

Tocilizumab Intravenous (Actemra®, Tyenne®, Tofidence™)

When requesting a tocilizumab intravenous product for non-oncology indications, the individual requiring treatment must be diagnosed with one of the following FDA-approved indications or off-label compendial uses and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-Approved Non-oncology Indications

Tocilizumab Intravenous is indicated for the treatment of:

- Rheumatoid arthritis (RA)
- Polyarticular juvenile idiopathic arthritis (pJIA)
- Systemic juvenile idiopathic arthritis (sJIA)
- Giant cell arteritis (GCA)

Approved Non-oncology Off-label Compendial Uses

- Still's disease, adult onset
- Polymyalgia rheumatica (PMR)
- Inflammatory arthritis associated with checkpoint inhibitor therapy

Coverage Guidelines

Rheumatoid Arthritis (RA)

The individual must meet the following criteria for initial authorization:

- Is 18 years of age or older;
- Had a 3-month trial of one of the following:
 - o At least one biologic agent; OR
 - o At least one conventional synthetic disease-modifying antirheumatic drug (DMARD) (e.g., methotrexate, leflunomide, sulfasalazine, and hydroxychloroquine);
- Tocilizumab intravenous is prescribed by or in consultation with a rheumatologist.

The individual must meet the following criteria for re-authorization:

- Has been established on tocilizumab intravenous or subcutaneous therapy for at least 6 months (*Note: A patient who has received < 6 months of therapy, or who is restarting therapy, is reviewed under initial authorization criteria.*);
- Meets one of the following:
 - o Has experienced a beneficial clinical response from baseline when assessed by at least one objective measure (e.g., Clinical Disease Activity Index [CDAI], Patient Activity Scale [PAS]-II, Rapid Assessment of Patient Index Data 3 [RAPID-3], Simplified Disease Activity Index [SDAI], etc.); OR

- o Has experienced an improvement in at least one symptom compared to baseline (e.g., decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints).

Polyarticular Juvenile Idiopathic Arthritis (pJIA)

The individual must meet the following criteria for initial authorization:

- Is 2 years of age or older;
- Meets one of the following:
 - o Has tried at least one other systemic therapy for this condition (e.g., etanercept, adalimumab, methotrexate, sulfasalazine, leflunomide, or nonsteroidal anti-inflammatory drug [NSAID]); OR
 - o Tocilizumab intravenous will be started concurrently with methotrexate, leflunomide, or sulfasalazine; OR
 - o Has an absolute contraindication to methotrexate, leflunomide, or sulfasalazine (e.g., pregnancy, breast feeding, alcoholic liver disease, immunodeficiency syndrome, blood dyscrasias); OR
 - o Has aggressive disease;
- Tocilizumab intravenous is prescribed by or in consultation with a rheumatologist.

The individual must meet the following criteria for re-authorization:

- Has been established on tocilizumab intravenous or subcutaneous therapy for at least 6 months (*Note: A patient who has received < 6 months of therapy, or who is restarting therapy, is reviewed under initial authorization criteria.*);
- Meets one of the following:
 - o Has experienced a beneficial clinical response from baseline when assessed by at least one objective measure (e.g., Physician Global Assessment [MD Global], Parent/Patient Global Assessment of Overall Well-being [PGA], Juvenile Arthritis Disease Activity Score [JDAS], serum markers [e.g., C-reactive protein], and/or reduced dosage of corticosteroids); OR
 - o Has experienced an improvement in at least one symptom compared to baseline (e.g., less joint pain or tenderness, decreased duration of morning stiffness or fatigue, improved function or activities of daily living).

Systemic Juvenile Idiopathic Arthritis (sJIA)

The individual must meet the following criteria for initial authorization:

- Is 2 years of age or older;
- Meets one of the following:
 - o Has tried one other systemic agent for this condition (e.g., anakinra, canakinumab, methotrexate, leflunomide, sulfasalazine, corticosteroid); OR
 - o Had at least 1-month trial of a nonsteroidal anti-inflammatory drug (NSAID);
- Tocilizumab intravenous is prescribed by or in consultation with a rheumatologist.

The individual must meet the following criteria for re-authorization:

- Has been established on tocilizumab intravenous or subcutaneous therapy for at least 6 months (*Note: A patient who has received < 6 months of therapy, or who is restarting therapy, is reviewed under initial authorization criteria.*);
- Meets one of the following:
 - o Has experienced a beneficial clinical response from baseline when assessed by at least one objective measure (e.g., serum markers [e.g., C-reactive protein, erythrocyte sedimentation rate], improvement in rash or skin manifestations, resolution of fever, and/or reduced dosage of corticosteroids); OR
 - o Has experienced an improvement in at least one symptom compared to baseline (e.g., less joint pain, tenderness, stiffness, swelling; decreased fatigue; and/or improved function or activities of daily living).

Giant Cell Arteritis (GCA)

The individual must meet all of the following criteria for initial authorization:

- Is 18 years of age or older;
- Has tried one systemic corticosteroid (e.g., prednisone);
- Tocilizumab intravenous is prescribed by or in consultation with a rheumatologist.

The individual must meet the following criteria for re-authorization:

- Has been established on tocilizumab intravenous or subcutaneous therapy for at least 6 months (*Note: A patient who has received < 6 months of therapy, or who is restarting therapy, is reviewed under initial authorization criteria.*);
- Meets one of the following:
 - o Has experienced a beneficial clinical response from baseline when assessed by at least one objective measure (e.g., C-reactive protein, erythrocyte sedimentation rate, resolution of fever, and/or reduced dosage of corticosteroids); OR
 - o Has experienced an improvement in at least one symptom compared to baseline (e.g., decreased headache, decreased scalp or jaw pain, decreased fatigue, and/or improved vision).

Still's Disease, Adult Onset

The individual must meet all of the following criteria for initial authorization:

- Is 18 years of age or older;
- Meets one of the following:
 - o Has tried a corticosteroid and had a 2-month trial of or intolerance to at least one conventional synthetic disease-modifying antirheumatic drug or one biologic agent (e.g., methotrexate, canakinumab, anakinra); OR
 - o Has moderate to severe active systemic features of this condition (e.g., fever, rash, lymphadenopathy, hepatomegaly, serositis); OR

- o Has active systemic features with concerns of progression to macrophage activation syndrome;
- Tocilizumab intravenous is prescribed by or in consultation with a rheumatologist.

The individual must meet the following criteria for re-authorization:

- Has been established on tocilizumab intravenous or subcutaneous therapy for at least 6 months (*Note: A patient who has received < 6 months of therapy, or who is restarting therapy, is reviewed under initial authorization criteria.*);
- Meets one of the following:
 - o Has experienced a beneficial clinical response from baseline when assessed by at least one objective measure (e.g., C-reactive protein, erythrocyte sedimentation rate, improvement in rash or skin manifestations, resolution of fever, and/or reduced dosage of corticosteroids); OR
 - o Has experienced an improvement in at least one symptom compared to baseline (e.g., less joint pain/tenderness, less stiffness, decreased fatigue, improved function or activities of daily living).

Polymyalgia Rheumatica (PMR)

The individual must meet the following criteria for initial authorization:

- Is 18 years of age or older;
- Has tried one systemic corticosteroid (e.g., prednisone);
- Tocilizumab intravenous is prescribed by or in consultation with a rheumatologist.

The individual must meet the following criteria for re-authorization:

- Has been established on tocilizumab intravenous or subcutaneous therapy for at least 6 months (*Note: A patient who has received < 6 months of therapy, or who is restarting therapy, is reviewed under initial authorization criteria.*);
- Meets one of the following:
 - o Has experienced a beneficial clinical response from baseline when assessed by at least one objective measure (e.g., C-reactive protein, erythrocyte sedimentation rate, resolution of fever, and/or reduced dosage of corticosteroids); OR
 - o Has experienced an improvement in at least one symptom compared to baseline (e.g., decreased shoulder, neck, upper arm, hip, or thigh pain, improved range of motion, decreased fatigue, or decreased stiffness).

Inflammatory Arthritis Associated with Checkpoint Inhibitor Therapy

The individual must meet all of the following criteria for initial authorization:

- Is 18 years of age or older;
- Is symptomatic despite a trial of at least one systemic corticosteroid (e.g., methylprednisolone, prednisone);
- Has tried at least one systemic nonsteroidal anti-inflammatory drug (NSAID);

- Tocilizumab intravenous is prescribed by or in consultation with a rheumatologist or an oncologist.

The individual must meet the following criteria for re-authorization:

- Has been established on tocilizumab intravenous or subcutaneous therapy for at least 6 months (*Note: A patient who has received < 6 months of therapy, or who is restarting therapy, is reviewed under initial authorization criteria.*);
- Meets one of the following:
 - o Has experienced a beneficial clinical response from baseline when assessed by at least one objective measure (e.g., C-reactive protein, erythrocyte sedimentation rate, and/or reduced dosage of corticosteroids); OR
 - o Has experienced an improvement in at least one symptom compared to baseline (e.g., less joint pain/tenderness, less swelling, decreased fatigue, and/or improved function or activities of daily living).

Approval duration (initial): 6 months

Approval duration (renewal): 12 months

Dosing Recommendations

Rheumatoid Arthritis

The recommended starting dose is 4 mg/kg administered intravenously every 4 weeks followed by an increase to 8 mg/kg administered intravenously every 4 weeks based on clinical response.

Polyarticular Juvenile Idiopathic Arthritis

- For patients weighing less than 30 kg: the recommended dose is 10 mg/kg administered intravenously every 4 weeks.
- For patients weighing 30 kg or more: the recommended dose is 8 mg/kg administered intravenously every 4 weeks.

Systemic Juvenile Idiopathic Arthritis

- For patients weighing less than 30 kg: the recommended dose is 12 mg/kg administered intravenously every 2 weeks.
- For patients weighing 30 kg or more: the recommended dose is 8 mg/kg administered intravenously every 2 weeks.

Giant Cell Arteritis

The recommended dose is 6 mg/kg administered intravenously every 4 weeks in combination with a tapering course of glucocorticoids. Tocilizumab intravenous can be used alone following discontinuation of glucocorticoids.

Still's Disease

The recommended dose is up to 8 mg/kg per dose administered intravenously every 2 weeks.

Polymyalgia Rheumatica

The recommended dose is up to 6 mg/kg to a maximum of 600 mg per dose administered intravenously every 4 weeks.

Inflammatory Arthritis Associated with Checkpoint Inhibitor Therapy

The recommended dose is up to 8 mg/kg to a maximum of 800 mg per dose administered intravenously every 4 weeks.

References

1. Actemra® injection for intravenous infusion [prescribing information]. South San Francisco, CA: Genentech; September 2024.
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. The NCCN Management of Immunotherapy-Related Toxicities Clinical Practice Guidelines in Oncology (version 1.2025 – December 20, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 26, 2025.
4. 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.
5. 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.
6. 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.
7. 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.
8. 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.
9. 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.
10. 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.
11. De Bandt M, Saint-Marcoux B. Tocilizumab for multirefractory adult-onset Still's disease. *Ann Rheum Dis*. 2009;68(1):153-154.
12. 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.
13. 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.
14. 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.
15. 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.
16. 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.
17. 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.
18. 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.
19. Dejaco C, Ramiro S, Bond M, et al. EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice: 2023 update. *Ann Rheum Dis*. 2023;ard-2023-224543.
20. 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.
21. Stone JH, Tuckwell K, Dimonaco S, et al. Trial of tocilizumab in giant-cell arteritis. *N Engl J Med*. 2017;377(4):317-328.

22. DeJaco C, Singh YP, Perel P, et al. 2015 Recommendations for the management of polymyalgia rheumatica: a European League Against Rheumatism/American College of Rheumatology collaborative initiative. *Ann Rheum Dis*. 2015;74(10):1799-807.
23. Tyenne® injection for intravenous infusion [prescribing information]. Lake Zurich, IL: Fresenius Kabi USA, LLC; February 2025.
24. Tofidence™ injection for intravenous infusion [prescribing information]. Cambridge, MA: Biogen MA Inc; March 2025.