Policy Title:	Tocilizumab Products: Actemra, Tofidence, Tyenne **NON-ONCOLOGY POLICY** (Intravenous)		
		Department:	PHA
Effective Date:	01/01/2020		
Review Date:	09/25/2019, 12/18/2019, 1/22/2020, 8/3/2020, 11/9/2020, 5/13/2021, 10/21/21, 4/14/2022, 8/10/23, 12/07/2023, 1/10/2024, 12/18/2024, 1/2025, 7/28/26		

Purpose: To support safe, effective, and appropriate use of tocilizumab

Scope: Medicaid, Commercial, Medicare

Policy Statement:

Tocilizumab is covered under the Medical Benefit when used within the following guidelines for non-oncology indications. Use outside of these guidelines may result in non-payment unless approved under an exception process. **For oncology indications, please refer to NHPRI Oncology Policy**

Procedure:

Coverage of tocilizumab will be reviewed prospectively via the prior authorization process based on criteria below.

Summary of Evidence:

Tocilizumab is an interleukin-6 (IL-6) receptor antagonist indicated for treatment of adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs), adult patients with giant cell arteritis, slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD), patients 2 years of age and older with active polyarticular juvenile idiopathic arthritis, patients 2 years of age and older with active systemic juvenile idiopathic arthritis. The efficacy and safety of intravenously administered Actemra was assessed in five randomized, double-blind, multicenter studies in patients greater than 18 years with active rheumatoid arthritis diagnosed according to American College of Rheumatology (ACR) criteria. The primary endpoint was the proportion of Actemra patients who achieved an ACR 20 response at Week 24. In all intravenous studies, patients treated with 8 mg per kg Actemra had higher ACR 20, ACR 50, and ACR 70 response rates versus MTX- or placebo-treated patients at week 24. During the 24 week-controlled portions of Studies I to V, patients treated with Actemra at a dose of 4 mg per kg in patients with inadequate response to DMARDs or TNF antagonist therapy had lower response rates compared to patients treated with Actemra 8 mg per kg. The clinical efficacy of Actemra was assessed in a phase 3 multicenter, randomized, double-blind, placebo-controlled study in patients with Systemic Sclerosis (SSc) (Study WA29767). Patients were not permitted to use biologic agents (such as TNF antagonists), alkylating agents, or cyclophosphamide. The primary efficacy endpoint was change from baseline at Week 48 in modified Rodnan skin score (mRSS). In the overall population of Study WA29767, there was not a statistically significant difference in the mean change

from baseline to Week 48 in mRSS (primary endpoint) in patients receiving Actemra compared to placebo (difference: -1.73; 95% CI: -3.78, 0.32). The efficacy of Actemra was assessed in a three-part study, WA19977 (NCT00988221), including an open-label extension in children 2 to 17 years of age with active polyarticular juvenile idiopathic arthritis (PJIA), who had an inadequate response to methotrexate or inability to tolerate methotrexate. Treatment with a stable dose of methotrexate was permitted but was not required during the study. Concurrent use of disease modifying antirheumatic drugs (DMARDs), other than methotrexate, or other biologics (e.g., TNF antagonists or T cell co-stimulation modulator) were not permitted in the study. Part I consisted of a 16-week active Actemra treatment lead-in period (n=188) followed by Part II, a 24-week randomized double-blind placebo-controlled withdrawal period, followed by Part III, a 64-week open-label period. The primary endpoint was the proportion of patients with a JIA ACR 30 flare at week 40 relative to week 16. Actemra treated patients experienced significantly fewer disease flares compared to placebo-treated patients (26% [21/82] versus 48% [39/81]; adjusted difference in proportions -21%, 95% CI: -35%, -8%). During the withdrawal phase (Part II), more patients treated with Actemra showed JIA ACR 30/50/70 responses at Week 40 compared to patients withdrawn to placebo. The efficacy of Actemra for the treatment of active SJIA was assessed in WA18221 (NCT00642460), a 12-week randomized, double blind, placebo-controlled, parallel group, 2-arm study. The primary endpoint was the proportion of patients with at least 30% improvement in JIA ACR core set (JIA ACR 30 response) at Week 12 and absence of fever (no temperature at or above 37.5°C in the preceding 7 days). The JIA ACE response rate with the absence of a fever in the Actemra treatment group had an 85% respond rate meanwhile placebo had a 24% response rate.

Initial Approval Criteria:

For all indications

- Submission of the member's chart or medical record is required, documenting medical necessity based on the criteria corresponding to the applicable indication; AND
- Physician has assessed baseline disease severity utilizing an objective measure/tool; AND
- Member is free of any clinically important active infection, including clinically important localized infections; AND
- Member has been evaluated and screened for the presence of latent tuberculosis (TB) infection prior to initiating treatment and will receive ongoing monitoring for the presence of TB during treatment; AND
- Member will not receive live vaccines during therapy; AND
- Tocilizumab will not be used concomitantly with an injectable biologic response modifier including TNF-inhibitors (e.g., adalimumab (e.g., Hadlima), Enbrel (etanercept), Cimzia (certolizumab), infliximab (e.g., Inflectra), etc.) and IL-inhibitors (e.g., Cosentyx (secukinumab), ustekinumab (e.g., Stelara, Otulfi, Selarsdi, Steqeyma, and Yesintek, etc.), Tremfya (guselkumab), Ilumya (tildrakizumab), Skyrizi (risankizumab), Bimzelx (bimekizumab), etc.) or other oral non-biologic agent (e.g., Otezla (apremilast), tofacitinib (Xeljanz), Olumiant (baricitinib), Rinvoq (upadacitinib), etc.); AND
- If requesting Actemra (tocilizumab) or Tofidence (tocilizumab-bavi), the member must have had an inadequate response, intolerance, or contraindication to at least a 3-month trial of Tyenne (tocilizumab-aazg)
- Medicare members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

Moderately to severely active rheumatoid arthritis (RA)

- Member is 18 years or older; AND
- Prescribed by, or in consultation with, a specialist in rheumatology; AND
- Documentation has been submitted of one of the following criteria:
    - Member has been tested for either of the following biomarkers and the test was positive:
        - Rheumatoid factor (RF)
        - Anti-cyclic citrullinated peptide (anti-CCP); OR
    - Member has been tested for ALL of the following biomarkers:
        - RF
        - Anti-CCP
        - C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR); AND
- Member has documented moderate to severe active disease; AND
- Documentation has been submitted that the member meets both of the following criteria:
    - Member has had an inadequate response, intolerance, or contraindication to at least a 3-month trial of methotrexate or any other conventional disease-modifying antirheumatic drug (DMARD) despite adequate dosing; AND
    - Member has had an inadequate response, intolerance or contraindication to at least a 3-month trial of adalimumab at maximum tolerated doses.

Active systemic juvenile idiopathic arthritis (sJIA) / moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)

- Member is at least 2 years of age or older; AND
- Prescribed by, or in consultation with, a specialist in rheumatology; AND
- Documentation has been submitted that the member has active systemic juvenile idiopathic arthritis (sJIA) or polyarticular juvenile idiopathic arthritis (pJIA)
- Documentation has been submitted of one of the following criteria:
    - Member has had an inadequate response, intolerance, or contraindication to at least a 1-month trial of either oral non-steroidal anti-inflammatory drugs (NSAIDs) OR an oral disease modifying anti-rheumatic agent (DMARD) (e.g., methotrexate, leflunomide, sulfasalazine, etc.) at an adequate dose and duration; OR
    - Member has risk factors for disease severity and potentially a more refractory disease course (see Appendix B), and also meets one of the following:
        - High-risk joints are involved (e.g., cervical spine, wrist, or hip)
        - High disease activity
        - Is judged to be at high risk for disabling joint disease; AND
- Documentation has been submitted that the member has had an inadequate response, intolerance or contraindication to at least a 3-month trial of adalimumab at maximum tolerated doses.

Cytokine Release Syndrome

- Prescribed by, or in consultation with, a specialist in oncology or hematology; AND
- Member has received or will be receiving chimeric antigen receptor (CAR) T cell therapy; AND
    - Tocilizumab is available and being ordered to have on-hand, prior to the administration of CAR-T therapy, if needed for the treatment of CRS; OR
    - Used for management of G1-4 neurotoxicity as additional therapy if the patient has concurrent CRS; OR
- Member has received or will be receiving T-cell engaging bispecific agents; AND
    - Used as prophylaxis to reduce the risk of CRS prior to administering the first dose of any bispecific antibody (i.e., talquetamab, teclistamab, elranatamab, or linvoseltamab) in patients with multiple myeloma; OR
    - Used as supportive care in patients with acute lymphoblastic leukemia (ALL) who have severe CRS related to blinatumomab therapy; OR
    - Used for the management of G1 prolonged steroid-refractory CRS (>24-48 hours) or if patient is at high-risk for CRS; OR
    - Used for the management of G2-4 CRS

Management of Immune Checkpoint Inhibitor Related Toxicities

- Prescribed by, or in consultation with, a specialist in oncology, hematology, or rheumatology; AND
- Member has been receiving therapy with an immune checkpoint inhibitor (e.g. nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab, cemiplimab, ipilimumab, dostarlimab, nivolumab/relatlimab-rmbw, retifanlimab, tislelizumab, toripalimab etc.); AND
- Used as additional disease modifying antirheumatic therapy (DMARD) for any of the following immunotherapy-related toxicities:
    - Giant cell arteritis; OR
    - Moderate or severe inflammatory arthritis; AND
        - Member's symptoms have not improved after holding immunotherapy; AND
            - Member has not responded to oral corticosteroids; OR
            - Member is unable to taper corticosteroids; OR
    - Polymyalgia rheumatica and is unable to taper prednisone OR has no improvement in symptoms from prednisone; OR
    - Used as additional corticosteroid-sparing immunosuppression for management of any of the following immunotherapy related toxicities:
        - G2 elevated alanine transaminase/aspartate transaminase (ALT/AST); AND

- Liver enzymes suggest worsening or no improvement after 3-7 days of prednisone; OR
- G3 or G4 elevated ALT/AST; AND
  - AST/ALT does not improve after 1-2 days of prednisone/methylprednisolone; OR
- G2 elevated alkaline phosphatase AND
  - Alkaline phosphatase worsens or does not improve within 3 days after initiating corticosteroids; OR
- G3 or G4 elevated alkaline phosphatase; AND
- Alkaline phosphatase does not improve after 1-2 days of prednisone/methylprednisolone

Neuromyelitis Optica Spectrum Disorder (NMOSD)

- Member has a confirmed diagnosis based on the following:
  - Member is seropositive for aquaporin-4 (AQP4) IgG antibodies; AND
    - Member has at least one core clinical characteristic §; AND
    - Alternative diagnoses have been excluded (e.g., myelin oligodendrocyte glycoprotein (MOG) antibody disease (MOGAD), multiple sclerosis, sarcoidosis, cancer, chronic infection, etc.); OR
  - Member is seronegative for AQP-4 IgG antibodies OR has unknown AQP-4-IgG status; AND
    - Member has at least two core clinical characteristics § occurring as a result of one or more clinical attacks; AND
    - Member experienced ALL of the following:
      - At least 1 core clinical characteristic must be acute optic neuritis, acute myelitis with, or area postrema syndrome; AND
      - Fulfillment of additional typical MRI finding requirements for each area affected, ψ; AND
    - Alternative diagnoses have been excluded (e.g., myelin oligodendrocyte glycoprotein (MOG) antibody disease (MOGAD multiple sclerosis, sarcoidosis, cancer, chronic infection, etc.); AND
- Used as a single agent or in combination with immunosuppressive therapy (e.g. azathioprine, methotrexate, mycophenolate, etc.)

Giant Cell Arteritis (GCA) †

- Prescribed by, or in consultation with, a specialist in rheumatology; AND
- Member has large vessel arteritis that has at some point been verified with biopsy or with imaging of the large vessels (color Doppler ultrasound [CDUS], MRI, PET-CT, or CT angiography); AND

- Member has active disease and an elevated c-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR); AND
- Member has had an inadequate response, contraindication, or intolerance to glucocorticoid therapy alone; AND
- Used in combination with a tapering course of glucocorticoids *(NOTE: tocilizumab can be used alone following discontinuation of glucocorticoids.)*

§ Core Clinical Characteristics of NMOSD: ▪ Acute Optic neuritis ▪ Acute myelitis ▪ Area postrema syndrome (APS): episode of otherwise unexplained hiccups and/or nausea and vomiting (lasting for at least 48 hours or with MRI evidence of a dorsal brainstem lesion) ▪ Acute brainstem syndrome other than APS ▪ Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions ▪ Acute cerebral syndrome with NMOSD-typical brain lesions
ψ Typical MRI findings in NMOSD related to clinical presentation (T2 unless noted otherwise) ▪ Optic neuritis: Normal cerebral MRI (or only nonspecific white matter lesions) OR longitudinally extensive optic nerve lesion (≥ half of the length of the optic nerve or involving optic chiasm; T2 or T1/Gd) ▪ Myelitis: Intramedullary lesion ≥ 3 contiguous VS (LETM) OR focal atrophy ≥ 3 contiguous VS in patients with a history of acute myelitis ▪ Area postrema syndrome (APS): Lesion in the dorsal medulla oblongata/area postrema ▪ Other brainstem syndrome: Periependymal brainstem lesion (4th ventricle) ▪ ¥ Diencephalic syndrome: Periependymal lesion (3rd ventricle) OR hypothalamic/thalamic lesion ▪ § Cerebral syndrome: Extensive periependymal lesion (lateral ventricle; often with Gd) OR long (> 1⁄2 length), diffuse, heterogeneous or edematous corpus callosum lesion OR long corticospinal tract lesion (unilateral or bilateral, contiguously involving internal capsule and cerebral peduncle) OR large, confluent (unilateral or bilateral) subcortical or deep white matter lesion

LETM = *longitudinally extensive transverse myelitis lesions*

VS=vertebral segments

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); **Φ** Orphan Drug

Continuation of Therapy Criteria:

- Member continues to meet initial criteria; AND

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: serious infection, severe neutropenia, severe thrombocytopenia, severe hepatotoxicity, gastrointestinal perforation, immunosuppression, severe hypersensitivity reactions, demyelinating disorders, etc.; AND

Non-Oncology Indications

Rheumatoid arthritis (RA)

- Documentation is submitted of member's positive clinical response with the requested medication as evidenced by improvement of disease activity by at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

Juvenile Idiopathic Arthritis (sJIA/pJIA)

- Documentation is submitted of member's positive clinical response with the requested medication as evidenced by low disease activity or improvement in any of the following from baseline:
  - Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
  - Number of joints with limitation of movement
  - Functional ability

NMOSD

- Documentation is submitted of member's positive clinical response as evidenced by stabilization or improvement in any of the following: neurologic symptoms as evidenced by a decrease in acute relapses or improvement of stability, reduced hospitalizations, reduction or discontinuation in plasma exchange treatments, and/or reduction or discontinuation of corticosteroids without relapse

Giant Cell Arteritis

- Documentation is submitted of member's positive clinical response as evidenced by low disease activity or improvement in signs and symptoms compared to baseline such as headache, temporal artery tenderness, visual symptoms, inflammatory parameters, (e.g., erythrocyte sedimentation rate [ESR], C-reactive protein), improvement of periodic imaging studies (color Doppler ultrasound [CDUS], MRI, PET-CT, or CT angiography), etc.

Management of Immune Checkpoint Inhibitor Related Toxicities and Cytokine Release Syndrome

- May not be renewed

Coverage durations:

Indication	Duration of initial approval	Continuation of therapy coverage
Adult Rheumatoid Arthritis	6 months	6 months
Polyarticular Juvenile Idiopathic Arthritis	6 months	6 months
Systemic Juvenile Idiopathic Arthritis	6 months	6 months
Immune Checkpoint Inhibitor Related Toxicities	1 dose	Cannot be renewed
Cytokine Release Syndrome	Up to 4 doses	Cannot be renewed
NMOSD	6 months	6 months
Giant Cell Arteritis	6 months	6 months, up to a maximum of 18 months of therapy

Per §§ 42 CFR 422.101, this clinical medical policy only applies to Medicare in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD).

Policy Rationale:
Tocilizumab was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Actemra according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For Medicare members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.

Dosage/Administration:

Indication	Dose	Maximum dose (1 billable unit = 1 mg)
Adult Rheumatoid Arthritis	4 mg/kg IV every 4 weeks May increase to 8 mg/kg every 4 weeks based on clinical response	800 units every 28 days

Polyarticular Juvenile Idiopathic Arthritis	Weight ≥ 30 kg: 8 mg/kg IV every 4 weeks Weight < 30 kg: 10 mg/kg IV every 4 weeks	800 units every 28 days
Systemic Juvenile Idiopathic Arthritis	Weight ≥ 30 kg 8 mg/kg IV every 2 weeks Weight < 30 kg 12 mg/kg IV every 2 weeks	800 units every 14 days
Management of Immune Checkpoint Inhibitor Related Toxicities	4 mg/kg IV once	3200 units for one course of therapy
NMOSD	8 mg/kg intravenously, every 4 weeks	800 units every 28 days
Giant Cell Arteritis	6 mg/kg intravenously, every 4 weeks Doses exceeding 600 mg per infusion are not recommended	600 units every 28 days
Cytokine Release Syndrome	Weight ≥ 30 kg: 12 mg/kg IV Weight < 30 kg: 8 mg/kg IV Doses exceeding 800 mg per infusion are not recommended in CRS Dose may be repeated up to three additional times if clinical signs or symptoms worsen or do not improve. Doses should be at least 8 hours apart.	

Investigational use: All therapies are considered investigational when used at a dose or for a condition other than those that are recognized as medically accepted indications as defined in any one of the following standard reference compendia: American Hospital Formulary Service Drug information (AHFS-DI), Thomson Micromedex DrugDex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs, or Peer-reviewed published medical literature indicating that sufficient evidence exists

to support use. Neighborhood does not provide coverage for drugs when used for investigational purposes.

Applicable Codes:
Below is a list of billing codes applicable for covered treatment options. The below tables are provided for reference purposes and may not be all-inclusive. Requests received with codes from tables below do not guarantee coverage. Requests must meet all criteria provided in the procedure section.

The following HCPCS/CPT code is:

HCPCS/CPT Code	Description
J3262	Injection, tocilizumab, 1 mg (Actemra)
Q5133	Injection, tocilizumab-bavi (tofidence), biosimilar, 1 mg
Q5135	Injection, tocilizumab-aazg (tyenne), biosimilar, 1 mg

References:

1. Actemra [package insert]. South San Francisco, CA; Genentech, Inc; December 2025. Accessed June 2026.
2. Tofidence [package insert]. Cambridge, MA; Biogen MA Inc.; May 2026. Accessed June 2026.
3. Tyenne [package insert]. Lake Zurich, IL; Fresenius Kabi USA, LLC. May 2026. Accessed June 2026.
4. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care Res (Hoboken). 2015 Nov 6. doi: 10.1002/acr.22783.
5. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care Res (Hoboken). 2011 Apr;63(4):465-82.
6. Ringold S, Weiss PF, Beukelman T, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. Arthritis Rheum. 2013 Oct;65(10):2499-512.
7. DeWitt EM, Kimura Y, Beukelman T, et al. Consensus treatment plans for new-onset systemic juvenile idiopathic arthritis. Arthritis Care Res (Hoboken). 2012 Jul;64(7):1001-10.
8. Nishimoto N, Kanakura Y, Aozasa K, et al. Humanized anti-interleukin-6 receptor antibody treatment of multicentric Castleman disease. Blood 2005;106:2627-2632
9. Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis. 2017 Mar 6. pii: annrheumdis-2016-210715.

10. Fraser JA, Weyand CM, Newman NJ, Biousse V. The treatment of giant cell arteritis. Rev Neurol Dis. 2008 Summer;5(3):140-52.
11. Dasgupta B, Borg FA, Hassan N, et al. BSR and BHPR guidelines for the management of giant cell arteritis. Rheumatology (Oxford). 2010 Aug;49(8):1594-7.
12. National Institute for Health and Care Excellence. NICE 2009. Rheumatoid Arthritis in Adults: Management. Published 25 February 2009. Clinical Guideline [CG79]. https://www.nice.org.uk/guidance/cg79/resources/rheumatoid-arthritis-in-adultsmanagement-pdf-975636823525.
13. National Institute for Health and Care Excellence. NICE 2010. Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after failure of a TNF inhibitor. Published 10 October 2012. Clinical Guideline [TA195]. https://www.nice.org.uk/guidance/ta195/resources/adalimumab-etanercept-infliximabrituximab-and-abatacept-for-the-treatment-of-rheumatoid-arthritis-after-the-failure-of-atnf-inhibitor-pdf-82598558287813.
14. Ward MM, Guthri LC, Alba MI. Rheumatoid Arthritis Response Criteria And PatientReported Improvement in Arthritis Activity: Is an ACR20 Response Meaningful to Patients". Arthritis Rheumatol. 2014 Sep; 66(9): 2339–2343. doi: 10.1002/art.38705
15. Ringold S, Bittner R, Neggi T, et al. Performance of rheumatoid arthritis disease activity measures and juvenile arthritis disease activity scores in polyarticular-course juvenile idiopathic arthritis: Analysis of their ability to classify the American College of Rheumatology pediatric measures of response and the preliminary criteria for flare and inactive disease. Arthritis Care Res (Hoboken). 2010 Aug;62(8):1095-102.
16. Consolaro A, Giancane G, Schiappapietra B, et al. Clinical outcome measures in juvenile idiopathic arthritis. Pediatric Rheumatology 18 April 2016 14:23.
17. Stroud C, Hedge A, Cherry C, et al. Tociluzumab for the management of immune mediated adverse events secondary to PD-1 blockage. Journal of Oncology Pharmacy Practice. 2017 December. https://doi.org/10.1177/1078155217745144.