POLICY Document for ACTEMRA

The overall objective of this policy is to support the appropriate and cost effective use of the medication, specific to use of preferred medication options, lower cost site of care and overall clinically appropriate use. This document provides specific information to each of the three sections of the overall policy.

Section 1: Preferred Product
- Policy information specific to preferred medications

Section 2: Site of Care
- Policy information specific to site of care (outpatient, hospital outpatient, home infusion)

Section 3: Clinical Criteria
- Policy information specific to the clinical appropriateness for the medication

Section 1: Preferred Product

EXCEPTIONS CRITERIA
DISEASE-MODIFYING ANTIRHEUMATIC DRUGS FOR AUTOIMMUNE CONDITIONS

I. PREFERRED PRODUCTS: ORENCIA, REMICADE, SIMPONI ARIA

This prior authorization program informs prescribers of preferred autoimmune products for treatment of plaque psoriasis, inflammatory joint related conditions, or inflammatory bowel disease. The prior authorization process evaluates if a clinical exception exists for use of a non-preferred autoimmune drug for these specific conditions. Coverage for a non-preferred autoimmune drug is provided when all preferred drugs have been tried, and either are not tolerated, ineffective, or contraindicated for the patient.

II. PLAN DESIGN SUMMARY

This program applies to non-preferred autoimmune products used in the treatment of plaque psoriasis, inflammatory joint related conditions, or inflammatory bowel disease. Coverage for targeted products (those which are non-preferred and not covered for the prescribed indication) is provided based on clinical circumstances that would exclude the use of the preferred product(s) for the indication. For plaque psoriasis indication, this program does not apply to members currently receiving therapy with a non-preferred product for which there is no preferred product in the same

subclass (e.g., interleukin antagonist). For inflammatory joint or bowel disease indications, coverage for the non-preferred product will continue in situations where the patient is currently receiving treatment.

Each PA request is reviewed based on all utilization management (UM) programs implemented.

Table. Disease-modifying antirheumatic drugs for autoimmune conditions

	Products*
Preferred	• **Orencia** (abatacept) • **Remicade** (infliximab) • **Simponi Aria** (golimumab, intravenous)
Non-Preferred	• **Actemra** (tocilizumab) • **Cimzia** (certolizumab pegol) • **Entyvio** (vedolizumab) • **Inflectra** (infliximab-dyyb) • **Stelara** (ustekinumab)

*If applicable for approved indication

III. EXCEPTION CRITERIA

A. Coverage for a non-preferred product is provided when ANY of the following criteria are met:

1. Member has had an inadequate response to treatment with a preferred product
2. Member has experienced an intolerable adverse event to all applicable preferred products
3. For indications where Remicade is the only preferred product option (i.e., Crohn's disease, ulcerative colitis, etc.), member has a contraindication to therapy with Remicade (i.e., moderate to severe heart failure defined as NYHA Functional Class III to IV or risk of lymphoma or serious injection) *(Note: does not apply to Inflectra)*
4. Member is currently receiving therapy with the requested product through insurance (excludes obtainment as samples or via manufacturer's patient assistance programs) and has received at least a 28-day supply within the past 90 days

Section 2: Site of Care

GUIDELINES FOR HOSPITAL OUTPATIENT SPECIALTY MEDICATION INFUSION

I. INTRODUCTION

There is a wide variation in the site-of-service utilization patterns for specific medications and therapy classes. This is driven by several factors. Some of these specialty medications are derived from pooled blood plasma, and therefore have the potential for an increased risk of infusion-related complications. These differences can affect patient tolerance and a physician's decision to utilize a more acute site of care such as the outpatient hospital. However, many patients that have been established on this treatment with one to several infusions safely administered may be candidates for infusions in a less acute lower-cost site of care.
Outpatient hospital infusion costs may be 2-3 times more compared to other sites of care suggesting an immediate opportunity exists for lowering spend on select specialty medications that require infusion.
Services for patients requiring infused specialty medications may be provided through a physician's in office infusion program or free standing ambulatory infusion center. These options provide access to quality care at a lower cost that may be more convenient for the patient. In addition, many patients who receive home or in office infusion therapy have been shown to experience better outcomes, fewer complications and, improved quality of life and preference, including more personalized attention which helps avoid stress.

This document describes the medical necessity criteria required for hospital outpatient infusion of the medications included in this policy.

II. GENERAL REQUIREMENTS: OUTPATIENT MEDICAL NECESSITY

Infusion in a hospital outpatient setting may be considered medically necessary for medications included in this policy when the criteria below OR individual medication policy criteria are met as outlined section III.

A. Clinical documentation that supports one or more of the following:

1. History of repeated moderate adverse reactions not responding to conventional interventions OR,
2. Laboratory confirmation of autoantibody development
3. The patient is medically unstable which may include respiratory, cardiovascular, or renal conditions that may predispose the member to a severe adverse event that cannot be managed in an alternate setting without appropriate medical personnel and equipment.
4. The patient has previously experienced a severe adverse event during or immediately after an infusion including but not limited to: anaphylaxis, anaphylactoid reactions, myocardial infarction, thromboembolism, or seizures.
5. Significant venous access issues requiring phlebotomy

B. Patient specific criteria that meets the following:

1. All alternate non-hospital outpatient settings are not within a reasonable distance from the member's home (10-30miles) AND,
2. The patient's home has been determined to be inappropriate for home infusion by a social worker, case manager or previous home nurse assessment or home infusion services are not available due to limited network access

III. MEDICATION SPECIFIC CRITERIA FOR HOSPITAL OUTPATIENT MEDICAL NECESSITY

In addition to the general criteria in Section II, the following guidelines will be applied:

A. TOCILIZUMAB
One or more of the following criteria must be met:

1. To determine tolerance of the therapy, the first two infusions may be permitted in the hospital outpatient setting.
2. Pediatric patients who are less than 21 years of age. The use of non-hospital based alternate site infusion services are at the discretion of the prescribing physician.
3. Patients who have experienced moderate infusion reactions including hypertension, hypotension, tachycardia, syncope, etc that have not responded to standard interventions including infusion rate adjustment and premedication.

IV. GENERAL CONSIDERATIONS: HOME INFUSION

Home Infusion therapy has the potential to deliver cost-effective, quality care.
Efforts to support patients who can receive infused medications care in a lower-cost setting versus an inpatient or clinic-based setting seems appealing, particular if that lower-cost setting is the patient's home.
The home infusion provider will complete an assessment to determine the appropriateness of a patient, caregiver if applicable, and their home prior to initiating care. This assessment may include an evaluation of the following:

A. Accessibility to 911 services and urgent care. Volunteer services may be acceptable if urgent care is readily available.
B. Adequate refrigeration is available if required.
C. Home is not located in a high crime area as determined by local authorities
D. Home environment does not meet general cleanliness standards determined by onsite home nursing assessment

V. BACKGROUND

Therapeutic monoclonal antibodies are laboratory-engineered substances that recognize and bind to a protein on the surface of a cell. Each mAB recognizes a different protein, or antigen. mAB's may be administered alone, in combination with other drugs, or as a carrier of agents. There are four types of antibodies defined by their source: Murine, chimeric (30:70 ratio of mouse to human sequences), humanized (~90% human sequences) and human. Monoclonal antibodies induce

moderate acute infusion reactions in 5-10% of patients. Reactions may occur with any dose of therapy; however, they are more common with the first two doses. The mAB's with the highest risk include murine and chimeric. The humanized and human mAB's carry a lesser risk because they carry fewer non-human components.

Tocilizumab is an interleukin-6 receptor inhibitor indicated in adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more disease-modifying antirheumatic drug (DMARD) therapies. Tocilizumab may be used as monotherapy or may be combined with methotrexate or other DMARDs. Tocilizumab is indicated as monotherapy or in combination with methotrexate for the treatment of active systemic juvenile idiopathic arthritis in children age 2 years and older.

Serious adverse reactions that have been reported include: gastrointestinal perforation, decreased platelet count (1% to 4%), neutropenia (rheumatoid arthritis, 1.8% to 3.7%; polyarticular or systemic juvenile idiopathic arthritis, 3.7% to 17%), anaphylaxis, hypersensitivity reaction (0% to 0.9%), opportunistic infection, tuberculosis, upper respiratory infection (rheumatoid arthritis, 6% to 8%; systemic juvenile idiopathic arthritis, 5% or higher), cancer, and severe infectious disease.
Infusion reactions have been reported as follows: (Rheumatoid arthritis, 7% to 8%; polyarticular juvenile idiopathic arthritis, 16% to 20.2%)

Section 3: Clinical Criteria

ACTEMRA (tocilizumab)

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Moderately to severely active rheumatoid arthritis
2. Active polyarticular juvenile idiopathic arthritis
3. Active systemic juvenile idiopathic arthritis
4. Giant cell arteritis

B. Compendial Uses
1. Unicentric Castleman's disease
2. Multicentric Castleman's disease

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Moderately to severely active rheumatoid arthritis (RA)

1. Authorization of 24 months may be granted for members who have received Actemra or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Actemra.

2. Authorization of 24 months may be granted for treatment of moderately to severely active RA when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week).
   b. Member has an intolerance or contraindication to methotrexate (see Appendix).

B. Active Polyarticular Juvenile Idiopathic Arthritis (pJIA)

1. Authorization of 24 months may be granted for members who have received Actemra or Orencia in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Actemra.

2. Authorization of 24 months may be granted for treatment of active pJIA when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least a 3-month trial of a TNF inhibitor (e.g., Enbrel, Humira, or Remicade).
   b. Member has experienced an intolerable adverse event or has contraindication to a TNF inhibitor.

C. Active Systemic Juvenile Idiopathic Arthritis (sJIA)

1. Authorization of 24 months may be granted for members who have received Actemra or Kineret in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Actemra.
2. Authorization of 24 months may be granted for treatment of active sJIA when any of the following criteria is met:
   a. Member has an inadequate response to at least a 2-week trial of corticosteroids.
   b. Member has an inadequate response to at least a 3-month trial of methotrexate or leflunomide.

D. Giant Cell Arteritis

1. Authorization of 12 months may be granted for treatment of giant cell arteritis.

E. Unicentric and Multicentric Castleman's Disease

1. Authorization of 12 months may be granted for treatment of unicentric or multicentric Castleman's disease.

III. CONTINUATION OF THERAPY

A. Rheumatoid Arthritis, Polyarticular Juvenile Idiopathic Arthritis and Systemic Juvenile Idiopathic

Authorization of 24 months may be granted for all members (including new members) who meet all initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Actemra as evidenced by low disease activity or improvement in signs and symptoms of the condition.

B. Giant Cell Arteritis

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

C. Unicentric and Multicentric Castleman's Disease

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

IV. OTHER

For all indications: Member has a pretreatment tuberculosis (TB) screening with a TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB)

Note: Members who have received Actemra or any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) in a paid claim through a pharmacy or medical benefit within the previous 120 days of the continuation request are exempt from requirements related to TB screening in this Policy.

Actemra for subcutaneous administration is not FDA-approved for pJIA or sJIA and will not be authorized for these conditions.

V. APPENDIX

A. Examples of Contraindications to Methotrexate

1. Alcoholism, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction

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SECTION 1

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SECTION 3

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