Policy Title: Actemra (tocilizumab) NON-ONCOLOGY POLICY
(Intravenous)

<table>
<thead>
<tr>
<th>Department:</th>
<th>PHA</th>
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Effective Date: 01/01/2020


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); AND
- 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)

Cytokine Release Syndrome (CRS)
• Patient is 2 years or older; AND
• Patient has received or will be receiving chimeric antigen receptor (CAR) T cell therapy; AND
  o Tocilizumab is being ordered to have on-hand, prior to the administration of CAR-T therapy, if needed for the treatment of CRS; OR
  o Patient has a confirmed diagnosis of CAR-T therapy induced severe or life-threatening CRS
• Used as supportive care in patients with refractory CRS secondary to anti-CD19 therapy (i.e., blinatumomab)

Management of Immune Checkpoint Inhibitor related Inflammatory Arthritis
• Patient has been receiving therapy with an immune checkpoint inhibitor (e.g. nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab, etc.); AND
• Patient has inflammatory arthritis related to their immunotherapy; AND
• Documented severe disease; AND
• Patient’s condition is refractory to corticosteroids (i.e., no improvement within 2 weeks of starting therapy)

Neuromyelitis Optica Spectrum Disorder (NMOSD)
• Patient has a confirmed diagnosis based on the following:
  o 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.)

§ 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

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 mm³),
thrombocytopenia (platelet count below 100,000 per mm³), 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].

**Cytokine Release Syndrome**

- May not be renewed

**Management of Immune Checkpoint Inhibitor related Inflammatory Arthritis**

- 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

**Coverage durations:**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Duration of initial approval</th>
<th>Continuation of therapy coverage</th>
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<tbody>
<tr>
<td>Adult Rheumatoid Arthritis</td>
<td>6 months</td>
<td>6 months</td>
</tr>
<tr>
<td>Polyarticular Juvenile Idiopathic Arthritis</td>
<td>6 months</td>
<td>6 months</td>
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<tr>
<td>Systemic Juvenile Idiopathic Arthritis</td>
<td>6 months</td>
<td>6 months</td>
</tr>
</tbody>
</table>
### Dosage/Administration:

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dose</th>
<th>Maximum dose (1 billable unit = 1 mg)</th>
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</thead>
<tbody>
<tr>
<td><strong>Adult Rheumatoid Arthritis</strong></td>
<td>4 mg/kg IV every 4 weeks</td>
<td>800 units every 28 days</td>
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<tr>
<td></td>
<td>May increase to 8 mg/kg every 4 weeks based on clinical response</td>
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<tr>
<td><strong>Polyarticular Juvenile Idiopathic Arthritis</strong></td>
<td>Weight ≥ 30 kg: 8 mg/kg IV every 4 weeks</td>
<td>800 units every 28 days</td>
</tr>
<tr>
<td></td>
<td>Weight &lt; 30 kg: 10 mg/kg IV every 4 weeks</td>
<td></td>
</tr>
<tr>
<td><strong>Systemic Juvenile Idiopathic Arthritis</strong></td>
<td>Weight ≥ 30 kg 8 mg/kg IV every 2 weeks</td>
<td>800 units every 14 days</td>
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<td></td>
<td>Weight &lt; 30 kg 12 mg/kg IV every 2 weeks</td>
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<tr>
<td><strong>Cytokine Release Syndrome (CRS)</strong></td>
<td>Weight ≥ 30 kg 8 mg/kg IV every 8 hours, if needed, up to a maximum of 4 total doses*</td>
<td>3200 units for one course of therapy</td>
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<tr>
<td></td>
<td>Weight &lt; 30 kg 12 mg/kg IV every 8 hours, if needed, up to a maximum of 4 total doses*</td>
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<td></td>
<td>*If no clinical improvement in the signs and symptoms of CRS occurs after the first dose, up to 3 additional doses may be administered. The interval between consecutive doses should be at least 8 hours. May be used with or without corticosteroids</td>
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<tr>
<td><strong>Immune Checkpoint Inhibitor related inflammatory arthritis</strong></td>
<td>4 mg/kg IV once</td>
<td>800 units for one course of therapy</td>
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<tr>
<td><strong>NMOSD</strong></td>
<td>8 mg/kg intravenously, every 4 weeks</td>
<td>800 units every 28 days</td>
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</tbody>
</table>
**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:

<table>
<thead>
<tr>
<th>HCPCS/CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J3262</td>
<td>Injection, tocilizumab, 1 mg</td>
</tr>
</tbody>
</table>

**References:**
   https://www.nice.org.uk/guidance/ta195/resources/adalimumab-eterancept-infliximabrituximab-
   and-abatacept-for-the-treatment-of-rheumatoid-arthritis-after-the-failure-of-tatnf-inhibitor-pdf-
   82598558287813.