Policy Title:	Actemra (tocilizumab) **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, 01/10/2024		

Purpose: To support safe, effective, and appropriate use of Actemra (tocilizumab).

Scope: Medicaid, Commercial, Medicare-Medicaid Plan (MMP)

Policy Statement:

Actemra (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 Actemra (tocilizumab) will be reviewed prospectively via the prior authorization process based on criteria below.

Summary of Evidence:

Actemra's efficacy and safety have been demonstrated in numerous clinical trials across its approved indications. In RA, Actemra has shown significant improvement in signs and symptoms, as well as inhibition of structural joint damage in those who have had an inadequate response to one or more Disease-Modifying Anti-Rheumatic Drugs (DMARDs). Clinical evidence also supports its effectiveness in managing GCA, SSc-ILD, PJIA, CRS, COVID-19, and SJIA.

Initial Criteria:

- Patient has been evaluated and screened for the presence of latent TB infection prior to initiating treatment; **AND**
- Patient does not have an active infection, including clinically important localized infections; **AND**
- Must not be administered concurrently with live vaccines; **AND**
- Patient is not on concurrent treatment with another another IL-inhibitor, TNF-inhibitor, biologic response modifier or other non-biologic agent (i.e., abrocitinib, apremilast, tofacitinib, baricitinib, upadacitinib, deucravacitinib, etc);
- MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements

Rheumatoid Arthritis

- Patient is 18 years or older; **AND**
- Physician has assessed baseline disease severity utilizing an objective measure/tool; **AND**
- Documented moderate to severe active disease; **AND**
- Patient has had at least a 3-month trial and failed previous therapy with ONE formulary oral disease modifying anti-rheumatic agent (DMARD) such as methotrexate, azathioprine, hydroxychloroquine, sulfasalazine, leflunomide, etc.; AND
- May be used as a single agent or in combination with other non-biologic DMARDs (e.g., methotrexate, hydroxychloroquine, leflunomide, sulfasalazine, etc.); **AND**
- Patient has had an inadequate response, intolerance or contraindication to at least a 3-month trial of adalimumab at maximum tolerated doses

Juvenile Idiopathic Arthritis (JIA)

- Patient is 2 years or older ; **AND**
- Patient has active systemic juvenile idiopathic arthritis (SJIA) or polyarticular juvenile idiopathic arthritis (PJIA) ; **AND**
- Physician has assessed baseline disease severity utilizing an objective measure/tool; **AND**
- Patient has had at least a 1-month trial and failure (unless contraindicated or intolerant) of previous therapy with either oral non-steroidal anti-inflammatory drugs (NSAIDs) OR a systemic glucocorticoid (prednisone, methylprednisolone, etc.); **AND**
- May be used alone or in combination with methotrexate; **AND**
- Patient has had an inadequate response, intolerance or contraindication to at least a 3-month trial of adalimumab at maximum tolerated doses

Management of Immune Checkpoint Inhibitor Related Toxicities

- Patient has been receiving therapy with an immune checkpoint inhibitor (e.g. nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab, cemiplimab, ipilimumab, dostarlimab, nivolumab/relatlimab-rmbw, retifanlimab,etc.); AND
  - Used as additional therapy for the management of immunotherapy-related giant cell arteritis; **OR**
  - Used as additional disease modifying antirheumatic therapy (DMARD) for moderate or severe immunotherapy-related inflammatory arthritis; **AND**
    - Patient's symptoms have not improved after holding immunotherapy; **AND**
      - Patient has not responded to oral corticosteroids; **OR**
      - Patient is unable to taper corticosteroids; **OR**
  - Patient has polymyalgia rheumatica and is unable to taper prednisone OR has no improvement in symptoms from prednisone

Neuromyelitis Optica Spectrum Disorder (NMOSD)

- Patient has a confirmed diagnosis based on the following:
  - Patient is seropositive for aquaporin-4 (AQP4) IgG antibodies; **AND**
    - Patient 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
  - Patient is seronegative for AQP-4 IgG antibodies OR has unknown AQP-4-IgG status; **AND**
    - Patient has at least two core clinical characteristics occurring as a result of one or more clinical attacks §; **AND**
    - Patient experienced ALL of the following:
      - At least 1 core clinical characteristic must be acute optic neuritis, acute myelitis with LETM*, 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) †

- Patient 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**
- Patient has active disease and an elevated c-reactive protein (CRP) and erythrocyte sedimentation rate (ESR); **AND**
- Patient has had an inadequate response, contraindication, or intolerance to glucocorticoid therapy alone; **AND**
- Used in combination with a tapering course of glucocorticoids *(NOTE: Actemra 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*

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

Continuation of Therapy Criteria:

- Patient continues to meet initial criteria; AND
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: neutropenia (absolute neutrophil count (ANC) below 1000 per mm^3), thrombocytopenia (platelet count below 100,000 per mm^3), hepatotoxicity (ALT or AST above 3-5 times the upper limit of normal), gastrointestinal perforation, severe hypersensitivity reactions, demyelinating disorders, etc.; AND
- Patient is receiving ongoing monitoring for presence of TB or other active infections

Non-Oncology Indications

Rheumatoid arthritis (RA)

- Disease response as indicated by improvement in signs and symptoms compared to baseline such as the number of tender and swollen joint counts, reduction of C-reactive protein, improvement of patient global assessment, and/or an improvement on a disease activity scoring tool [e.g. an improvement on a composite scoring index such as Disease Activity Score-28 (DAS28) of 1.2 points or more or a ≥20% improvement on the American College of Rheumatology-20 (ACR20) criteria]

Juvenile Idiopathic Arthritis (SJIA/PJIA)

- Disease response as indicated by improvement in signs and symptoms compared to baseline such as the number of tender and swollen joint counts and/or an improvement on a disease activity scoring tool [e.g. an improvement on a composite scoring index such as Juvenile Arthritis Disease Activity Score (JADAS) or the American College of Rheumatology (ACR) Pediatric (ACR-Pedi 30) of at least 30% improvement from baseline in three of six variables].

Management of Immune Checkpoint Inhibitor Related Toxicities

- May not be renewed

NMOSD

- Disease response as indicated by stabilization/improvement in any of the following: neurologic symptoms as evidenced by a decrease in acute relapses or improvement of stability, reduced hospitalizations, reduction/discontinuation in plasma exchange treatments, and/or reduction/discontinuation of corticosteroids without relapse

Giant Cell Arteritis

- Disease response as indicated by improvement in signs and compared to baseline such as headache, temporal artery tenderness, visual symptoms, inflammatory parameters, (e.g., erythrocyte sedimentation rate [ESR], C-reactive protein), etc.

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
NMOSD	6 months	6 months
Giant Cell Arteritis	6 months	6 months

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

Policy Rationale:
Actemra 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 INTEGRITY (Medicare-Medicaid Plan) 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
	The interval between consecutive doses should be at least 8 hours. May be used with or without corticosteroids	
Immune Checkpoint Inhibitor Related Toxicities inflammatory arthritis	4 mg/kg IV once	800 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

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

References:

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14. Consolaro A, Giancane G, Schiappapietra B, et al. Clinical outcome measures in juvenile idiopathic arthritis. Pediatric Rheumatology 18 April 2016 14:23.
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