Interleukin (IL)-1 Inhibitors Prior Authorization with Quantity Limit Criteria Program Summary

This prior authorization program applies to Commercial, NetResults A series, SourceRx and Health Insurance Marketplace formularies.

OBJECTIVE

The intent of the Interleukin (IL)-1 Inhibitors prior authorization (PA) with Quantity Limit program is to ensure that patients prescribed therapy meet the selection requirements defined in product labeling and/or clinical guidelines and/or clinical studies. The PA defines appropriate use as the Food and Drug Administration (FDA) labeled indication or as supported by the highest level of clinical evidence. Criteria will limit the approved dose to at or below the maximum FDA labeled dose. Doses above the set limit will be approved if the requested quantity is below the FDA limit and cannot be dose optimized.

TARGETED AGENTS

Arcalyst® (rilonacept)
Ilaris® (canakinumab)

QUANTITY LIMIT FOR PRIOR AUTHORIZATION

Brand (generic)	GPI	Multisource Code	Quantity Limit
Arcalyst® (rilonacept) subcutaneous injection			
220 mg single-use vial	66450060002120	M, N, O, or Y	4-220 mg vials/28 days*
Ilaris® (canakinumab) subcutaneous injection			
150 mg/mL single-use vial	66460020002015	M, N, O, or Y	2- 150 mg vials/28 days^
180 mg single-use vial	66460020002120	M, N, O, or Y	2-180 mg vials/28 days^

*Loading dose of up to 320 mg on Day 0.
^Labeled dose is up to 300mg every 4 weeks for SJIA.

PRIOR AUTHORIZATION (PA) CRITERIA FOR APPROVAL

Initial Evaluation

The requested agent will be approved when ALL of the following are met:

1. The patient has an FDA labeled indication for the requested agent
   AND
2. The patient is at least the minimal age noted in the FDA labeled indication
   AND
3. If the diagnosis is SJIA, BOTH of the following:
   a. Verified active systemic features (e.g. ongoing fever, anemia, rash, C-Reactive Protein levels >50 mg/L, ≥2 joint with active arthritis, etc)
      AND
   b. ONE of the following
      i. The patient has tried and failed at least ONE prerequisite medication
         OR

ii. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to all of the prerequisite agents

AND

4. If the diagnosis is Familial Mediterranean Fever (FMF), then ONE of the following:
    a. The patient has tried and failed at least ONE prerequisite medication
    OR
    b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to all of the prerequisite agents

AND

5. The patient does not have any FDA labeled contraindication(s) to the requested agent

AND

6. The patient does not have an active or chronic infection (e.g. tuberculosis, HIV, hepatitis B/C)

AND

7. If the patient is currently being treated with another biologic (IL-1 inhibitor, IL-6 inhibitor, TNF-α blocking agent, etc), the agent will be discontinued before initiating the requested agent

AND

8. ONE of the following:
    a. The quantity (dose) requested is less than or equal to the program quantity limit
    OR
    b. ALL of the following:
        i. The requested quantity (dose) is greater than the program quantity limit
        AND
        ii. The requested quantity (dose) is less than or equal to the FDA labeled dose
        AND
        iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit
    OR
    c. ALL of the following:
        i. The requested quantity (dose) is greater than the program quantity limit
        AND
        ii. The requested quantity (dose) is greater than the FDA labeled dose
        AND
        iii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of approval: 12 months (Arcalyst will also have a loading dose once)

Renewal Evaluation

The requested agent will be approved when ALL of the following are met:

1. The patient has been previously approved for therapy through Prime Therapeutics Prior Authorization process

AND

2. The patient has shown clinical improvement (i.e. improvement in serum levels of C-Reactive Protein (CRP), improvement in Serum Amyloid A (SAA), slowing of disease progression, decrease in symptom severity and/or frequency)

AND

3. The patient is not currently being treated with another biologic immunomodulator agent

AND

4. The patient does not have an active or chronic infection (e.g. tuberculosis, HIV, hepatitis B/C)
   AND
5. The patient does not have any FDA labeled contraindication(s) to the requested agent
   AND
6. ONE of the following:
   a. The quantity (dose) requested is less than or equal to the program quantity limit
      OR
   b. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
         AND
      ii. The requested quantity (dose) is less than or equal to the FDA labeled dose
         AND
      iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

      OR
   c. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
         AND
      ii. The requested quantity (dose) is greater than the FDA labeled dose
         AND
      iii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of approval: 12 months

FDA APPROVED INDICATIONS AND DOSAGE[1,2,5]

Available Products[1,2]	Indication	Route of administration	Dosage and Administration
Arcalyst (rilonacept)	Treatment of CAPS including FCAS and MWS in adults and children 12 years of age and older.	Subcutaneous injection	≥18 years old: 320 mg subcutaneously on day 0 then 160 mg once weekly 12-17 years old: 4.4mg/kg subcutaneously (up to 320 mg) on day 0 then 2.2mg/kg (up to 160 mg) once weekly
Ilaris (canakinumab)	Periodic Fever Syndromes: • Treatment of CAPS including FCAS and MWS, in adults and children 4 years of age and older • TRAPS in adult and pediatric patients • HIDS/MKD in adult and pediatric patients • FMF in adult and pediatric patients Active Systemic Juvenile Idiopathic Arthritis (SJIA) (≥2 years old)	Subcutaneous injection	CAPS/FCAS/MWS: <u>>40 kg:</u> 150 mg subcutaneously (SC) every 8 weeks <u>≥15-40 kg:</u> 2 mg/kg SC every 8 weeks (inadequate response: can increase to 3 mg/kg SC every 8 weeks) TRAPS/HIDS/MKD/FMF: ≤40 kg: 2 mg/kg SC every 4 weeks (inadequate response: can increase to 4 mg/kg every 4 weeks) >40 kg: 150 mg SC every 4 weeks (inadequate response: can increase to 300 mg every 4 weeks) SJIA: 4mg/kg (maximum of 300mg) for body weight ≥7.5kg subcutaneously every 4 weeks

CAPS**-** Cryopyrin-associated Periodic Syndromes
FCAS- Familial Cold Autoinflammatory Syndrome
MWS- Muckle-Wells Syndrome
SJIA- Systemic Juvenile Idiopathic Arthritis
TRAPS – Tumor Necrosis Factor Receptor Associated Periodic SyndromeHIDS – Hyperimmunoglobulin D Syndrome
MKD – Mevalonate Kinase Deficiency
FMF – Familial Mediterranean Fever

CLINICAL RATIONALE

Periodic Fever Syndromes:

CAPS/FCAS/MWS

CAPS is a rare disease affecting an estimated 300 people in the United States. CAPS consists of three phenotypically related disorders all associated with mutations in the CIAS-1 gene.[3] The mildest form, FCAS is characterized by intermittent cold-induced rash, with fever and arthralgia. MWS is characterized by urticaria, deafness, and reactive amyloid A amyloidosis. The most severe form is neonatal onset multisystem inflammatory disorder (NOMID) and presents in neonates with inflammation affecting many organ systems. Not all patients with CAPS have the gene mutation for altered cryopyrin.[4] Prior to the development of rilonacept and canakinumab, CAPS was treated with antihistamines, NSAIDs, corticosteroids, and immunosuppressants. Both rilonacept and canakinumab inhibit interleukin-1 (IL-1).

Inhibition of IL-1 is the mechanism of anakinra for the treatment of rheumatoid arthritis.[5] Canakinumab and rilonacept are not approved for any disease state other than CAPS.

Formerly known as Familial Hibernian Fever, Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), is another rare autoinflammatory disorder (prevalence of approximately one per million) caused by a genetic defect in the gene that encordes the 55 kDa receptor for tumor necrosis factor (TNF). This genetic disorder is characterized by recurrent episodes of fever often lasting over a week without any associated viral or bacterial infections (episodes every 5-6 weeks is typical, but can vary). Many times a rash will spread from the torso down the extremities and the patient will experience chest pain due to inflammation surrounding the lungs and heart. Depending on the mutation, some patients may develop secondary amyloidosis.[14,15]

Hyperimmunoglobulin D syndrome (HIDS) also known as Mevalonate Kinase Deficiency (MKD) has somewhat similar manifestations as TRAPS, but is due to a mutation in the mevalonate kinase gene. It also clinically presents as unremitting fever lasting several days accompanied by chills with no associated infections. There often is also lymphadenopathy, splenomegaly, arthralgia/arthritis, abdominal pain, and rash. Time between attacks vary by patient, but are commonly seen every month to two months.[16,17]

Similar to TRAPS, HIDS/MKD, patients with Familial Mediterranean Fever (FMF) experience recurrent episodes of fever with abdominal, chest or joint pain lasting 1-3 days and can dissipate without treatment. An erysipelas-like skin lesion found on the lower leg/ankle/foot is reported in 7-40 percent of patients. The diagnosis is based on clinical symptoms, ethnic origin and family history. Genetic testing is a supportive measure for diagnosis as some patient's genetic testing is not diagnostic (there may only be one or no pathogenic MEFV mutation). FMF cannot be cured, but it can be controlled with life-long use of colchicine. It is estimated that about 10% of patients do not respond adequately or cannot tolerate colchicine and move onto an IL-1 inhibitor.[18-20]

Systemic Juvenile Idiopathic Arthritis (SJIA)

Systemic juvenile idiopathic arthritis (SJIA) was formerly called Still's disease and is the rarest subset (4-15%) of juvenile idiopathic arthritis (JIA). As of recent, it is thought that the inflammatory process underlying SJIA is different than other categories within JIA and involves interleukins IL-1 and IL-6. Patients typically present with fever, rash, and arthritis. The American College of Rheumatology (ACR) 2013 SJIA initial therapy treatment update for active systemic features includes nonsteroidal anti-inflammatory drugs (NSAIDs), systemic glucocorticoids (oral or intravenous) and Anakinra (IL-1). Many children with SJIA have refractory disease, in which agents targeting interleukins IL-1 and IL-6 are used. ACR suggests continued disease activity be managed with canakinumab (IL-1), tocilizumab (IL-6), TNF-α inhibitors, methotrexate, leflunomide or options included in initial therapy not yet utilized. Treatment suggestions/decisions are based on the patient's physician global assessment (MD global) and active joint count (AJC). Macrophage activation syndrome (MAS), a life-threatening condition including fever, enlarged organs, cytopenias, coagulopathy amongst many other systemic abnormalities, has been associated with approximately 10 percent of SJIA cases.[6-13]

Interleukin-1 blockade may interfere with immune response to infections. Serious, life-threatening infections have been reported in patients taking rilonacept or canakinumab. Treatment with these agents should not be initiated in patients with active or chronic infections. Administration of rilonacept or canakinumab should be discontinued if a patient develops a serious infection.[1,2]

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