AETNA BETTER HEALTH® Coverage Policy/Guideline					
Name:	Kineret			Page:	1 of 11
Effective Date:	5/1/2024			Last Review Date:	11/2023; 4/2024
Applies to:	☐Illinois ☐New Jersey ☒Pennsylvania Kids	☐Florida ☒Maryland ☐Virginia		☒Florida Kids ☐Michigan ☒Kentucky PRMD	

Intent:

The intent of this policy/guideline is to provide information to the prescribing practitioner outlining the coverage criteria for Kineret under the patient's prescription drug benefit.

Description:

A. FDA-Approved Indications
   1. Moderately to severely active rheumatoid arthritis (RA), in patients 18 years of age or older who have failed 1 or more disease modifying antirheumatic drugs (DMARDs)
   2. Cryopyrin-Associated Periodic Syndromes (CAPS), including Neonatal-Onset Multisystem Inflammatory Disease (NOMID)
   3. Deficiency of Interleukin-1 Receptor Antagonist (DIRA)

B. Compendial Uses
   1. Systemic juvenile idiopathic arthritis (sJIA)
   2. Adult-onset Still's disease
   3. Multicentric Castleman disease
   4. Recurrent pericarditis
   5. Hyperimmunoglobulin D syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)
   6. Schnitzler syndrome
   7. Gout and pseudogout (calcium pyrophosphate deposition)
   8. CAR T-Cell-Related Toxicities – Cytokine release syndrome (CRS)
   9. Erdheim-Chester Disease

All other indications are considered experimental/investigational and not medically necessary.

Applicable Drug List:

Non-preferred: Kineret

Policy/Guideline:

Documentation for all indications:
The patient is unable to take THREE preferred products (a preferred adalimumab product, Enbrel, Kevzara or Rinvoq), where indicated, for the given diagnosis due to a trial and inadequate treatment response or intolerance, or a contraindication. Documentation is required for approval.

Documentation:

A. Rheumatoid arthritis (RA)

1. For initial requests:
   a. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   b. Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).
2. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B. Adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (sJIA)

1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C. Neonatal-onset multisystem inflammatory disease (NOMID): For continuation requests: Chart notes, medical record documentation, or laboratory results supporting positive clinical response.

D. Deficiency of interleukin-1 receptor antagonist (DIRA): For initial requests: *IL1RN* mutation status.

E. Recurrent pericarditis

1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy.
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

F. Hyperimmunoglobulin D syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD): For initial requests: Chart notes, medical record documentation, or laboratory result (if applicable) indicating number of active flares within the last 6 months and Physician's Global Assessment (PGA) score or C-reactive protein (CRP) level.

G. Gout and pseudogout flares and CAR T-Cell-related toxicities: For initial requests: Chart notes, medical record documentation, or claims history supporting previous

medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

Prescriber Specialty:
This medication must be prescribed by or in consultation with one of the following:

A. Rheumatoid arthritis, adult-onset Still's disease, systemic juvenile idiopathic arthritis, gout, and pseudogout: rheumatologist
B. Cryopyrin-associated periodic syndromes (CAPS), including neonatal-onset multisystem inflammatory disease (NOMID), deficiency of interleukin-1 receptor antagonist (DIRA), and hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD): rheumatologist or immunologist
C. Recurrent pericarditis: cardiologist, rheumatologist, or immunologist
D. Schnitzler syndrome: rheumatologist, dermatologist, or immunologist
E. Multicentric Castleman disease, CAR T-cell-related toxicities, and Erdheim-Chester disease: oncologist or hematologist

Criteria for Initial Approval:

A. Rheumatoid arthritis (RA)

1. Authorization of 12 months may be granted for adult members who have previously received a biologic or targeted synthetic drug indicated for moderately to severely active rheumatoid arthritis.
2. Authorization of 12 months may be granted for adult members for treatment of moderately to severely active RA when all of the following criteria are met:
    i. Member meets either of the following criteria:
        a. Member has been tested for either of the following biomarkers and the test was positive:
            1. Rheumatoid factor (RF)
            2. Anti-cyclic citrullinated peptide (anti-CCP)
        b. Member has been tested for ALL of the following biomarkers:
            1. RF
            2. Anti-CCP
            3. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)
    ii. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week), or the member has an intolerance or contraindication to methotrexate (see Appendix).
    iii. Member has experienced an inadequate response to at least a 3-month trial of a biologic or a targeted synthetic drug (e.g., Rinvoq, Xeljanz) or has an intolerance to a biologic or targeted synthetic drug.

B. Adult-onset Still's disease (AOSD)

1. Authorization of 12 months may be granted for members who have received a biologic indicated for active adult-onset Still's disease.
2. Authorization of 12 months may be granted for treatment of active adult-onset Still's disease when both of the following criteria are met:
   i. Member has active systemic features (e.g., fever, arthralgia/arthritis, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, sore throat).
   ii. Member meets any of the following:
      a. Member has had an inadequate response to a trial of nonsteroidal anti-inflammatory drugs (NSAIDs).
      b. Member has had an inadequate response to a trial of corticosteroids.
      c. Member has had an inadequate response to a trial of a conventional synthetic drug (e.g., methotrexate).

C. Systemic juvenile idiopathic arthritis (sJIA)

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active systemic juvenile idiopathic arthritis.
2. Authorization of 12 months may be granted for treatment of active systemic juvenile idiopathic arthritis when both of the following criteria are met:
   i. Member has active systemic features (e.g., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, serositis).
   ii. Member has had an inadequate response to non-steroidal anti-inflammatory drugs (NSAIDs) or systemic glucocorticoids.

D. Neonatal-onset multisystem inflammatory disease (NOMID)

Authorization of 12 months may be granted for treatment of cryopyrin-associated periodic syndromes (CAPS), including NOMID (also known as chronic infantile neurologic cutaneous and articular [CINCA] syndrome).

E. Deficiency of interleukin-1 receptor antagonist (DIRA)

Authorization of 12 months may be granted for treatment of genetically confirmed deficiency of interleukin-1 receptor antagonist (DIRA) due to *IL1RN* mutations.

F. Recurrent pericarditis

Authorization of 12 months may be granted for treatment of recurrent pericarditis when both of the following criteria are met:

1. Member has had at least two episodes of pericarditis.

2. Member has failed at least 2 agents of standard therapy (e.g., colchicine, non-steroidal anti-inflammatory drugs [NSAIDs], corticosteroids).

G. Multicentric Castleman disease

Authorization of 12 months may be granted for treatment of multicentric Castleman disease when both of the following criteria are met:

1. The requested medication will be used as a single agent.
2. The disease has progressed following treatment of relapsed/refractory or progressive disease.

H. Hyperimmunoglobulin D syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)

Authorization of 12 months may be granted for treatment of HIDS/MKD when both of the following criteria are met:

1. Member has had active flares within the last 6 months.
2. Physician's Global Assessment (PGA) score greater than or equal to 2 or C-reactive protein (CRP) greater than 10 mg/L.

I. Schnitzler syndrome

Authorization of 12 months may be granted for treatment of Schnitzler syndrome when both of the following criteria are met:

1. Member has an urticarial rash, monoclonal IgM (or IgG) gammopathy, and at least two of the following signs and symptoms: fever, joint pain or inflammation, bone pain, lymphadenopathy, hepatomegaly, splenomegaly, leukocytosis, elevated erythrocyte sedimentation rate (ESR), or abnormalities on bone morphological study (e.g., increased bone density).
2. Other possible causes of the signs and symptoms have been ruled out, including but not limited to: hyperimmunoglobulin D syndrome, adult-onset Still's disease, urticarial hypocomplementemic vasculitis, acquired C1 inhibitor deficiency, and cryoglobulinemia.

J. Management of gout and pseudogout flares

Authorization of 6 months may be granted for management of flares for gout or pseudogout (also known as calcium pyrophosphate deposition disease) when either of the following criteria is met:

1. Member has had an inadequate response or intolerance to maximum tolerated doses of non-steroidal anti-inflammatory drugs (NSAIDs), colchicine, and oral and injectable corticosteroids.
2. Member has a contraindication to NSAIDs and colchicine and has a clinical reason to avoid repeated courses of corticosteroids.

K. Cytokine release syndrome

Authorization of 1 month may be granted for the management of chimeric antigen receptor (CAR) T-cell-induced cytokine release syndrome when either of the following criteria is met:

1. Cytokine release syndrome is refractory to high-dose corticosteroids and anti-IL-6 therapy.
2. Kineret will be used as a replacement for the second dose of tocilizumab when supplies are limited or unavailable.

L. Erdheim-Chester Disease

Authorization of 12 months may be granted for the treatment of Erdheim-Chester disease.

Continuation of Therapy:

A. Rheumatoid arthritis (RA)

Authorization of 12 months may be granted for all adult members (including new members) who are using the requested medication for moderately to severely active rheumatoid arthritis and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B. Adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (sJIA)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for adult-onset Still's disease or systemic juvenile idiopathic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
2. Number of joints with limitation of movement
3. Functional ability
4. Systemic features (e.g., fever, evanescent rash, lymphadenopathy, hepatomegaly, splenomegaly, serositis)

C. Neonatal-onset multisystem inflammatory disease (NOMID)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for CAPS, including NOMID (also known as CINCA), and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Fever
2. Skin rash
3. Joint pain and/or inflammation
4. Central nervous system (CNS) symptoms (e.g., meningitis, headache, cerebral atrophy, uveitis, hearing loss)
5. Inflammatory markers (e.g., serum amyloid A [SAA], C-reactive protein [CRP], erythrocyte sedimentation rate [ESR])

D. Recurrent pericarditis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for recurrent pericarditis and who achieve or maintain a positive clinical response as evidenced by decreased recurrence of pericarditis or improvement in signs and symptoms of the condition when there is improvement in any of the following:

1. Pericarditic chest pain
2. Pericardial rubs
3. Electrocardiogram (ECG)
4. Pericardial effusion
5. C-reactive protein (CRP)

E. Multicentric Castleman disease

Authorization of 12 months may be granted for continued treatment of multicentric Castleman disease in members requesting reauthorization who have not experienced disease progression or an unacceptable toxicity.

F. Cytokine release syndrome

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

G. All other indications

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for an indication outlined in criteria for initial

approval and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

Other Criteria:
Member has had a documented negative tuberculosis (TB) test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic drugs or targeted synthetic drugs associated with an increased risk of TB.

*If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

Member cannot use the requested medication concomitantly with any other biologic drug or targeted synthetic drug.

APPENDIX: Examples of clinical reasons to avoid pharmacologic treatment with methotrexate

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Drug interaction
3. Risk of treatment-related toxicity
4. Pregnancy or currently planning pregnancy
5. Breastfeeding
6. Significant comorbidity prohibits use of systemic agents (e.g., liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
7. Hypersensitivity
8. History of intolerance or adverse event

Approval Duration and Quantity Restrictions:

Approval:
Initial Approval: Gout and pseudogout flares = 6 months; cytokine release syndrome = 1 month; all others = 12 months
Renewal Approval: Gout and pseudogout flares = 6 months; cytokine release syndrome = 1 month; all others = 12 months

Quantity Level Limit:

Medication	Standard Limit	Exception Limit*
Kineret (anakinra) injection 100 mg/0.67 mL single-use prefilled syringe	30 syringes per 30 days	360 syringes per 30 days

*Exception limits apply to loading doses.

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