       Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).
     - **ii.** Patient meets at least ONE of the following (a or b):
       - **a)** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating a tocilizumab product); OR
         Note: Examples of objective measures are serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), resolution of fever, and/or reduced dosage of corticosteroids.
       - **b)** Compared with baseline (prior to initiating a tocilizumab product), patient experienced an improvement in at least one symptom, such as decreased headache, scalp, or jaw pain; decreased fatigue; and/or improved vision.

4. **Polyarticular Juvenile Idiopathic Arthritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and ii):
     - **i.** Patient is ≥ 2 years of age; AND

ii. Patient meets ONE of the following conditions (a, b, c, or d):
- **a)** Patient has tried one other systemic therapy for this condition; OR
  Note: Examples of other systemic therapies include methotrexate, sulfasalazine, leflunomide, or a nonsteroidal anti-inflammatory drug (NSAID). A biologic (refer to **Appendix** for examples of biologics used for polyarticular juvenile idiopathic arthritis) also counts as a trial of one systemic therapy.
- **b)** Patient will be starting on a tocilizumab intravenous product concurrently with methotrexate, sulfasalazine, or leflunomide; OR
- **c)** Patient has an absolute contraindication to methotrexate, sulfasalazine, or leflunomide; OR
  Note: Examples of absolute contraindication to methotrexate include pregnancy, breast feeding, alcoholic liver disease, immunodeficiency syndrome, and blood dyscrasias.
- **d)** Patient has aggressive disease, as determined by the prescriber; AND

iii. The medication is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving a Tocilizumab Intravenous or Subcutaneous Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least ONE of the following (a or b):
- **a)** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating a tocilizumab product); OR
  Note: Examples of objective measures include Physician Global Assessment (MD global), Parent/Patient Global Assessment of Overall Well-Being (PGA), Parent/Patient Global Assessment of Disease Activity (PDA), Juvenile Arthritis Disease Activity Score (JDAS), Clinical Juvenile Arthritis Disease Activity Score (cJDAS), Juvenile Spondyloarthritis Disease Activity Index (JSpADA), serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), and/or reduced dosage of corticosteroids.
- **b)** Compared with baseline (prior to initiating a tocilizumab product), patient experienced an improvement in at least one symptom, such as improvement in limitation of motion, less joint pain or tenderness, decreased duration of morning stiffness or fatigue, improved function or activities of daily living.

5. Rheumatoid Arthritis. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):

i. Patient is ≥ 18 years of age; AND

ii. Patient has tried ONE conventional synthetic disease-modifying antirheumatic drug (DMARD) for at least 3 months; AND
Note: Examples of one conventional DMARD tried include methotrexate (oral or injectable), leflunomide, hydroxychloroquine, and sulfasalazine. An exception to the requirement for a trial of one conventional synthetic DMARD can be made if the patient has already had a 3-month trial of at least one biologic (refer to **Appendix** for examples of biologics used for rheumatoid arthritis). A patient who has already tried a biologic for rheumatoid arthritis is not required to "step back" and try a conventional synthetic DMARD.

ii. The medication is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving a Tocilizumab Intravenous or Subcutaneous Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least ONE of the following (a or b):

a) Patient experienced a beneficial clinical response when assessed by at least one objective measure; OR
Note: Examples of standardized and validated measures of disease activity include Clinical Disease Activity Index (CDAI), Disease Activity Score (DAS) 28 using erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), Patient Activity Scale (PAS)-II, Rapid Assessment of Patient Index Data 3 (RAPID-3), and/or Simplified Disease Activity Index (SDAI).
b) Patient experienced an improvement in at least one symptom, such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths.

6. Systemic Juvenile Idiopathic Arthritis. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):
i. Patient is ≥ 2 years of age; AND
ii. The patient has tried one other systemic therapy for this condition; AND
Note: Examples of other systemic therapies include a corticosteroid (oral, intravenous), a conventional synthetic disease-modifying antirheumatic drug (DMARD) [e.g., methotrexate, leflunomide, sulfasalazine], a 1-month trial of a nonsteroidal anti-inflammatory drug (NSAID), Kineret (anakinra subcutaneous injection), or Ilaris (canakinumab subcutaneous injection). A biosimilar of Actemra does not count.
iii. The medication is prescribed by or in consultation with a rheumatologist.
B) Patient is Currently Receiving a Tocilizumab Intravenous or Subcutaneous Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):
i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).
ii. Patient meets at least ONE of the following (a or b):
a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of objective measures include resolution of fever, improvement in rash or skin manifestations, clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), and/or reduced dosage of corticosteroids.
b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as less joint pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

Other Uses with Supportive Evidence

7. Castleman Disease. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Approval. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
i. Patient is ≥ 18 years of age; AND
ii. Patient is negative for the human immunodeficiency virus (HIV) and human herpesvirus-8 (HHV-8); AND
iii. The medication is being used for relapsed or refractory disease; AND
iv. The medication is prescribed by or in consultation with an oncologist or hematologist.
B) Patient is Currently Receiving a Tocilizumab Intravenous or Subcutaneous Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):
i. Patient has been established on therapy for at least 6 months; AND

Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least ONE of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of objective measures include clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate, fibrinogen, albumin, and/or hemoglobin), increased body mass index, and/or reduction in lymphadenopathy.

b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as improvement or resolution of constitutional symptoms (e.g., fatigue, physical function).

8. Inflammatory Arthritis Associated with Checkpoint Inhibitor Therapy. Approve for the duration noted if the patient meets ONE of the following (A or B):
Note: Examples of checkpoint inhibitors are Keytruda (pembrolizumab intravenous infusion), Opdivo (nivolumab intravenous infusion), Yervoy (ipilimumab intravenous infusion), Tecentriq (atezolizumab intravenous infusion), Bavencio (avelumab intravenous infusion), Imfinzi (durvalumab intravenous infusion), and Libtayo (cemiplimab-rwlc intravenous infusion).

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):

i. Patient is ≥ 18 years of age; AND

ii. Patient is symptomatic despite a trial of at least ONE systemic corticosteroid; AND
Note: Examples of a corticosteroid include methylprednisolone and prednisone.

iii. Patient has tried at least ONE systemic non-steroidal anti-inflammatory agent (NSAID); AND
Note: Examples of systemic NSAIDs include ibuprofen and naproxen

iv. The medication is prescribed by or in consultation with a rheumatologist or an oncologist.

B) Patient is Currently Receiving a Tocilizumab Intravenous or Subcutaneous Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least ONE of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of objective measures include clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate) and/or reduced dosage of corticosteroids.

b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as less joint pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

9. Polymyalgia Rheumatica. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):

i. Patient is ≥ 18 years of age; AND

ii. Patient has tried one systemic corticosteroid; AND
Note: An example of a systemic corticosteroid is prednisone.

iii. The medication is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving a Tocilizumab Subcutaneous or Intravenous Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on therapy for at least 6 months; AND

Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least ONE of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating a tocilizumab product); OR
Note: Examples of objective measures are serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), resolution of fever, and/or reduced dosage of corticosteroids.

b) Compared with baseline (prior to initiating a tocilizumab product), patient experienced an improvement in at least one symptom, such as decreased shoulder, neck, upper arm, hip, or thigh pain or stiffness; improved range of motion; and/or decreased fatigue.

10. Still's Disease, Adult Onset. Approve for the duration noted if the patient meets the following criteria (A or B):

i. Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):

i. Patient is ≥ 18 years of age; AND

ii. Patient meets ONE of the following (a, b, or c):

a) Patient meets BOTH of the following [(1) and (2)]:

(1) Patient has tried one corticosteroid; AND

(2) Patient has tried one conventional synthetic disease-modifying antirheumatic drug (DMARD) such as methotrexate given for at least 2 months or was intolerant to a conventional synthetic DMARD; OR

b) Patient has at least moderate to severe active systemic features of this condition, according to the prescriber; OR
Note: Examples of moderate to severe active systemic features include fever, rash, lymphadenopathy, hepatomegaly, splenomegaly, and serositis.

c) Patient has active systemic features with concerns of progression to macrophage activation syndrome, as determined by the prescriber; AND

iii. The medication is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving a Tocilizumab Intravenous or Subcutaneous Product. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on this medication for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least ONE of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of objective measures include resolution of fever, improvement in rash or skin manifestations, clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), and/or reduced dosage of corticosteroids.

b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as less joint pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Actemra Intravenous is not recommended in the following situations:

1. COVID-19 (Coronavirus Disease 2019) – Non-Hospitalized Patient. Tocilizumab intravenous is only indicated in hospitalized adults with COVID who are receiving systemic corticosteroids and requiring supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal

membrane oxygenation (ECMO).[1] For COVID-19, the dose is 8 mg/kg (to a maximum of 800 mg) given as a single intravenous infusion. A second dose may be administered at least 8 hours after the initial infusion if clinical signs or symptoms worsen or do not improve after the first dose.

2. **Concurrent Use with a Biologic or with a Targeted Synthetic Oral Small Molecule Drug.** This medication should not be administered in combination with another biologic or with a targeted synthetic oral small molecule drug used for an inflammatory condition (see Appendix for examples). Combination therapy is generally not recommended due to a potentially higher rate of adverse events and lack of controlled clinical data supporting additive efficacy.
   Note: This does NOT exclude the use of conventional synthetic disease-modifying antirheumatic drug (e.g., methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with this medication.

3. **Crohn's Disease.** In a 12-week pilot study conducted in Japan, 36 adults with active Crohn's disease (Crohn's Disease Activity Index [CDAI] ≥ 150 and increased C-reactive protein) were randomized, in a double-blind fashion to tocilizumab 8 mg/kg intravenous every 2 weeks; or alternating infusions of tocilizumab 8 mg/kg every 4 weeks and placebo (i.e., alternating with placebo every 2 weeks), or to placebo every 2 weeks.[23] At baseline the CDAI means ranged from 287 to 306. Patients had been treated with corticosteroids, mesalamine-type drugs, metronidazole, or elemental diet. Six patients in the placebo group, four patients on tocilizumab intravenous every 4 weeks and one patient on tocilizumab intravenous every 2 weeks dropped out. The mean reduction in the CDAI score in the tocilizumab 8 mg/kg every 2 week group was 88 points (from mean 306 to 218). Further studies are needed.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Actemra® intravenous infusion [prescribing information]. South San Francisco, CA: Genentech; December 2022.
2. Schoels MM, van der Heijde D, Breedveld FC, et al. Blocking the effects of interleukin-6 in rheumatoid arthritis and other inflammatory rheumatic diseases: systematic literature review and meta-analysis informing a consensus statement. *Ann Rheum Dis*. 2013;72(4):583-589.
3. Yescarta™ intravenous infusion [prescribing information]. Santa Monica, CA: Kite Pharma; May 2019.
4. Kymriah™ intravenous infusion [prescribing information]. East Hanover, NJ: Novartis Oncology; June 2019.
5. Lee DW, Gardner R, Porter DL, et al. Current concepts in the diagnosis and management of cytokine release syndrome. *Blood*. 2014;124(2):188-195.
6. The NCCN Management of Immunotherapy-Related Toxicities Clinical Practice Guidelines in Oncology (version 1.2024 – December 7, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 21, 2024.
7. Ringold S, Angeles-Han ST, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for non-systemic polyarthritis, sacroiliitis, and enthesitis. *Arthritis Care Res (Hoboken)*. 2019;71(6):717-734.
8. Onel KB, Horton DB, Lovell DJ, et al. 2021 American College of Rheumatology guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for oligoarthritis, temporomandibular joint arthritis, and systemic juvenile idiopathic arthritis. *Arthritis Rheumatol*. 2022 Apr;74(4):553-569.
9. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol*. 2021;73(7):1108-1123.
10. The NCCN Castleman Disease Clinical Practice Guidelines in Oncology (version 1.2024 – January 18, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 21, 2024.
11. Riera E, Olivé A, Narváez J, et al. Adult onset Still's disease: review of 41 cases. *Clin Exp Rheumatol*. 2011;29(2):331-336.
12. Puéchal X, de Bandt M, Berthelot JM, et al. Tocilizumab in refractory adult Still's disease. *Arthritis Care Res (Hoboken)*. 2011;63(1):155-159.
13. Perdan-Pirkmajer K, Praprotnik S, Tomšič M. A case of refractory adult-onset Still's disease successfully controlled with tocilizumab and a review of the literature. *Clin Rheumatol*. 2010;29(12):1465-1467.

14. Sabnis GR, Gokhale YA, Kulkarni UP. Tocilizumab in Refractory Adult-Onset Still's Disease with Aseptic Meningitis-Efficacy of Interleukin-6 Blockade and Review of the Literature. *Semin Arthritis Rheum*. 2011;40(4):365-368.
15. De Bandt M, Saint-Marcoux B. Tocilizumab for multirefractory adult-onset Still's disease. *Ann Rheum Dis*. 2009;68(1):153-154.
16. Yoshimura M, Makiyama J, Koga T, et al. Successful treatment with tocilizumab in a patient with refractory adult-onset Still's disease (AOSD). *Clin Exp Rheumatol*. 2010;28(1):141-142.
17. Nakahara H, Mima T, Yoshio-Hoshino N, et al. A case report of a patient with refractory adult-onset Still's disease who was successfully treated with tocilizumab over 6 years. *Mod Rheumatol*. 2009;19(1):69-72.
18. Matsumoto K, Nagashima T, Takatori S, et al. Glucocorticoid and cyclosporine refractory adult onset Still's disease successfully treated with tocilizumab. *Clin Rheumatol*. 2009;28(4):485-487.
19. Iwamoto M, Nara H, Hirata D, et al. Humanized monoclonal anti-interleukin-6 receptor antibody for treatment of intractable adult-onset Still's disease. *Arthritis Rheum*. 2002;46(12):3388-3389.
20. Rech J, Ronneberger M, Englbrecht M, et al. Successful treatment of adult-onset Still's disease refractory to TNF and IL-1 blockade by IL-6 receptor blockade. *Ann Rheum Dis*. 2011;70(2):390-392.
21. Furst DE, Keystone EC, So AK, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2012. *Ann Rheum Dis*. 2013;72 Suppl 2:ii2-34.
22. Xeljanz® tablets [prescribing information]. New York, NY: Pfizer; February 2016.
23. Ito H, Takazoe M, Fukuda Y, et al. A pilot randomized trial of a human anti-interleukin-6 receptor monoclonal antibody in active Crohn's disease. *Gastroenterology*. 2004;126:989-996.
24. Centers for Disease Control and Prevention (Web site). Coronavirus (COVID-19). Available at: https://www.cdc.gov/coronavirus/2019-ncov/index.html/. Accessed on April 21, 2024.
25. Dejaco C, Ramiro S, Bond M, eta al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice: 2023 update. *Ann Rheum Dis*. 2023:ard-2023-224543.
26. Xu X, Han M, Li T, et al. Effective treatment of severe COVID-19 patients with tocilizumab. *Proc Natl Acad Sci U S A*. 2020;117(20):10970-10975.
27. Strohbehn GW, Heiss BL, Rouhani SJ, et al. COVIDOSE: A Phase II Clinical Trial of Low-Dose Tocilizumab in the Treatment of Noncritical COVID-19 Pneumonia. *Clin Pharmacol Ther*. 2021;109(3):688-696.
28. Dastan F, Saffaei A, Haseli S, et al. Promising effects of tocilizumab in COVID-19: A non-controlled, prospective clinical trial. *Int Immunopharmacol*. 2020;88:106869.
29. Galvan-Roman JM, Rodriguez-Garcia SC, Roy-Vallejo E, et al. IL-6 serum levels predict severity and response to tocilizumab in COVID-19: An observational study. *J Allergy Clin Immunol*. 2021;147(1):72-80.
30. Zhao H, Zhu Q, Zhang C, et al. Tocilizumab combined with favipiravir in the treatment of COVID-19: A multicenter trial in a small sample size. *Biomed Pharmacother*. 2021;133:110825.
31. Tuckwell K, Collinson N, Dimonaco S, et al. Newly diagnosed vs. relapsing giant cell arteritis: baseline data from the GiACTA trial. *Semin Arthritis Rheum*. 2017;46(5):657-664.
32. Stone JH, Tuckwell K, Dimonaco S, et al. Trial of tocilizumab in giant-cell arteritis. *N Engl J Med*. 2017 ;377(4):317-328.

APPENDIX

[*] Not an all-inclusive list of indications. Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn's disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; [^] Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; AA – Alopecia areata; TYK2 – Tyrosine kinase 2.