Overview
Ilaris is a human anti-interleukin-1β (IL-1β) monoclonal antibody that binds to human IL-1β and neutralizes its activity by blocking its interaction with IL-1 receptors. It does not bind IL-1α or IL-1 receptor antagonist (IL-1ra). IL-1 cytokine signaling is important in the pathogenesis of autoinflammatory conditions. Ilaris is indicated for the following uses:

1. Treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children aged 4 years and older;
2. Systemic juvenile idiopathic arthritis (SJIA) in patients ≥ 2 years of age;
3. Tumor necrosis factor receptor associated periodic syndrome (TRAPS), in adult and pediatric patients;
4. Hyperimmunoglobulin D Syndrome (HIDS)/mevalonate kinase deficiency (MKD), in adult and pediatric patients; AND
5. Familial Mediterranean Fever (FMF), in adult and pediatric patients.

Arcalyst® (rilonacept for SC injection) is another IL-1 blocker and is approved for the treatment of CAPS. Arcalyst, given once weekly by SC injection, was effective in the treatment of CAPS in patients with MWS (n = 3) and FCAS (n = 44). Kineret® (anakinra for SC injection), a recombinant nonglycosylated form of the naturally occurring IL-1Ra, is an IL-1 antagonist that is indicated for neonatal onset multisystem inflammatory disorder (NOMID) and for the treatment of rheumatoid arthritis. Kineret has also been used off-label to treat various other forms of CAPS. Kineret is given by SC injection once daily. Treatment of CAPS with antihistamines, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and immunosuppressants (e.g., azathioprine, cyclosporine, mycophenolate mofetil) is usually not effective. Of note, neither Kineret nor Arcalyst are indicated in TRAPS, HIDS/MKD, or FMF. Although neither Kineret nor Arcalyst are indicated in SJIA, Kineret is used for this condition and features prominently in guidelines for SJIA.

Policy Statement
Prior authorization is recommended for prescription benefit coverage of Ilaris. Because of the specialized skills required for evaluation and diagnosis of patients treated with Ilaris as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Ilaris to be prescribed by or in consultation with a physician who specializes in the condition being treated. 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.

Automation: None.
Recommended Authorization Criteria
Coverage of Ilaris is recommended in those who meet the following criteria:

FDA-Approved Indications

1. Cryopyrin-Associated Periodic Syndromes (CAPS) (including Familial Cold Autoinflammatory Syndrome [FCAS], Muckle-Wells Syndrome [MWS], and Neonatal Onset Multisystem Inflammatory Disease [NOMID] or Chronic Infantile Neurological Cutaneous and Articular [CINCA] Syndrome).
   A) Initial Therapy. Approve for 3 months if the patient meets the following conditions (i and ii):
      i. Patient is ≥ 4 years of age; AND
      ii. Ilaris is prescribed by or in consultation with a rheumatologist, geneticist, allergist/immunologist, or dermatologist.
   B) Patients Currently Receiving Ilaris. Approve for 1 year if the patient has had a response, as determined by the prescriber.

2. Familial Mediterranean Fever (FMF).
   A) Initial Therapy. Approve for 4 months if Ilaris 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 has had a response, as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Ilaris.

3. Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD).
   A) Initial Therapy. Approve for 4 months if Ilaris 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 has had a response, as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Ilaris.

   A) Initial Therapy. Approve for 3 months (which is adequate for three doses) if the patient meets ALL of the following conditions (i, ii, and iii):
      i. Patient is ≥ 2 years of age; AND
      ii. Patient meets ONE of the following conditions (a, b, or c):
         a) Patient has tried at least TWO other biologics for SJIA (e.g., Actemra® [tocilizumab infusion], Kineret, Oencia® [abatacept infusion], tumor necrosis factor [TNF] inhibitors [e.g., Enbrel® {etanercept injection}, Humira® {adalimumab injection}, Remicade® {infliximab infusion}); OR
         b) Patient has features of poor prognosis (e.g., arthritis of the hip, radiographic damage, 6-month duration of significant active systemic disease, defined by: fever, elevated inflammatory markers, or requirement for treatment with systemic glucocorticoids), as determined by the prescribing physician AND has tried Actemra or Kineret; OR
         c) Patient has features of SJIA with active systemic features with concerns of progression to macrophage activation syndrome (MAS), as determined by the prescribing physician, AND has tried Kineret.
      iii. Ilaris is prescribed by or in consultation with a rheumatologist.
   B) Patient is Currently Receiving Ilaris. Approve for 1 year if the patient has had a response (e.g., resolution of fevers; improvement in limitation of motion; less joint pain or tenderness; decreased
duration of morning stiffness or fatigue; improved function or activities of daily living; reduced dosage of corticosteroids), as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Ilaris.

5. Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS).
   A) Initial Therapy. Approve for 4 months if Ilaris 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 has had a response, as determined by the prescriber. The patient may not have a full response, but there should have been a recent or past response to Ilaris.

REFERENCES
1. Ilaris® for subcutaneous injection [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2016.


**Other References Utilized:**