Effective Date **7/15/2024**
Coverage Policy Number **IP0228**

Tocilizumab Intravenous

Table of Contents

Related Coverage Resources

COVID-19 Drug and Biologic Therapeutics - (2016)
Oncology Medications - (1403)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for the following tocilizumab intravenous products:

- Actemra® (tocilizumab intravenous infusion)
- Tyenne® (tocilizumab-aazg intravenous infusion)

The use of intravenous tocilizumab in COVID-19 is addressed in a separate coverage policy. Refer to the related coverage policy link above (COVID-19 Drug and Biologic Therapeutics).

The use of intravenous tocilizumab for oncology indications (for example, Castleman's disease) is addressed in a separate coverage policy. Refer to the related coverage policy link above (Oncology Medications).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Tocilizumab (Actemra, Tyenne) intravenous is considered medically necessary when ONE of the following is met (1, 2, 3, 4, 5, 6, 7 or 8):

1. **Cytokine Release Syndrome Associated with Chimeric Antigen Receptor (CAR) T-Cell Therapy.**

   Examples of CAR T-cell therapy include Abecma (idecabtagene vicleucel injection), Breyanzi (lisocabtagene maraleucel intravenous infusion), Kymriah (tisagenlecleucel intravenous infusion), Tecartus (brexucabtagene intravenous infusion), and Yescarta (axicabtagene ciloleucel intravenous infusion).

   If the patient has Cytokine Release Syndrome due to COVID-19 (coronavirus disease 2019) refer to related coverage policy link above (COVID-19 Drug and Biologic Therapeutics).

2. **Giant Cell Arteritis.** Individual meets **ALL** of the following criteria (A, B and C):
   A. Individual is 18 years of age or older
   B. Medication is being prescribed by, or in consultation with, a rheumatologist or a prescriber who specializes in Giant Cell Arteritis
   C. Documented inadequate response, contraindication or intolerance to **ONE** systemic corticosteroid (for example, prednisone)

3. **Inflammatory Arthritis Associated with Checkpoint Inhibitor Therapy.** Individual meets the **ALL** of the following criteria (A, B, C and D):
   A. Individual developed inflammatory arthritis while receiving a checkpoint inhibitor

      For example, Keytruda (pembrolizumab IV infusion), Opdivo (nivolumab IV infusion), Yervoy (ipilimumab IV infusion), Tecentriq (atezolizumab IV infusion), Bavencio (avelumab IV infusion), Imfinzi (durvalumab IV infusion), Libtayo® (cemiplimab-rwlc intravenous infusion).

   B. Documented inadequate response, contraindication or intolerance to **ONE** systemic corticosteroid (for example, methylprednisolone, prednisone)
   C. Documented inadequate response, contraindication or intolerance to **ONE** nonsteroidal anti-inflammatory drug (NSAID) [for example, ibuprofen, naproxen]
   D. Medication is prescribed by, or in consultation with, a rheumatologist or an oncologist

4. **Polyarticular Juvenile Idiopathic Arthritis.** Individual meets the following criteria (A):
   A. Medication is being prescribed by, or in consultation with, a rheumatologist or a prescriber who specializes in polyarticular juvenile idiopathic arthritis

5. **Polymyalgia Rheumatica**. Individual meets **ALL** of the following criteria (A, B and C):
   A. Individual is 18 years of age or older
   B. Medication is prescribed by, or in consultation with, a rheumatologist or a prescriber who specializes in Polymyalgia Rheumatica
   C. Documentation of an inadequate response, contraindication or intolerance to **ONE** systemic corticosteroid (for example, prednisone)

6. **Rheumatoid Arthritis.** Individual meets **ALL** of the following criteria (A, B and C):
   A. Individual is 18 years of age or older
   B. Medication is being prescribed by, or in consultation with, a rheumatologist or a prescriber who specializes rheumatoid arthritis
   C. Documentation of **ONE** of the following:
      i. Individual has had an inadequate response to **ONE** conventional synthetic disease-modifying anti-rheumatic drug (csDMARD) [for example, methotrexate, hydroxychloroquine, leflunomide, sulfasalazine]
      ii. Individual has a contraindication or intolerance to csDMARD therapy

iii. Individual has already tried a biologic or targeted synthetic DMARD for Rheumatoid Arthritis

Refer to the Appendix for biologics and tsDMARDs used for Rheumatoid Arthritis

7. **Systemic Juvenile Idiopathic Arthritis.** Individual meets the following criteria (A):
   A. Medication is prescribed by, or in consultation with, a rheumatologist or a prescriber who specializes in Systemic Juvenile Idiopathic Arthritis

8. **Still's Disease.** Individual meets **ALL** of the following criteria (A, B, and C):
   A. Individual is 18 years of age or older
   B. Medication is prescribed by, or in consultation with, a rheumatologist or a prescriber who specializes in Still's Disease
   C. **EITHER** of the following (i or ii):
      i. **BOTH** of the following (a and b):
         a. Documented inadequate response, contraindication or intolerance to **ONE** corticosteroid (for example, prednisone)
         b. Documented inadequate response after at least 2 months, contraindication or intolerance to **ONE** conventional synthetic disease-modifying antirheumatic drug (csDMARD) [for example, methotrexate]
      ii. Individual has already tried a biologic for Still's Disease

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Tocilizumab (Actemra, Tyenne) intravenous is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Examples of a response include:

1. **Cytokine Release Syndrome Associated with Chimeric Antigen Receptor (CAR) T-Cell Therapy**: Not applicable for continuation beyond initial approval duration.

2. **Giant Cell Arteritis:** improvement in serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), resolution of fever, and/or reduced dosage of corticosteroids.

3. **Inflammatory Arthritis Associated with Checkpoint Inhibitor Therapy:** Less joint pain, morning stiffness, or fatigue, improved function or activities of daily living, decreased soft tissue swelling in joints or tendon sheaths, improved laboratory values, reduced dosage of corticosteroids.

4. **Polyarticular Juvenile Idiopathic Arthritis:** Improvement in limitation of motion; less joint pain or tenderness; improved function or activities of daily living; decreased duration of morning stiffness or fatigue; reduced dosage of corticosteroids; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values.

5. **Polymyalgia Rheumatica**: decreased shoulder, neck, upper arm, hip, or thigh pain or stiffness; improved range of motion; and/or decreased fatigue, improvement in serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), resolution of fever, or reduced dosage of corticosteroids.

6. **Rheumatoid Arthritis.** Less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values; reduced dosage of corticosteroids.

7. **Systemic Juvenile Idiopathic Arthritis:** Improvement in limitation of motion; less joint pain or tenderness; improved function or activities of daily living; decreased duration of morning stiffness or fatigue; reduced dosage of corticosteroids; decreased soft tissue swelling in joints or tendon sheaths; improved laboratory values.

8. **Still's Disease:** resolution of fever, improvement in rash or skin manifestations, clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), reduced dosage of corticosteroids, less joint pain/tenderness, stiffness, or swelling, decreased fatigue and/or improved function or activities of daily living.

Authorization Duration

Initial approval duration:
- **Cytokine Release Syndrome Associated with Chimeric Antigen Receptor (CAR) T-Cell Therapy**: 1 week (4 doses only)
- For **ALL** other covered uses: up to 12 months

Reauthorization approval duration:
- **Cytokine Release Syndrome Associated with Chimeric Antigen Receptor (CAR) T-Cell Therapy**: Not applicable for continuation beyond initial approval duration
- For **ALL** other covered uses: up to 12 months

Conditions Not Covered

Tocilizumab (Actemra, Tyenne) intravenous is considered experimental, investigational or unproven for **ANY** other use including the following (this list may not be all inclusive):

1. **Concurrent Use with a Biologic or with a Targeted Synthetic Disease-Modifying Antirheumatic Drug (tsDMARD).** Data are lacking evaluating concomitant use of tocilizumab intravenous in combination with another biologic or with a targeted synthetic DMARD used for an inflammatory condition (see Appendix for examples). Combination therapy with another biologic or targeted synthetic DMARD has the potential for higher rate of adverse effects and lack of controlled trial data in support of additive efficacy.[21-22]

   This does NOT exclude the use of conventional synthetic DMARDs (e.g., methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with tocilizumab intravenous.

2. **Crohn's Disease.** In a 12-week pilot study conducted in Japan, 36 adults with active Crohn's disease (Crohn's Disease Activity Index [CDAI] at least 150 and increased C-reactive protein) were randomized, in a double-blind fashion to tocilizumab 8 mg/kg intravenous every 2 weeks; or alternating infusions of tocilizumab 8 mg/kg every 4 weeks and placebo (i.e., alternating with placebo every 2 weeks), or to placebo every 2 weeks.23 At baseline the CDAI means ranged from 287 to 306. Patients had been treated with corticosteroids, mesalamine-type drugs, metronidazole, or elemental diet. Six patients in the placebo group, four patients on tocilizumab intravenous every 4 weeks and one patient on tocilizumab intravenous every 2 weeks dropped out. The mean reduction in the CDAI score in the tocilizumab 8 mg/kg every 2 week group was 88 points (from mean 306 to 218). Further studies are needed.

Coding / Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J3262	Injection, tocilizumab, 1 mg

Background

Overview
Tocilizumab intravenous infusion, an interleukin-6 (IL-6) receptor inhibitor, is indicated for the following conditions:[1]

- **Coronavirus Disease 2019 (COVID-19)**, in hospitalized adults who are receiving systemic corticosteroids and require supplemental oxygen, non-invasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation (ECMO).
- **Cytokine release syndrome**, in patients ≥ 2 years of age with severe or life-threatening disease associated with chimeric antigen receptor (CAR) T-cell therapy.
- **Giant cell arteritis** in adults.
- **Polyarticular juvenile idiopathic arthritis**, for the treatment of active disease in patients ≥ 2 years of age.
- **Rheumatoid arthritis**, for treatment of adults with moderate to severe active disease who have had an inadequate response to one or more disease modifying antirheumatic drugs (DMARDs).
- **Systemic juvenile idiopathic arthritis**, for the treatment of active disease in patients ≥ 2 years of age.

Dosing Information
In rheumatoid arthritis, many dose modifications are recommended for the management of dose-related laboratory changes such as increased liver enzymes, neutropenia, and thrombocytopenia.[1] In conditions other than rheumatoid arthritis, reduced dosing of tocilizumab intravenous generally follows the recommendations for rheumatoid arthritis. Dose interruptions of tocilizumab intravenous are recommended for certain laboratory abnormalities and are similar to those recommended in rheumatoid arthritis. Dosing modifications are determined by the prescriber. Specifically for cytokine release syndrome associated with CAR T-cell therapy, the median number of tocilizumab intravenous doses administered in the pivotal trial was one dose (range, 1 to 4 doses).

Guidelines/Clinical Efficacy
IL-6 blockers are mentioned in multiple guidelines for treatment of inflammatory conditions. Clinical data also support use of tocilizumab in other conditions.

- **Cytokine Release Syndrome:** The National Comprehensive Cancer Network (NCCN) clinical practice guidelines for Management of Immunotherapy-Related Toxicities (version 1.2024 – December 7, 2023) give specific recommendations for use of tocilizumab in the management of inflammatory arthritis, cytokine release syndrome, and CAR T-cell-related toxicities.[6]
    - For cytokine release syndrome and CAR T-cell-related toxicities, tocilizumab is recommended for all grades of disease.
    - For immune checkpoint inhibitor-related inflammatory arthritis, infliximab and tocilizumab are among the alternatives that may be considered for severe arthritis not responding to steroids.
- **Giant Cell Arteritis and Polymyalgia Rheumatica:** Recommendations from the European League Against Rheumatism (EULAR) [2023] state the diagnosis of giant cell arteritis may be made without biopsy if there is a high suspicion of giant cell arteritis and a positive imaging test.[25] In the pivotal trial evaluating tocilizumab subcutaneous for giant cell arteritis (n = 251), patients were treated with

corticosteroids in an open-label fashion (20 mg to 60 mg/day) during the screening period prior to treatment with tocilizumab subcutaneous.[31,32] Sustained remission at Week 52 was achieved in 56% of patients who received tocilizumab subcutaneous every week + 26-week prednisone taper and 53% of patients who received Actemra every other week + 26-week prednisone taper vs. in 14% of patients in the 26-week prednisone taper and 18% of patients in the 52-week prednisone taper.

- **Polyarticular Juvenile Idiopathic Arthritis:** Guidelines for the treatment of juvenile idiopathic arthritis from the American College of Rheumatology (ACR) [2021] address oligoarthritis and temporomandibular joint (TMJ) arthritis.[31] For oligoarthritis, a biologic is recommended following a trial of a conventional synthetic DMARD. In patients with TMJ arthritis, scheduled nonsteroidal anti-inflammatory drugs (NSAIDs) and/or intra-articular glucocorticoids are recommended first-line. A biologic is a therapeutic option if there is an inadequate response or intolerance. Additionally, rapid escalation to a biologic ± conventional synthetic DMARD (methotrexate preferred) is often appropriate given the impact and destructive nature of TMJ arthritis. In these guidelines, there is not a preferred biologic that should be initiated for JIA. ACR/Arthritis Foundation has guidelines for the treatment of juvenile idiopathic arthritis (2019) specific to juvenile non-systemic polyarthritis, sacroiliitis, and enthesitis.[7] For patients without risk factors, initial therapy with a DMARD is conditionally recommended over a biologic (including tocilizumab). Biologics (e.g., Actemra) are conditionally recommended as initial treatment when combined with a DMARD over biologic monotherapy.
- **Rheumatoid Arthritis:** Guidelines from ACR (2021) recommend addition of a biologic or a targeted synthetic DMARD for a patient taking the maximum tolerated dose of methotrexate who is not at target.[9]
- **Systemic Juvenile Idiopathic Arthritis:** Guidelines for the treatment of JIA from the ACR (2021) address systemic juvenile idiopathic arthritis (SJIA).[8] A brief trial of NSAIDs and/or an interleukin (IL)-1 or IL-6 inhibitor are recommended as initial monotherapy for patients with SJIA without macrophage activation syndrome. In a patient who presents with macrophage activation syndrome, an IL-1 or IL-6 blocker and/or systemic glucocorticoids are recommended.
- **Castleman's Disease:** The NCCN clinical practice guidelines for Castleman Disease (version 1.2024 – January 18, 2024) mention tocilizumab as a second-line therapy for relapsed or refractory unicentric Castleman disease in patients who are negative for the human immunodeficiency virus and human herpesvirus-8.[10] For multicentric Castleman's disease, the guidelines list tocilizumab as a subsequent therapy for relapsed, refractory, or progressive disease.
- **COVID-19 (Coronavirus Disease 2019):** By inhibiting IL-6, tocilizumab is speculated to be associated with better clinical outcomes in COVID-19, such as decreased systemic inflammation, improved survival rate, better hemodynamics, and improvement of respiratory distress.[24]
- **Still's Disease:** Still's disease presents in adults with features similar to those of SJIA.[11] Tocilizumab IV has been effective in reducing fever, symptoms, and markers of inflammation in patients who were refractory to treatment with prednisone, methotrexate, Kineret, and/or a tumor necrosis factor inhibitor.[11-20]

Actemra intravenous infusion, an interleukin-6 (IL-6) receptor inhibitor, is indicated for the following conditions:[1]

- **Cytokine release syndrome**, in patients greater than or equal to 2 years of age with severe or life-threatening disease associated with chimeric antigen receptor (CAR) T-cell therapy.
- **Giant cell arteritis** in adults.
- **Polyarticular juvenile idiopathic arthritis**, for the treatment of active disease in patients greater than or equal to 2 years of age.
- **Rheumatoid arthritis**, for treatment of adults with moderate to severe active disease who have had an inadequate response to one or more disease modifying antirheumatic drugs (DMARDs).
- **Systemic juvenile idiopathic arthritis**, for the treatment of active disease in patients greater than or equal to 2 years of age.

Dosing Information

In rheumatoid arthritis, many dose modifications are recommended for the management of dose-related laboratory changes such as increased liver enzymes, neutropenia, and thrombocytopenia.[1] In conditions other than rheumatoid arthritis, reduced dosing of Actemra intravenous generally follows the recommendations for rheumatoid arthritis. Dose interruptions of Actemra intravenous are recommended for certain laboratory abnormalities and are similar to those recommended in rheumatoid arthritis. Dosing modifications are determined by the prescriber. Specifically for cytokine release syndrome associated with CAR T-cell therapy,

the median number of Actemra intravenous doses administered in the pivotal trial was one dose (range, 1 to 4 doses).

Cytokine Release Syndrome Associated with Chimeric Antigen Receptor (CAR) T-Cell Therapy
- Patient is < 30 kg: Up to 12 mg/kg to a maximum of 800 mg per dose
- Patient is ≥ 30 kg: Up to 8 mg/kg to a maximum of 800 mg per dose
- Interval of at least 8 hours between doses

Giant Cell Arteritis
- Up to 6 mg/kg to a maximum of 600 mg per dose
- Interval of at least 4 weeks between doses

Inflammatory Arthritis Associated with Checkpoint Inhibitor Therapy
- Up to 8 mg/kg to a maximum of 800 mg per dose
- Interval of at least 4 weeks between doses

Polymyalgia Rheumatica
- Up to 6 mg/kg to a maximum of 600 mg per dose
- Interval of at least 4 weeks between doses

Polyarticular Juvenile Idiopathic Arthritis
- Patient is < 30 kg: Up to 10 mg/kg up to a maximum of 800 mg per dose
- Patient is ≥ 30 kg: Up to 8 mg/kg up to a maximum of 800 mg per dose
- Interval of at least 4 weeks between doses

Rheumatoid Arthritis
- Up to 8 mg/kg to a maximum of 800 mg per dose
- Interval of at least 4 weeks between doses

Systemic Juvenile Idiopathic Arthritis
- Patient is < 30 kg: Up to 12 mg/kg per dose
- Patient is ≥ 30 kg: Up to 8 mg/kg per dose
- Interval of at least 1 week between doses

Still's Disease
- Up to 8 mg/kg per dose
- Interval of at least 2 weeks between doses

Guidelines/Clinical Efficacy
IL-6 blockers are mentioned in multiple guidelines for treatment of inflammatory conditions. Clinical data also support use of Actemra in other conditions.

- **Cytokine Release Syndrome:** The National Comprehensive Cancer Network (NCCN) clinical practice guidelines for Management of Immunotherapy-Related Toxicities (version 1.2022 – February 22, 2022) give specific recommendations for use of Actemra in the management of inflammatory arthritis, cytokine release syndrome, and CAR T-cell-related toxicities.[6]
  - For cytokine release syndrome and CAR T-cell-related toxicities, Actemra is recommended for all grades of disease.
  - For immune checkpoint inhibitor-related inflammatory arthritis, infliximab and Actemra are among the alternatives that may be considered for refractory or severe arthritis not responding to steroids.

- **Giant Cell Arteritis and Polymyalgia Rheumatica:** Recommendations from the European League Against Rheumatism (EULAR) [2018] state the diagnosis of giant cell arteritis may be made without biopsy if there is a high suspicion of giant cell arteritis and a positive imaging test.[31] In the pivotal trial

evaluating Actemra subcutaneous for giant cell arteritis (n = 251), patients were treated with corticosteroids in an open-label fashion (20 mg to 60 mg/day) during the screening period prior to treatment with Actemra subcutaneous.[32-33] Sustained remission at Week 52 was achieved in 56% of patients who received Actemra subcutaneous every week + 26-week prednisone taper and 53% of patients who received Actemra every other week + 26-week prednisone taper vs. in 14% of patients in the 26-week prednisone taper and 18% of patients in the 52-week prednisone taper.

- **Polyarticular Juvenile Idiopathic Arthritis:** Guidelines for the treatment of JIA from the American College of Rheumatology (ACR) [2021] address oligoarthritis and temporomandibular joint (TMJ) arthritis.[31] For oligoarthritis, a biologic is recommended following a trial of a conventional synthetic DMARD. In patients with TMJ arthritis, scheduled nonsteroidal anti-inflammatory drugs (NSAIDs) and/or intra-articular glucocorticoids are recommended first-line. A biologic is a therapeutic option if there is an inadequate response or intolerance. Additionally, rapid escalation to a biologic ± conventional synthetic DMARD (methotrexate preferred) is often appropriate given the impact and destructive nature of TMJ arthritis. In these guidelines, there is not a preferred biologic that should be initiated for JIA. ACR/Arthritis Foundation has guidelines for the treatment of juvenile idiopathic arthritis (2019) specific to juvenile non-systemic polyarthritis, sacroiliitis, and enthesitis.[7] For patients without risk factors, initial therapy with a DMARD is conditionally recommended over a biologic (including Actemra). Biologics (e.g., Actemra) are conditionally recommended as initial treatment when combined with a DMARD over biologic monotherapy.

- **Rheumatoid Arthritis:** Guidelines from ACR (2021) recommend addition of a biologic or a targeted synthetic DMARD for a patient taking the maximum tolerated dose of methotrexate who is not at target.[9]

- **Systemic Juvenile Idiopathic Arthritis:** Guidelines for the treatment of JIA from the ACR (2021) address systemic juvenile idiopathic arthritis (SJIA).[31] A brief trial of NSAIDs and/or an interleukin (IL)-1 or IL-6 inhibitor are recommended as initial monotherapy for patients with SJIA without macrophage activation syndrome. In a patient who presents with macrophage activation syndrome, an IL-1 or IL-6 blocker and/or systemic glucocorticoids are recommended.

- **Stills Disease:** Still's disease presents in adults with features similar to those of SJIA.[11] Actemra IV has been effective in reducing fever, symptoms, and markers of inflammation in patients who were refractory to treatment with prednisone, methotrexate, Kineret, and/or a tumor necrosis factor inhibitor.[11-20]

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APPENDIX

Table 1. Approved TNFis for Targeted Indications.

	Rheumatology					Dermatology	Gastroenterology	
	RA	JIA	AS	nr-axSpA	PsA	PsO	CD	UC
Tumor Necrosis Factor Inhibitors								
Cimzia	√	--	√	√	√	√	√	--
Enbrel	√	√	√	--	√	√	--	--
Humira	√	√	√	--	√	√	√	√
Infliximab Products	√	--	√	--	√	√	√	√
Simponi Subcutaneous	√	--	√	--	√	--	--	√
Simponi Aria	√	√	√	--	√	--	--	--

TNFis – Tumor necrosis factor inhibitors; RA – Rheumatoid arthritis; JIA – Juvenile idiopathic arthritis; AS – Ankylosing spondylitis; nr-axSpA – Non-radiographic spondyloarthritis; PsA – Psoriatic arthritis; PsO – Plaque psoriasis; CD – Crohn's disease; UC – Ulcerative colitis.

Table 2. Approved IL-17, IL-23, and IL-12/23 Blockers for Targeted Indications.

	Rheumatology				Dermatology		Gastroenterology	
	Ankylosing Spondylitis	ERA	nr-axSpA	PsA	AD	Plaque Psoriasis	Crohn's Disease	Ulcerative Colitis
Interleukin-13 Blocker								
Adbry	--	--	--	--	√	--	--	--
Interleukin-17 Blockers								
Cosentyx	√	√	√	√	--	√	--	--
Siliq	--	--		--	--	√	--	--
Taltz	√	--	√	√	--	√	--	--
Interleukin-23 Blockers								
Ilumya	--	-- --	--	--	--	√	--	--
Skyrizi	--	--	--	√	--	√	√	--
Tremfya	--	--	--	√	--	√	--	--
Interleukin-12/23 Blockers								
Stelara Subcutaneous	--	--	--	√	--	√	√^	√^
Stelara Intravenous	--	--	--	--	--	--	√#	√#

AD - Atopic Dermatitis, ERA - Enthesitis-Related Arthritis, IL – Interleukin; nr-axSpA – Non-radiographic spondyloarthritis; ^ Maintenance dosing only; # Induction dosing only.

Table 3. Approved Oral tsDMARDs for Targeted Indications.

	Rheumatology				Dermatology		Gastro-enterology
	Rheumatoid Arthritis	Juvenile Idiopathic Arthritis	Ankylosing Spondylitis	Psoriatic Arthritis	Atopic Dermatitis	Plaque Psoriasis	Ulcerative Colitis
	Janus Kinases Inhibitors						
Cibinqo	--	--	--	--	√	--	--
Olumiant	√	--	--	--	--	--	--
Rinvoq	√	--	√	√	√	--	√
Xeljanz tablets	√	√#	√	√	--	--	√
Xeljanz oral solution	--	√#	--	--	--	--	--
Xeljanz XR	√	--	√	√	--	--	√
Phosphodiesterase Type 4 Inhibitor							
Otezla	--	--	--	√	--	√	--
Sphingosine 1-Phosphate Receptor Modulator							
Zeposia	--	--	--	--	--	--	√

tsDMARDs – Targeted synthetic disease-modifying antirheumatic drugs; # Indicated in polyarticular JIA.

Table 4. Other Approved Biologics for Targeted Indications.

	Rheumatology		
	Rheumatoid Arthritis	**Juvenile Idiopathic Arthritis**	**Psoriatic Arthritis**
Interleukin-6 Blockers			
Actemra Intravenous	√	√^	--
Actemra Subcutaneous	√	√^	--
Kevzara	√	--	--
Interleukin-1 Blocker			
Kineret	√	--	--
T-Cell Costimulation Modulator			
Orencia Intravenous	√	√#	√
Orencia Subcutaneous	√	√#	√
CD20-Directed Cytolytic Antibody			
Rituximab Intravenous Products	√	--	--

^ Indicated in polyarticular and systemic JIA; # Indicated in polyarticular JIA.