Blue Cross Blue Shield Blue Care Network of Michigan

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Effective Date: 12/09/2021

Ilaris® (canakinumab)

HCPCS: J0638

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved age
   b. Diagnosis of:
      i. Still's disease, including adult-onset Still's disease and systemic juvenile idiopathic arthritis (sJIA)
         1. Trial and treatment failure with one of the following: methotrexate, leflunomide, glucocorticoids, NSAIDs
         2. Trial and failure, contraindication, or intolerance to Kineret and Actemra
      ii. Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS)
      iii. Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)
      iv. Familial Mediterranean Fever (FMF) in patients who have tried and failed colchicine
      v. Cryopyrin-Associated Periodic Syndromes (CAPS) with phenotypes: Familial Cold Auto-Inflammatory Syndrome (FCAS) or Muckle-Wells Syndrome (MWS)
         1. Laboratory evidence of a genetic mutation (such as in the Cold-Induced Auto-inflammatory Syndrome 1 (CIAS1 – also referred to as the NLRP-3))
            OR
         2. Elevated inflammatory markers (C-reactive protein [CRP] and serum amyloid A) plus at least two of six typical CAPS manifestations:
            a) Urticaria-like rash
            b) Cold-triggered episodes
            c) Sensorineural hearing loss
            d) Musculoskeletal symptoms
            e) Chronic aseptic meningitis
            f) Skeletal abnormalities
   c. Not to be used in combination with other biologics or targeted DMARDs
   d. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN utilization management medical drug list.

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B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing.
   b. Initial Authorization Period: One year at a time
   c. Renewal criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit.

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Bachground Information:

- Ilaris is an interleukin (IL)-1β blocker that is approved for the following indications:
    - Periodic Fever Syndromes:
        - Cryopyrin-Associated Periodic Syndromes (CAPS) in adults and children 4 years of age and older including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS)
        - Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS) in adult and pediatric patients
        - Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD) in adult and pediatric patients
        - Familial Mediterranean Fever (FMF) 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 and older
- Periodic Fever Syndromes are a group of rare autoinflammatory diseases that cause disabling and persistent fevers which may be accompanied by joint pain, swelling, muscle pain and skin rashes with complications that can be life-threatening.
    - The most common syndrome is FMF, which mainly affects people of Eastern Mediterranean ancestry. It affects 1 in 250 to 1 in 1,000 individuals in these populations, many of whom are children. FMF is characterized by episodic attacks of fever lasting one to three days and accompanied, in most cases, by abdominal pain, pleurisy, and arthralgias/arthritis.
    - TRAPS is characterized by recurrent fevers over months or years. Other clinical features include focal myalgias, conjunctivitis, and rash. Fever and associated symptoms commonly last at least five days and often continue for more than two weeks.
    - HIDS/MKD is characterized by episodic attacks of fever lasting three to seven days accompanied, in most cases, by chills, cervical lymphadenopathy, abdominal pain, vomiting, and/or diarrhea.
    - CAPS are a group of rare genetic diseases affecting approximately 200 to 300 people in the United States, attributed to a specific genetic mutation. There are two types of CAPS recognized that affect the majority of patients.

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- Familial Cold Auto-Inflammatory Syndrome (FCAS) – patients have recurrent intermittent episodes of fever and rash that primarily followed natural, artificial (e.g., air conditioning) or both types of generalized cold exposure.

- Muckle-Wells Syndrome (MWS) – patients have chronic fever and rash that may wax and wane in intensity; sometimes exacerbated by generalized cold exposure. This syndrome may be associated with deafness or amyloidosis.

- The diagnosis of CAPS is confirmed by genetic testing for NALP3 mutations. However, in some patients the mutation is not detectable for various reasons. For these situations, diagnostic criteria include raised inflammatory markers (C-reactive protein [CRP] and serum amyloid A) plus at least two of six typical CAPS manifestations:

    - Urticaria-like rash
    - Cold-triggered episodes
    - Sensorineural hearing loss
    - Musculoskeletal symptoms
    - Chronic aseptic meningitis
    - Skeletal abnormalities

- Arcalyst® (rilonacept) is another IL-1β blocker indicated for the treatment of CAPS. Both products appear to have similar efficacy. Ilaris has a more convenient dosing regimen and is indicated for a younger age population.

- Still's disease (adult onset (AOSD) and systemic juvenile idiopathic arthritis (sJIA)

    - sJIA is a rare subtype of juvenile idiopathic arthritis that causes body-wide inflammation. It accounts for 4-15% of JIA and is defined as arthritis in > 1 joint for at least 6 weeks duration in a child age < 16 years with or preceded by a fever of at least 2 weeks duration that is documented to be daily for at least 3 days and accompanied by one or more of the following: evanescent erythematous rash, generalized lymphadenopathy, hepatomegaly or splenomegaly, and serositis. The condition can occur in adulthood with similar features and is referred to as adult onset Still's disease.

    - The underlying inflammatory process appears to be distinct from other categories of autoimmune arthritis, with interleukin (IL)-1 and IL-6 playing a central role. The goal of therapy focuses on prompt control of active inflammation and symptoms and prevention of disease- and or treatment-related morbidities like growth disturbances, joint damage and functional limitations.

    - Treatment varies depending on the degree of synovitis and the presence of active systemic features (fever, rash, lymphadenopathy, hepatomegaly or splenomegaly, serositis).

    - Per the 2013 update of the 2011 American College of Rheumatology (ACR) recommendations for the treatment of JIA, sJIA treatment is typically initiated with a short-term course of systemic glucocorticoid monotherapy or NSAID monotherapy. Disease-modifying anti-rheumatic drugs (DMARDs, preferably methotrexate (MTX) or leflunomide (LEF) per the recommendation) may be beneficial to those without active systemic features but with active joint involvement. Anakinra may be of benefit as initial therapy for those with moderate to severe active systemic features irrespective of the number of joints involved.

    - For those with continued disease activity despite initial treatment, potential treatment options may include (in no particular order): abatacept, anakinra, tocilizumab, canakinumab, tumor necrosis factor inhibitors (TNFi; adalimumab, etanercept and infliximab), glucocorticoids, and DMARDs. The recommended choice and

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order of therapy is dependent on the continued presence (or lack) of active systemic features, the physician global assessment score, active joint count, and previously trialed treatments. The detailed recommendations for subsequent therapies can be found in the 2013 update of the ACR Recommendations for the treatment of JIA (see figures 1 and 2 within the recommendation).

- Ilaris (canakinumab) and Actemra (tocilizumab) are the only biologic agents FDA approved to treat sJIA, and Ilaris is the only drug approved for adult onset-Still's disease. There are no guidelines for treating AOSD; however, literature recommends a similar treatment approach as with sJIA. The use of Kineret for sJIA and both Kineret and Actemra for AOSD is supported by various trials, case studies, and case series. Additionally, the efficacy of Kineret and Actemra in sJIA provides further evidence supporting the use of both agents in AOSD. The significantly lower cost of Actemra and Kineret make these agents more cost-effective alternatives to Ilaris for the treatment of sJIA and AOSD.

- The safety and effectiveness of Ilaris in treating these conditions were established in multiple clinical trials. The use of Ilaris in combination with other biologic agents or targeted disease-modifying antirheumatic drugs is not recommended due to a lack of robust clinical evidence to support the safety and efficacy of concurrent use.

References:

1. Ilaris [prescribing information]. East Hanover, NJ: Novartis. June 2020.
2. Nigrovic, PA. Cryopyrin-associated periodic syndromes and related disorders. UpToDate, Waltham, MA, 2020.
3. Padeh, YC. Hyperimmunoglobulin D Syndrome: Management. UpToDate, Waltham, MA, 2020.
4. Kuemmerle-Deschner JB, Ozen S, Tyrrell PN et al. Diagnostic criteria for cryopyrin-associated periodic syndrome (CAPS). Ann Rheum Dis. 2017;76(6):942.
5. Mandl, L. Treatment of adult Still's disease. UpToDate, Waltham, MA, 2020.
6. Ringold et al. 2013 Update of the 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis. Arthritis and Rheumatism. Vol 65 No 10 October 2013.
7. Ringold et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the Treatment of JIA. Arthritis Care and Research. Vol 71 No 6 Jun 2019.

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>2.3</td><td>Effective Date: 12/09/2021</td><td>Removed FDA approved indications criteria</td></tr>
<tr><td>2.2</td><td>Effective Date: 02/04/2021</td><td>Added trial and failure of Actemra and Kineret to criteria for sJIA and AOSD</td></tr>
<tr><td>2.1</td><td>Effective Date: 12/03/2020</td><td>Updated step criteria for AOSD and sJIA. Added criteria bullet d – not to use in combination with biologics. Changed renewal criteria to be consistent across all diagnoses.</td></tr>
<tr><td>2.0</td><td>Effective Date; 9/28/2020</td><td>UM medical management system update for MAPPO AND BCNA
<table>
<tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr>
<tr><td>BCBS</td><td>Yes</td></tr>
<tr><td>BCN</td><td>Yes</td></tr>
<tr><td>MAPPO</td><td>Yes</td></tr>
<tr><td>BCNA</td><td>Yes</td></tr>
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<tr><td>1.9</td><td>Effective Date: 08/13/2020</td><td>Updates were made to the criteria, including adding criteria for a new indication</td></tr>
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1.8	Effective Date: 11/7/2019	Criteria updated for step therapy for SIJA
1.7	Effective Date: 08/15/2019	Annual Review of Medical Policy
1.6	Effective Date: 08/09/2018	Change in verbiage for preferred therapy
1.5	Effective Date: 05/03/2018	Annual Review of Medical Policy
1.4	Effective Date 05/04/2017	Added new criteria for TRAPS, HIDS/MKD, and FMF.
1.3	Effective Date 08/11/2016	Annual Update
1.2	Effective Date: 02/01/2015	UM medical management system update for BCN **Line of Business** / **PA Required in Medical Management System (Yes/No)** BCBS: Yes BCN: Yes MAPPO: No BCNA: No
1.1	Effective Date: 04/01/2014	UM medical management system update for BCBSM **Line of Business** / **PA Required in Medical Management System (Yes/No)** BCBS: Yes BCN: No MAPPO: No BCNA: No
1.0	Effective Date: 08/08/2013	Criteria Update **Line of Business** / **PA Required in Medical Management System (Yes/No)** BCBS: No BCN: No MAPPO: No BCNA: No

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

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