# Drug Coverage Policy

**Effective Date.....7/1/2024**
**Coverage Policy Number.....IP0235**
**Policy Title..... Ilaris**

# Inflammatory Conditions – Ilaris

- Ilaris® (canakinumab subcutaneous injection – Novartis)

***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 and have discretion in making individual coverage determinations. 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 Healthcare Coverage Policy

Ilaris, an interleukin-1β (IL-1β) blocker, is indicated for the following uses:[1]

- **Periodic Fever Syndromes:**
  - **Cryopyrin-associated periodic syndromes** (CAPS), including familial cold autoinflammatory syndrome (FCAS) and Muckle-Wells syndrome (MWS), for treatment of patients ≥ 4 years of age.
  - **Familial Mediterranean fever** (FMF), in adult and pediatric patients.

    - **Hyperimmunoglobulin D syndrome** (HIDS)**/mevalonate kinase deficiency** (MKD), in adult and pediatric patients.
    - **Tumor necrosis factor receptor associated periodic syndrome** (TRAPS), in adult and pediatric patients.
- **Active Still's disease**, including **adult-onset Still's disease** (AOSD) and **systemic juvenile idiopathic arthritis** (SJIA), in patients ≥ 2 years of age.
- **Gout flares** in adults in whom nonsteroidal anti-inflammatory drugs (NSAIDs) and colchicine are contraindicated, not tolerated, or do not provide an adequate response, and in whom repeated courses of corticosteroids are not appropriate.

In the pivotal trial for periodic fevers (TRAPS, HIDS/MKD, and FMF), patients were required to be at least 2 years of age with a disease flare, defined as a C-reactive protein level ≥ 10 mg/L. Prior to starting Ilaris, a minimum level of disease activity at baseline was required for FMF (at least one flare per month despite colchicine), HIDS/MKD (≥ three febrile acute flares within the previous 6 month period), and TRAPS (≥ six flares per year). In this study, patients were assessed for a response following 4 months of treatment with Ilaris.

**Guidelines**
Ilaris is used for a variety of periodic fever syndromes and inflammatory conditions. The European Alliance of Associations for Rheumatology (EULAR) and American College of Rheumatology (ACG) [2021] provide treatment guidelines for interleukin-1 (IL-1) mediated autoinflammatory diseases and indicate IL-blocking therapy has become the preferred treatment and a therapeutic trial with IL-1 blocking treatment may be started when strong clinical suspicion of a diagnosis of CAPS, TRAPS, MKD, or DIRA is entertained.[2] The guidelines also provide additional diagnosis specific treatment recommendations:

- **CAPS:** 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 appropriate weight gain and development in the growing patient.
- **TRAPS:** IL-1 blockers are more effective than traditional disease-modifying antirheumatic drugs (DMARDs) and other biologic DMARDs in achieving disease remission and preventing long-term complications.
- **MKD/HIDS**: In patients without chronic inflammation, on demand IL-1 blockage should be attempted at the onset of flares. In children, IL-1 blocking therapy is generally required.

*FMF*
Guidelines for familial Mediterranean fever from the EULAR (2016) note that treatment goals are to prevent the clinical attacks and to suppress chronic subclinical inflammation.[3] IL-1 blockade is an option for patients with protracted febrile myalgia. In patients who develop amyloidosis, the maximal tolerated dose of colchicine and biologics (especially IL-1 blockade) are recommended.

*Gout*
Guidelines for the management of gout flares from the ACR (2020) recommend colchicine, NSAIDs, or glucocorticoids (oral, intraarticular, or intramuscular) as appropriate first-line therapy.[4] If a patient is unable to tolerate or has contraindications to any of the first line conventional alternatives, IL-1 inhibitors are conditionally recommended.

*SIJA*
There are standardized treatment plans published for use of Ilaris.[5,6] At Month 3, patients with unchanged or worsening disease or patients whose steroid dose is > 50% of the starting dose should have an increase in prednisone plus either addition of methotrexate or change to Actemra. Guidelines from the ACR for the management of SJIA (2021) mention Ilaris as a treatment alternative, depending upon the manifestations of SJIA being treated.[7] While there are a number

of other effective options for treating synovitis in patients with active SJIA, effective options for treatment of macrophage activation syndrome are much more limited and include Kineret ® (anakinra subcutaneous injection), calcineurin inhibitors, and systemic corticosteroids (no preferential sequencing noted). Although use of Ilaris is uncertain in some situations, macrophage activation syndrome is a potentially life-threatening situation with limited treatment options.

## Medical Necessity Criteria

**Ilaris is considered medically necessary when ONE of the following is met:**

**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):
   Note: This includes familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and neonatal onset multisystem inflammatory disease (NOMID) formerly known as chronic infantile neurological cutaneous and articular syndrome (CINCA).
   **A)** Initial Therapy. Approve for 6 months if the patient meets BOTH of the following (i and ii):
      **i.** Patient is ≥ 4 years of age; AND
      **ii.** The medication is prescribed by or in consultation with a rheumatologist, geneticist, allergist/immunologist, or dermatologist.
   **B)** Patient is Currently Receiving Ilaris. 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: For a patient who has not received 6 months of therapy or who is restarting therapy with this medication, refer to Initial Therapy criteria above.
      **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.

   **Dosing.** Approve one of the following dosing regimens (A or B):
   **A)** Patient is ≥ 15 kg and ≤ 40 kg: Approve up to 3 mg/kg per dose administered subcutaneously no more frequently than once every 8 weeks; OR
   **B)** Patient is > 40 kg: Approve up to 150 mg per dose administered subcutaneously no more frequently than once every 8 weeks.

2. **Familial Mediterranean Fever (FMF).** 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, iii, iv, and v):
      **i.** Patient is ≥ 2 years of age; AND
      **ii.** Patient has had a trial of colchicine, unless contraindicated; AND

**iii.** Patient will be taking Ilaris in combination with colchicine, unless colchicine is contraindicated or not tolerated; AND

**iv.** Prior to starting Ilaris, the patient meets BOTH of the following (a and b):

**a)** C-reactive protein level is ≥ 10 mg/L OR elevated to at least two times the upper limit of normal for the reporting laboratory; AND

**b)** Patient has a history of at least one flare per month despite use of colchicine, OR was hospitalized for a severe flare; AND

**v.** The medication is prescribed by or in consultation with a rheumatologist, nephrologist, geneticist, gastroenterologist, oncologist, or hematologist.

**B)** Patient is Currently Receiving Ilaris. 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: For a patient who has not received 6 months of therapy or who is restarting therapy with this medication, refer to Initial Therapy criteria above.

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

**Dosing.** Approve one of the following dosing regimens (A or B):

**A)** Patient is ≤ 40 kg: Approve up to 4 mg/kg per dose administered subcutaneously no more frequently than once every 4 weeks; OR

**B)** Patient is > 40 kg: Approve up to 300 mg per dose administered subcutaneously no more frequently than once every 4 weeks.

**3. Gout, Acute Flare.** Approve for 6 months if the patient meets ALL of the following (A, B, C, and D):

**A)** Patient is ≥ 18 years of age; AND

**B)** Patient meets ONE of the following (i or ii):

**i.** Patient meets BOTH of the following (a and b):

**a)** Patient has an intolerance, contraindication, or lack of response to nonsteroidal anti-inflammatory drugs (NSAIDs) for the treatment of acute gout flares; AND

**b)** Patient has an intolerance, contraindication, or lack of response to colchicine for the treatment of acute gout flares; OR

**ii.** Patient meets BOTH of the following (a and b):

**a)** Patient has been previously treated with corticosteroids (oral or injectable) for an acute gout flare; AND

**b)** According to the prescriber, patient is unable to be retreated with a repeat course of corticosteroids (oral or injectable) for acute gout flares; AND

**C)** According to the prescriber, patient is receiving or will be taking concomitant urate lowering medication for the prevention of gout unless contraindicated; AND
Note: Examples of uric acid lowering drugs include allopurinol, febuxostat, or probenecid.

**D)** Ilaris is prescribed by or in consultation with a rheumatologist.

**Dosing.** Approve up to 150 mg administered subcutaneously no more frequently than once every 12 weeks.

**4. Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD).** 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 ≥ 2 years of age; AND
- **ii.** Prior to starting Ilaris, the patient meets BOTH of the following (a and b):
  - **a)** C-reactive protein level is ≥ 10 mg/L OR elevated to at least two times the upper limit of normal for the reporting laboratory; AND
  - **b)** Patient has a history of at least three febrile acute flares within the previous 6-month period OR was hospitalized for a severe flare; AND
- **iii.** The medication is prescribed by or in consultation with a rheumatologist, nephrologist, geneticist, oncologist, or hematologist.

**B)** Patient is Currently Receiving Ilaris. 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: For a patient who has not received 6 months of therapy or who is restarting therapy with this medication, refer to Initial Therapy criteria above.
- **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 decreased frequency of attacks, 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 decreased pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

**Dosing.** Approve one of the following dosing regimens (A or B):

**A)** Patient is ≤ 40 kg: Approve up to 4 mg/kg per dose administered subcutaneously no more frequently than once every 4 weeks; OR

**B)** Patient is > 40 kg: Approve up to 300 mg per dose administered subcutaneously no more frequently than once every 4 weeks.

**5. Stills Disease, Adult Onset.** Approve for the duration noted if the patient meets ONE of the following (A or B):

**A)** Initial Therapy. Approve for 6 months (which is adequate for three doses) if the patient meets ALL of the following (i, ii, and iii):
- **i.** Patient is ≥ 18 years of age; AND
  Note: If the patient is < 18 years of age, refer to criteria for systemic juvenile idiopathic arthritis.
- **ii.** Patient meets ONE of the following (a or b):
  - **a)** Patient has tried at least ONE other biologic; OR
    Note: Examples of biologics for Still's disease include a tocilizumab product (Actemra intravenous infusion, biosimilar; Actemra subcutaneous injection), Kineret (anakinra subcutaneous injection).
  - **b)** Patient was started on Ilaris while in the hospital; AND

**iii.** Ilaris is prescribed by or in consultation with a rheumatologist.

**B)** Patient is Currently Receiving Ilaris. 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: For a patient who has not received 6 months of therapy or who is restarting therapy with this medication, refer to Initial Therapy criteria above.

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

**Dosing.** Approve up to 4 mg/kg to a maximum of 300 mg per dose administered subcutaneously no more frequently than once every 4 weeks.

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

**A)** Initial Therapy. Approve for 6 months (which is adequate for three doses) if the patient meets ALL of the following (i, ii, and iii):

**i.** Patient is ≥ 2 years of age; AND

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

**a)** Patient has tried at least ONE other biologic; OR
Note: Examples of biologics for SJIA include a tocilizumab product (Actemra intravenous infusion, biosimilar; Actemra subcutaneous injection), Kineret (anakinra subcutaneous injection),.

**b)** Patient was started on Ilaris while in the hospital; AND

**iii.** Ilaris is prescribed by or in consultation with a rheumatologist.

**B)** Patient is Currently Receiving Ilaris. 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: For a patient who has not received 6 months of therapy or who is restarting therapy with this medication, refer to Initial Therapy criteria above.

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

**Dosing.** Approve up to 4 mg/kg to a maximum of 300 mg per dose administered subcutaneously no more frequently than once every 4 weeks.

7. **Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS).** 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 ≥ 2 years of age; AND
     - **ii.** Prior to starting Ilaris, the patient meets BOTH of the following (a and b):
       - **a)** C-reactive protein level is ≥ 10 mg/L OR elevated to at least two times the upper limit of normal for the reporting laboratory; AND
       - **b)** Patient has a history of at least six flares per year OR was hospitalized for a severe flare; AND
     - **iii.** The medication is prescribed by or in consultation with a rheumatologist, geneticist, nephrologist, oncologist, or hematologist.
   - **B)** Patient is Currently Receiving Ilaris. 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: For a patient who has not received 6 months of therapy or who is restarting therapy with this medication, refer to Initial Therapy criteria above.
     - **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 decreased frequency of attacks, 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 improvements in symptoms include such as decreased pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

   **Dosing.** Approve one of the following dosing regimens (A or B):
   - **A)** Patient is ≤ 40 kg: Approve up to 4 mg/kg per dose administered subcutaneously no more frequently than once every 4 weeks; OR
   - **B)** Patient is > 40 kg: Approve up to 300 mg per dose administered subcutaneously no more frequently than once every 4 weeks.

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.

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

## Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Concurrent Biologic Therapy.** Ilaris has not been evaluated and should not be administered in combination with another biologic agent for an inflammatory condition (see Appendix for examples).[1] An increased incidence of serious infections has been associated with another IL-1 blocker, Kineret, when given in combination with tumor necrosis factor inhibitor in patients with rheumatoid arthritis. Concomitant administration of Ilaris and other agents that block IL-1 or its receptors is not recommended.

2. **COVID-19 (Coronavirus Disease 2019).**
   Note: This includes requests for cytokine release syndrome associated with COVID-19.

3. **Rheumatoid Arthritis.** Efficacy is not established. In a 12-week, Phase II, placebo-controlled, double-blind study, 277 patients who had failed methotrexate were randomized to Ilaris or placebo.[8] Although the ACR 50 at Week 12 was higher for Ilaris 150 mg (given every 4 weeks) compared with placebo (26.5% vs. 11.4%, respectively; P = not significant), there was not a statistically significant difference in ACR 50 for the other Ilaris treatment groups (Ilaris 300 mg every 2 weeks; Ilaris 600 mg loading dose followed by 300 mg every 2 weeks).

## Coding Information

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 |
|---|---|
| J0638 | Injection, canakinumab, 1 mg |

## References


1. Ilaris® subcutaneous injection [prescribing information]. East Hanover, NJ: Novartis; August 2023.
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. Ozen S, Demirkaya E, Erer B, et al. EULAR recommendations for the management of familial Mediterranean fever. *Ann Rheum Dis*. 2016;75(4):644-651.
4. FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for the Management of Gout [published correction appears in Arthritis Care Res (Hoboken). 2020 Aug;72(8):1187] [published correction appears in Arthritis Care Res (Hoboken). 2021 Mar;73(3):458]. *Arthritis Care Res* (Hoboken). 2020;72(6):744-760.
5. Kimura Y, Morgan DeWitt E, Beukelman T, et al. Adding Canakinumab to the Childhood Arthritis and Rheumatology Research Alliance Consensus Treatment Plans for Systemic Juvenile Idiopathic Arthritis: comment on the article by DeWitt et al. *Arthritis Care Res (Hoboken)*. 2014;66(9):1430-1431.

6. DeWitt EM, Kimura Y, Beukelman T, et al. Consensus treatment plans for new-onset systemic juvenile idiopathic arthritis. *Arthritis Care Res (Hoboken).* 2012;64(7):1001-1010.
7. 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 Apr;74(4):553-569.
8. Alten R, Gomez-Reino J, Durez P, et al. Efficacy and safety of the human anti-IL-1β monoclonal antibody canakinumab in rheumatoid arthritis: results of a 12-week, Phase II, dose-finding study. *BMC Musculoskelet Disord.* 2011;12:153.

## Revision Details

| Type of Revision | Summary of Changes | Date |
|---|---|---|
| Annual Revision | Updated policy title, previously was Canakinumab<br><br>**For All Indications:** Added clarification throughout the policy for all indications that for a Patient Currently Receiving Ilaris. "Patient has been established on this medication for at least 6 months;<br>Note: For a patient who has not received 6 months of therapy or who is restarting therapy with this medication, refer to Initial Therapy criteria"<br><br>**Cryopyrin-Associated Periodic Syndromes (CAPS)** - Added patient is ≥ 4 years of age<br><br>**Stills Disease, Adult Onset and Systemic Juvenile Idiopathic Arthritis (SJIA)** - Added requirements for ONE of the following: trial of ONE other biologic; OR patient was started on Ilaris in the hospital.<br><br>**Conditions Not Covered:** Removed Behcet's Disease, Cardiovascular risk reduction and disorder prevention, Majeed Syndrome, Schnitzler Syndrome, Type 1 or 2 Diabetes. All continue to be considered experimental, investigational, or unproven. This was list maintenance and does not imply any updates to coverage status. | 7/1/2024 |

The policy effective date is in force until updated or retired.

## APPENDIX

| | Mechanism of Action | Examples of Inflammatory 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 |
| **Zymfentra®** (infliximab-dyyb SC injection) | Inhibition of TNF | CD, UC |
| **Infliximab IV Products** (Remicade®, biosimilars) | Inhibition of TNF | AS, CD, PsO, PsA, RA, UC |
| **Simponi®, Simponi® Aria™** (golimumab SC injection, golimumab IV infusion) | Inhibition of TNF | SC formulation: AS, PsA, RA, UC |
| **Actemra®** (tocilizumab IV infusion, tocilizumab SC injection) | Inhibition of IL-6 | IV formulation: AS, PJIA, PsA, RA |
| **Actemra®** (tocilizumab IV infusion, tocilizumab SC injection) | Inhibition of IL-6 | SC formulation: PJIA, RA, SJIA |
| **Kevzara®** (sarilumab SC injection) | Inhibition of IL-6 | IV formulation: PJIA, RA, SJIA |
| **Kevzara®** (sarilumab SC injection) | Inhibition of IL-6 | RA, PMR |
| **Orencia®** (abatacept IV infusion, abatacept SC injection) | T-cell costimulation modulator | SC formulation: JIA, PSA, RA |
| **Rituximab IV Products** (Rituxan®, biosimilars) | CD20-directed cytolytic antibody | 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 |
| **Stelara®** (ustekinumab SC injection, ustekinumab IV infusion) | Inhibition of IL-12/23 | SC formulation: CD, PsO, PsA, UC |
| **Siliq™** (brodalumab SC injection) | Inhibition of IL-17 | IV formulation: CD, UC |
| **Siliq™** (brodalumab SC injection) | Inhibition of IL-17RA | PsO |
| **Bimzelx®** (bimekizumab-bkzx SC injection) | Inhibition of IL-17A and IL-17F | PsO |
| **Cosentyx®** (secukinumab SC injection, secukinumab IV infusion) | Inhibition of IL-17A | SC formulation: AS, ERA, nr-axSpA, PsO, PsA |
| **Skyrizi®** (risankizumab-rzaa SC injection) | Inhibition of IL-23 | IV formulation: AS, nr-axSpA, PsA |
| **Taltz®** (ixekizumab SC injection) | Inhibition of IL-17A | AS, nr-axSpA, PsO, PsA |
| **Ilumya™** (tildrakizumab-asmn SC injection) | Inhibition of IL-23 | PsO |

* Not an all-inclusive list of indication (e.g., oncology indications and rare inflammatory conditions are not listed). 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.