



PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Kineret Prior Authorization

- Kineret® (anakinra subcutaneous injection – Swedish Orphan Biovitrim)

REVIEW DATE: 02/26/2025; selected revision 04/23/2025

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. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. 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.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Kineret, an interleukin-1 (IL-1) blocker, is indicated for the following uses:¹

- **Cryopyrin-associated periodic syndromes (CAPS)**, for treatment of neonatal-onset multisystem inflammatory disease (NOMID).
- **Deficiency of interleukin-1 receptor antagonist (DIRA)** treatment.
- **Rheumatoid arthritis**, to reduce the signs and symptoms and slow the progression of structural damage with moderately to severely active disease in adults who have failed one or more disease-modifying antirheumatic drugs (DMARDs); Kineret can be used ± DMARDs, other than tumor necrosis factor inhibitors (TNFis).

Guidelines

Kineret is used for treatment of a variety of periodic fever syndromes and inflammatory conditions.

CAPS and DIRA

The European Alliance of Associations for Rheumatology (EULAR) and American College of Rheumatology (ACR) [2021] provide treatment guidelines for IL-1 mediated autoinflammatory diseases: cryopyrin-associated periodic syndromes, tumor necrosis factor receptor-associated periodic syndrome, mevalonate kinase deficiency, and deficiency of the IL-1 receptor antagonist.² Guidelines indicate IL-1 blocking therapy has become the preferred treatment and a therapeutic trial with IL-1 blocking agents may be started when strong clinical suspicion of a diagnosis of CAPS, TRAPS, MKD, or DIRA is suspected. The guidelines also provide additional diagnosis-specific treatment recommendations:

- **CAPS:** CAPS encompasses three rare genetic syndromes (familial cold autoinflammatory syndrome, Muckle-Wells syndrome, and neonatal onset multisystem inflammatory disease formerly known as chronic infantile neurological cutaneous and articular syndrome) that are thought to be one condition along a spectrum of disease severity. IL-1 blockers are recommended as standard of care across the spectrum of disease for improved symptom control and reduced systemic and tissue/organ inflammation. The dose and/or frequency of administration should be adjusted to control disease activity, normalize markers of systemic inflammation, and for appropriate weight gain and development in the growing patient. In many cases, patients with CAPS reported an immediate clinical response to Kineret with rash, fever, and arthritis disappearing within a few days and not recurring during follow-up.³ Dramatic and persistent normalization of inflammatory markers and hematologic tests have also been achieved.
- **DIRA:** DIRA is caused by recessive loss-of-function pathogenic variants in the *IL1RN* gene.² Treatment with agents that block both IL- α and IL- β is recommended and includes Kineret and Arcalyst® (rilonacept subcutaneous injection). Kineret approval for the treatment of DIRA was based on a natural-history study in nine patients (aged 1 month to 9 years at baseline) with genetically confirmed DIRA.¹ Patients were treated with Kineret for up to 10 years. All nine patients achieved remission while on Kineret for DIRA. In some patients, skin and bone manifestations resolved within days and weeks, respectively.

Rheumatoid Arthritis

Current recommendations for the treatment of rheumatoid arthritis from the American College of Rheumatology (ACR) [2021] do not make a recommendation for the use of Kineret.⁴ The recommendations also note that Kineret is used infrequently for rheumatoid arthritis and that TNFi and other non-TNFi biologics (i.e., rituximab, Actemra® [tocilizumab intravenous infusion, tocilizumab subcutaneous injection], and Orencia® [abatacept intravenous infusion, abatacept subcutaneous injection]) are appropriate initial biologic therapy for most patients with rheumatoid arthritis.

Still's disease [including Systemic Juvenile Idiopathic Arthritis (SJIA) and Still's Disease, Adult Onset (AOSD)]

The European Alliance of Associations for Rheumatology (EULAR) and Pediatric Rheumatology European Society (PReS) joint clinical guidelines for management of

Still's disease (2024) indicate SJIA and AOSD are the same disease, differing in age of onset, and can be referred to collectively as Still's disease.⁶ Guidelines recommend an IL-1 or IL-6 inhibitor be initiated as early as possible after diagnosis. No preferred agent is provided. Macrophage activation syndrome (MAS), which is a life-threatening complication of Still's disease, should be treated with high dose steroids and if needed, other treatments which includes Kineret.

Guidelines for the treatment of JIA from the ACR (2021) address SJIA.⁵ A brief trial of NSAIDs and/or an 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 MAS, an IL-1 or IL-6 blocker and/or systemic glucocorticoids are recommended.

Kineret has been effective in reducing fever, symptoms, and markers of inflammation in patients with AOSD who were refractory to conventional treatment with a corticosteroid, nonsteroidal anti-inflammatory drug (NSAID), and/or conventional synthetic DMARDs such as methotrexate.⁷⁻¹³

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Kineret. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Kineret as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Kineret to be prescribed by or in consultation with a physician who specializes in the condition being treated.

All reviews for use of Kineret for COVID-19 and/or cytokine release syndrome associated with COVID-19 will be forwarded to the Medical Director.

• **Kineret® (anakinra subcutaneous injection – Swedish Orphan Biovitrim)**
is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. Cryopyrin-Associated Periodic Syndromes (CAPS). Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets BOTH of the following (i and ii):

i. The medication is being used for treatment of familial cold autoinflammatory syndrome (FCAS), Muckle-Wells Syndrome (MWS),

and/or neonatal onset multisystem inflammatory disease (NOMID) formerly known as chronic infantile neurological cutaneous and articular syndrome (CINCA); AND

- ii. The medication is prescribed by or in consultation with a rheumatologist, geneticist, allergist/immunologist, or a dermatologist; OR

B) Patient is Currently Receiving Kineret. Approve for 1 year if the patient meets BOTH of the following (i and ii):

- i. Patient has been established on this medication for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

- ii. Patient meets at least ONE of the following (a or b):

- a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR

Note: Examples of objective measures include resolution of fever, improvement in rash or skin manifestations, clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, amyloid A), reduction in proteinuria, and/or stabilization of serum creatinine.

- b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom.

Note: Examples of improvement in symptoms include fewer cold-induced attacks; less joint pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

2. Deficiency of Interleukin-1 Receptor Antagonist. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets BOTH of the following (i and ii):

- i. Genetic testing has confirmed bi-allelic pathogenic variants in the *IL1RN* gene; AND

- ii. The medication is prescribed by or in consultation with a rheumatologist, geneticist, dermatologist, or a physician specializing in the treatment of autoinflammatory disorders; OR

B) Patient is Currently Receiving Kineret. Approve for 1 year if the patient meets BOTH of the following (i and ii):

- i. Patient has been established on this medication for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

- ii. Patient meets at least ONE of the following (a or b):

- a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR

Note: Examples of objective measures include improvement in rash or skin manifestations, clinically significant improvement or normalization

of serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), reduction in proteinuria, and/or stabilization of serum creatinine.

- b)** Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom.

Note: Examples of improvement of symptoms include improvement of skin or bone symptoms; less joint pain/tenderness, stiffness, or swelling.

3. Rheumatoid Arthritis. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):

- i.** Patient is ≥ 18 years of age; AND

- ii.** Patient has had a 3-month trial of a biologic OR targeted synthetic disease-modifying antirheumatic drug (DMARD) for this condition, unless intolerant; AND

Note: This is a 3-month trial of at least one biologic other than the requested drug. A biosimilar of the requested biologic does not count. Refer to [Appendix](#) for examples of biologics and targeted synthetic DMARDs used for rheumatoid arthritis. Conventional synthetic DMARDs such as methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine do not count.

- iii.** The medication is prescribed by or in consultation with a rheumatologist; OR

B) Patient is Currently Receiving Kineret. Approve for 1 year if the patient meets BOTH of the following (i and ii):

- i.** Patient has been established on therapy for at least 6 months; AND

Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).

- ii.** Patient meets at least ONE of the following (a or b):

- a)** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR

Note: Examples of standardized and validated measures of disease activity include Clinical Disease Activity Index (CDAI), Disease Activity Score (DAS) 28 using erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), Patient Activity Scale (PAS)-II, Rapid Assessment of Patient Index Data 3 (RAPID-3), and/or Simplified Disease Activity Index (SDAI).

- b)** Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths.

Other Uses with Supportive Evidence

4. Still's Disease, Adult Onset (AOSD). Approve for the duration noted if the patient meets ONE of the following (A or B):

Note: Adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (SJIA) are considered the same disease (Still's disease) but differ in age of onset. For a patient < 18 years of age, refer to the SIJA indication below.

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):

i. Patient is \geq 18 years of age; AND

ii. Patient meets ONE of the following (a, b, or c):

a) Patient meets BOTH of the following [(1) and (2)]:

(1) Patient has tried one corticosteroid; AND

(2) Patient has had an inadequate response to one conventional synthetic disease-modifying antirheumatic drug (DMARD) such as methotrexate given for at least 2 months or was intolerant to a conventional synthetic DMARD; OR

Note: A previous trial of one biologic (e.g., Actemra [tocilizumab intravenous injection, tocilizumab subcutaneous injection], Arcalyst [rilonacept subcutaneous injection], Ilaris [canakinumab subcutaneous injection]) other than the requested drug also counts towards a trial of one other systemic agent for Still's disease. A biosimilar of the requested biologic does not count.

b) Patient has at least moderate to severe active systemic features of this condition, according to the prescriber; OR

Note: Examples of moderate to severe active systemic features include fever, rash, lymphadenopathy, hepatomegaly, splenomegaly, and serositis.

c) Patient has active systemic features with concerns of progression to macrophage activation syndrome, as determined by the prescriber; AND

iii. The medication is prescribed by or in consultation with a rheumatologist; OR

B) Patient is Currently Receiving Kineret. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on this medication for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least ONE of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR

Note: Examples of objective measures include 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), and/or reduced dosage of corticosteroids.

b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as less joint

pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

5. Systemic Juvenile Idiopathic Arthritis (SJIA). Approve for the duration noted if the patient meets ONE of the following (A or B):

Note: Systemic juvenile idiopathic arthritis (SJIA) and adult-onset Still's disease (AOSD) are considered the same disease (Still's disease) but differ in age of onset. For a patient ≥ 18 years of age, refer to AOSD indication above.

A) Initial Therapy. Approve for 6 months if the patient meets BOTH of the following (i and ii):

- i. Patient is ≥ 2 years of age; AND
- ii. The medication is prescribed by or in consultation with a rheumatologist;
OR

B) Patient is Currently Receiving Kineret. Approve for 1 year if the patient meets BOTH of the following (i and ii):

- i. Patient has been established on this medication for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

- ii. Patient meets at least ONE of the following (a or b):

- a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR

Note: Examples of objective measures include 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), and/or reduced dosage of corticosteroids.

- b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as less joint pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

CONDITIONS NOT COVERED

Kineret® (anakinra subcutaneous injection – Swedish Orphan Biovitrim) is(are) considered not medically necessary for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

- 1. Ankylosing Spondylitis.** Kineret has been beneficial in a few patients with ankylosing spondylitis, but results are not consistent.^{14,15} In a small open-label study, patients with active ankylosing spondylitis who were refractory to NSAIDs (n = 20) received Kineret 100 mg daily.¹⁵ The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score decreased over a 6-month period but was not significant (5.8 at baseline vs. 5.0 at Week 12, and 4.8 at Week 24). No significant change was found in Bath Ankylosing Spondylitis Functional Index (BASFI) and

patients' and physicians' global assessment of general pain during the study. After 12 weeks, both the assessment in ankylosing spondylitis (ASAS) 20 and 40 responses improved in 10.5% of patients (intention-to-treat analysis). After 24 weeks, ASAS 20 was attained in 26% of patients, ASAS 40 in 21% of patients, and ASAS 70 in 10.5% of patients. Guidelines for axial spondyloarthritis from the Assessment of SpondyloArthritis International Society (ASAS)/European Union Against Rheumatism (EULAR) [2016] do not mention Kineret as a treatment option.¹⁶

- 2. Concurrent Use with a Biologic or with a Targeted Synthetic Oral Small Molecule Drug.** This medication should not be administered in combination with another biologic or with a targeted synthetic oral small molecule drug used for an inflammatory condition (see [Appendix](#) for examples). Combination therapy is generally not recommended due to a potentially higher rate of adverse events and lack of controlled clinical data supporting additive efficacy.¹⁷

Note: This does NOT exclude the use of conventional synthetic disease-modifying antirheumatic drugs (e.g., methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with this medication.

- 3. Lupus Arthritis.** The effectiveness and safety of Kineret were evaluated in an open 3-month pilot trial in patients (n = 4) with systemic lupus erythematosus (SLE) and severe, therapy-refractory non-erosive polyarthritis (three patients had deforming Jaccoud's arthropathy) and no other uncontrolled major organ involvement.¹⁸ Patients were refractory to NSAIDs, antimalarials, corticosteroids, methotrexate, cyclophosphamide, and azathioprine. SLE was controlled with stable doses of corticosteroids and/or antirheumatic or immunosuppressive agents; pain was managed with NSAIDs and/or other medications. Patients had improved clinically after 4 weeks on Kineret, but after 12 weeks, the clinical activity parameters tended to increase again. The results from this study are preliminary and a larger controlled study is needed.
- 4. Osteoarthritis.** In a Phase II study in patients with painful osteoarthritis of the knee, Kineret 150 mg administered by intraarticular injection was well tolerated.¹⁹ The study was not designed to assess the analgesic efficacy of Kineret. Patients with osteoarthritis of the knee were enrolled in a multicenter, double-blind, placebo-controlled study and randomized to Kineret 50 mg, Kineret 150 mg, or placebo for intraarticular injection.²⁰ Although the injections were well tolerated, there were no significant differences in improvement in knee pain, stiffness, function or cartilage turnover between Kineret doses and placebo. Similar to other studies in this population, there was a significant placebo effect noted.

REFERENCES

1. Kineret® subcutaneous injection [prescribing information]. Stockholm, Sweden: Swedish Orphan Biovitrum; December 2020.
2. Romano M, Arici ZS, Piskin D, et al. The 2021 EULAR/American College of Rheumatology points to consider for diagnosis, management and monitoring of the interleukin-1 mediated autoinflammatory diseases: cryopyrin-associated periodic syndromes, tumour necrosis factor receptor-associated

- periodic syndrome, mevalonate kinase deficiency, and deficiency of the interleukin-1 receptor antagonist. *Ann Rheum Dis*. 2022;81(7):907-921.
3. Shinkai K, McCalmont TH, Leslie KS. Cryopyrin-associated periodic syndromes and autoinflammation. *Clin Exp Dermatol*. 2008;33:1-9.
 4. Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Care Res (Hoboken)*. 2021;73(7):924-939.
 5. Onel KB, Horton DB, Lovell DJ, et al. 2021 American College of Rheumatology Guideline for the Treatment of Juvenile Idiopathic Arthritis: Therapeutic Approaches for Oligoarthritis, Temporomandibular Joint Arthritis, and Systemic Juvenile Idiopathic Arthritis. *Arthritis Rheumatol*. 2022;74(4):553-569.
 6. Fautrel B, Mitrovic S, De Matteis A, et al. EULAR/PReS recommendations for the diagnosis and management of Still's disease, comprising systemic juvenile idiopathic arthritis and adult-onset Still's disease. *Ann Rheum Dis*. 2024;83(12):1614-1627.
 7. Riera E, Olivé A, Narváez J, et al. Adult onset Still's disease: review of 41 cases. *Clin Exp Rheumatol*. 2011;29(2):331-336.
 8. Lequerré T, Quartier P, Rosellini D, et al. Interleukin-1 receptor antagonist (anakinra) treatment in patients with systemic-onset juvenile idiopathic arthritis or adult onset Still's disease. Preliminary experience in France. *Ann Rheum Dis*. 2008;67:302-308.
 9. Fitzgerald AA, Leclercq SA, Yan A, et al. Rapid responses to anakinra in patients with refractory adult-onset Still's disease. *Arthritis Rheum*. 2005;52:1794-1803.
 10. Kötter I, Wacker A, Koch S, et al. Anakinra in patients with treatment-resistant adult-onset Still's disease: Four case reports with serial cytokine measurements and a review of the literature. *Semin Arthritis Rheum*. 2007;37:189-197.
 11. Kalliolias GD, Georgiou PE, Antonopoulos IA, et al. Anakinra treatment in patients with adult-onset Still's disease is fast, effective, safe and steroid sparing: experience from an uncontrolled trial. *Ann Rheum Dis*. 2007;66:842-843.
 12. Giampietro C, Ridene M, Lequerre T, et al. Anakinra in adult-onset Still's disease: long-term treatment in patients resistant to conventional therapy. *Arthritis Care Res (Hoboken)*. 2013;65(5):822-826.
 13. Ortiz-Sanjuán F1, Blanco R, Riancho-Zarrabeitia L, et al. Efficacy of anakinra in refractory adult-onset Still's disease: multicenter study of 41 patients and literature review. *Medicine (Baltimore)*. 2015;94(39):e1554.
 14. Tan AL, Marzo-Ortega H, O'Connor P, et al. Efficacy of anakinra in active ankylosing spondylitis: a clinical and magnetic resonance imaging study. *Ann Rheum Dis*. 2004;63:1041-1045.
 15. Haibel H, Rudwaleit M, Listing J, et al. Open label trial of anakinra in active ankylosing spondylitis over 24 weeks. *Ann Rheum Dis*. 2005;64:296-298.
 16. van der Heijde D, Ramiro S, Landewé R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis*. 2017;76(6):978-991.
 17. Furst DE, Keystone EC, So AK, et al. Updated consensus statement on biological agents for the treatment of rheumatic diseases, 2012. *Ann Rheum Dis*. 2013;72 Suppl 2:ii2-34.
 18. Ostendorf B, Iking-Konert C, Kurz K, et al. Preliminary results of safety and efficacy of the interleukin 1 receptor antagonist anakinra in patients with severe lupus arthritis. *Ann Rheum Dis*. 2005;64:630-683.
 19. Chevalier X, Giraudeau B, Conrozier T, et al. Safety study of intraarticular injection of interleukin 1 receptor antagonist in patients with painful knee osteoarthritis: a multicenter study. *J Rheumatol*. 2005;32:1317-1323.
 20. Chevalier X, Goupille P, Beaulieu AD, et al. Intraarticular injection of anakinra in osteoarthritis of the knee: a multicenter, randomized, double-blind, placebo-controlled study. *Arthritis Rheum*. 2009;61(3):344-352.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	01/25/2023
Annual Revision	No criteria changes.	02/28/2024
Selected Revision	<p>Systemic Juvenile Idiopathic Arthritis: The requirement for previous therapy was removed. Exceptions that apply to a patient who is not required to try another therapy prior to Kineret were removed (no longer needed).</p> <p>Still's Disease, Adult Onset: The condition was changed to as listed (previously was Still's Disease).</p>	04/24/2024
Selected Revision	<p>Rheumatoid Arthritis: For initial approval, a requirement that the patient is ≥ 18 years of age was added.</p> <p>Systemic Juvenile Idiopathic Arthritis: For initial approval, a requirement that the patient is ≥ 2 years of age was added.</p> <p>Still's Disease, Adult Onset: For initial approval, a requirement that the patient is ≥ 18 years of age was added.</p> <p>Conditions Not Covered : Concurrent use with a Biologic or with a Targeted Synthetic Oral Small Molecule Drug was changed to as listed (previously oral small molecule drug was listed as Disease-Modifying Antirheumatic Drug).</p>	09/11/2024
Annual Revision	<p>Cryopyrin-Associated Periodic Syndromes: An "allergist/immunologist" was added to the existing requirement that the medication is being prescribed by or in consultation with a rheumatologist, geneticist, or dermatologist. For a patient currently receiving Kineret, the examples of improvements in symptoms were moved to a Note.</p> <p>Deficiency of Interleukin-1 Receptor Antagonist: The term "mutation" was rephrased to "biallelic pathogenic variants". For a patient currently receiving Kineret, the examples of improvements in symptoms were moved to a Note.</p> <p>Rheumatoid Arthritis: The previous requirement "Patient experienced a beneficial clinical response when assessed by at least one objective measure" was reworded to "When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug)". The previous requirement "Patient experienced an improvement in at least one symptom..." was updated add "Compared with baseline (prior to initiating the requested drug)".</p> <p>Still's Disease, Adult-Onset: The following Note was added "Adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (SJIA) are considered the same disease (Still's disease) but differ in age of onset. For a patient < 18 years of age, refer to the SIJA indication below."</p> <p>Systemic Juvenile Idiopathic Arthritis: The following Note was added "Systemic juvenile idiopathic arthritis (SJIA) and adult-onset Still's disease (AOSD) are considered the same disease (Still's disease) but differ in age of onset. For a patient ≥ 18 years of age, refer to AOSD indication above."</p>	02/26/2025
Selected Revision	<p>Policy Statement: Removed "All reviews for COVID-19 and/or cytokine release syndrome associated with COVID-19 will be forwarded to the Medical Director."</p>	04/23/2025

	COVID-19 (Coronavirus Disease 2019): Diagnosis removed from Other Uses with Supportive Evidence.	
--	---	--

APPENDIX

	Mechanism of Action	Examples of Indications*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA, RA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Zymfentra® (infliximab-dyyb SC injection)	Inhibition of TNF	CD, UC
Simponi®, Simponi Aria® (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
Tocilizumab Products (Actemra® IV, biosimilar; Actemra SC, biosimilar)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PSA, RA
		IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA^, RA
Omvoh® (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	UC
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
Siliq® (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx® (secukinumab SC injection; secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, nr-axSpA, PsO, PsA
		IV formulation: AS, nr-axSpA, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Bimzelx® (bimekizumab-bkzx SC injection)	Inhibition of IL-17A/17F	PsO
Ilumya® (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PSA, PsO, UC
		IV formulation: CD, UC
Tremfya® (guselkumab SC injection, guselkumab IV infusion)	Inhibition of IL-23	SC formulation: PsA, PsO, UC
		IV formulation: UC
Entyvio® (vedolizumab IV infusion, vedolizumab SC injection)	Integrin receptor antagonist	CD, UC
Oral Therapies/Targeted Synthetic Oral Small Molecule Drugs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo™ (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA, AA
Litfulo® (ritlecitinib capsules)	Inhibition of JAK pathways	AA

Leqselvi® (deuruxolitinib tablets)	Inhibition of JAK pathways	AA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, nr-axSpA, RA, PsA, UC
Rinvoq® LQ (upadacitinib oral solution)	Inhibition of JAK pathways	PsA, PJIA
Sotyktu® (deucravacitinib tablets)	Inhibition of TYK2	PsO
Xeljanz® (tofacitinib tablets/oral solution)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC
Zeposia® (ozanimod tablets)	Sphingosine 1 phosphate receptor modulator	UC
Velsipity® (etrasimod tablets)	Sphingosine 1 phosphate receptor modulator	UC

* Not an all-inclusive list of indications. Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn’s disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; ^ Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; AA – Alopecia areata; TYK2 – Tyrosine kinase 2.

"Cigna Companies" refers to operating subsidiaries of The Cigna Group. All products and services are provided exclusively by or through such operating subsidiaries, including Cigna Health and Life Insurance Company, Connecticut General Life Insurance Company, Evernorth Behavioral Health, Inc., Cigna Health Management, Inc., and HMO or service company subsidiaries of The Cigna Group. © 2025 The Cigna Group.