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		
Revision Date:	09/25/2019, 12/18/2019, 1/22/2020, 8/3/2020, 11/9/2020		

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.

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 TNF-inhibitor, biologic response modifier or other non-biologic agent (i.e., apremilast, tofacitinib, baricitinib);
- 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); AND
- May be used alone or in combination with methotrexate; AND
- Patient must have failed or experienced intolerable side effects to two or more formulary TNF inhibitor agents, such as adalimumab (Humira)

Juvenile Idiopathic Arthritis (JIA)

- Patient is 2 years or older ; AND
- Patient has active systemic (SJIA) or polyarticular (PJIA) disease; 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 must have failed or experienced intolerable side effects to adalimumab (Humira)

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 etc.); AND
    - Used as additional therapy for the management of giant cell arteritis; OR
    - Patient has severe immunotherapy-related inflammatory arthritis ; AND
        - Used as additional disease modifying antirheumatic therapy ; AND
            - Patient's symptoms have not improved within 1 week after starting high dose corticosteroids OR
            - Patient is unable to taper corticosteroids by week 2

Neuromyelitis Optica Spectrum Disorder (NMOSD)

- Patient has a confirmed diagnosis based on the following:
    - Patient was found to be seropositive for aquaporin-4 (AQP4) IgG antibodies; AND
        - Patient has at least one core clinical characteristic §; AND
        - Alternative diagnoses have been excluded (e.g., multiple sclerosis, sarcoidosis, cancer, chronic infection, etc.); OR
    - Patient was found to be 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 optic neuritis, acute myelitis with LETM*, or area postrema syndrome; AND

  - Dissemination in space (≥2 different core clinical characteristics); AND
  - Fulfillment of additional MRI requirements, as applicable ψ; AND
- Alternative diagnoses have been excluded (e.g., 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 (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:
▪ Optic neuritis ▪ Acute myelitis ▪ Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting ▪ Acute brainstem syndrome ▪ Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD-typical diencephalic MRI lesions ▪ Symptomatic cerebral syndrome with NMOSD-typical brain lesions
ψ Core Clinical Characteristics of NMOSD
▪ Acute optic neuritis: requires brain MRI showing (a) normal findings or only nonspecific white matter lesions, OR (b) optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium-enhancing lesion extending over >1/2 optic nerve length or involving optic chiasm ▪ Acute myelitis: requires associated intramedullary MRI lesion extending over ≥3 contiguous segments (LETM) OR ≥3 contiguous segments of focal spinal cord atrophy in patients with history compatible with acute myelitis ▪ Area postrema syndrome: requires associated dorsal medulla/area postrema lesions ▪ Acute brainstem syndrome: requires associated peri-ependymal brainstem lesions

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, 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, 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

*** Requests will also be reviewed to National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) if applicable. ***

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	4 mg/kg IV once	800 units for one course of therapy

Toxicities inflammatory arthritis		
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 in GCA patients.	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

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