Clinical Policy: Anakinra (Kineret)
Reference Number: ERX.SPA.135
Effective Date: 10.01.16
Last Review Date: 05.19

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Anakinra (Kineret®) is an interleukin-1 (IL-1) receptor antagonist.

FDA Approved Indication(s)
Kineret is indicated for the treatment of:
- Rheumatoid arthritis (RA): Reduction in signs and symptoms and slowing the progression of structural damage in moderately to severely active rheumatoid arthritis, in patients 18 years of age or older who have failed 1 or more disease modifying antirheumatic drugs (DMARDs). Kineret can be used alone or in combination with DMARDs other than tumor necrosis factor blocking agents
- Cryopyrin-associated periodic syndromes (CAPS): Treatment of neonatal-onset multisystem inflammatory disease (NOMID)

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Kineret is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Rheumatoid Arthritis (must meet all):
      1. Diagnosis of RA;
      2. Prescribed by or in consultation with a rheumatologist;
      3. Age ≥ 18 years;
      4. Member meets one of the following (a or b):
         a. Failure of a ≥ 3 consecutive month trial of methotrexate (MTX) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
         b. If intolerance or contraindication to MTX (see Appendix D), failure of a ≥ 3 consecutive month trial of at least ONE conventional DMARD (e.g., sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
      5. Failure of 2 of the following, each used for ≥ 3 consecutive months unless contraindicated or clinically significant adverse effects are experienced: etanercept (Enbrel® is preferred), adalimumab (Humira® is preferred), Kevzara®, infliximab (Remicade® is preferred), Xeljanz®, Xeljanz XR®, or golimumab (Simponi Aria® is preferred);
      6. Dose does not exceed 100 mg per day.
   Approval duration: 6 months

   B. Cryopyrin-Associated Periodic Syndromes (must meet all):
      1. Diagnosis of NOMID;
      2. Prescribed by or in consultation with a rheumatologist;
      3. Dose does not exceed 8 mg/kg per day.
   Approval duration: 6 months
C. Other diagnoses/indications
   1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III
      (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy
   A. All Indications in Section I (must meet all):
      1. Currently receiving medication via health plan affiliated with Envolve Pharmacy Solutions or
         member has previously met initial approval criteria;
      2. Member is responding positively to therapy;
      3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
         a. RA: 100 mg per day;
         b. NOMID: 8 mg/kg per day.
   
      Approval duration: 12 months

   B. Other diagnoses/indications (must meet 1 or 2):
      1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions
         and documentation supports positive response to therapy.
      Approval duration: Duration of request or 6 months (whichever is less); or
      2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III
         (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:
   A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient
      documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or
      evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   CAPS: cryopyrin-associated periodic syndromes
   DMARD: disease modifying antirheumatic drugs
   FDA: Food and Drug Administration
   MTX: methotrexate
   IL-1: interleukin-1
   NOMID: neonatal-onset multisystem inflammatory disease
   RA: rheumatoid arthritis

   Appendix B: Therapeutic Alternatives
   This table provides a listing of preferred alternative therapy recommended in the approval criteria.
   The drugs listed here may not be a formulary agent for all relevant lines of business and may require
   prior authorization.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>azathioprine (Azasan®, Imuran®)</td>
<td>RA 1 mg/kg/day PO QD or divided BID</td>
<td>2.5 mg/kg/day</td>
</tr>
<tr>
<td>Cuprimine® (d-penicillamine)</td>
<td>RA* Initial dose: 125 or 250 mg PO QD Maintenance dose: 500 – 750 mg/day PO QD</td>
<td>1,500 mg/day</td>
</tr>
<tr>
<td>cyclosporine (Sandimmune®, Neoral®)</td>
<td>RA 2.5 – 4 mg/kg/day PO divided BID</td>
<td>4 mg/kg/day</td>
</tr>
<tr>
<td>hydroxychloroquine (Plaquinil®)</td>
<td>RA* Initial dose: 400 – 600 mg/day PO Maintenance dose: 200 – 400 mg/day PO</td>
<td>600 mg/day</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Dosing Regimen</td>
<td>Dose Limit/Maximum Dose</td>
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<td>---------------------------------</td>
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</tr>
<tr>
<td>leflunomide (Arava®)</td>
<td>RA 100 mg PO QD for 3 days, then 20 mg PO QD</td>
<td>20 mg/day</td>
</tr>
<tr>
<td>methotrexate (Rheumatrex®)</td>
<td>RA 7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week</td>
<td>30 mg/week</td>
</tr>
<tr>
<td>Ridaura® (auranofin)</td>
<td>RA 6 mg PO QD or 3 mg PO BID</td>
<td>9 mg/day (3 mg TID)</td>
</tr>
<tr>
<td>sulfasalazine (Azulfidine®)</td>
<td>RA 2 g/day PO in divided doses</td>
<td>3 gm/day</td>
</tr>
<tr>
<td>Enbrel (etanercept)</td>
<td>RA 25 mg SC twice weekly or 50 mg SC once weekly</td>
<td>50 mg/week</td>
</tr>
<tr>
<td>Humira (adalimumab)</td>
<td>RA 40 mg SC every other week (may increase to once weekly)</td>
<td>40 mg/week</td>
</tr>
<tr>
<td>Kevzara (sarilumab)</td>
<td>RA 200 mg SC once every two weeks</td>
<td>200 mg every 2 weeks</td>
</tr>
<tr>
<td>Remicade (infliximab)</td>
<td>RA In conjunction with MTX</td>
<td>10 mg/kg every 4 weeks</td>
</tr>
<tr>
<td>Simponi Aria (golimumab)</td>
<td>RA Initial dose: 3 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: 3 mg/kg IV every 8 weeks</td>
<td>2 mg/kg every 8 weeks</td>
</tr>
<tr>
<td>Xeljanz (tofacitinib)</td>
<td>RA 5 mg PO BID</td>
<td>10 mg/day</td>
</tr>
<tr>
<td>Xeljanz XR (tofacitinib)</td>
<td>RA 11 mg PO QD</td>
<td>11 mg/day</td>
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</table>

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

*Off-label*

**Appendix C: Contraindications/Boxed Warnings**
- Contraindication(s): known hypersensitivity to *E. coli*-derived proteins, Kineret, or any components of the product
- Boxed warning(s): none reported

**Appendix D: General Information**
- Definition of MTX or DMARD failure:
  - Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.
  - Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week. However,
excessive alcohol drinking can lead to worsening of the condition, so patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.

- Examples of positive response to therapy may include, but are not limited to:
  - Reduction in joint pain/swelling/tenderness
  - Improvement in ESR/CRP levels
  - Improvements in activities of daily living

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>100 mg SC QD</td>
<td>100 mg/day</td>
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<tr>
<td>NOMID</td>
<td>Initial dose:</td>
<td></td>
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<td></td>
<td>1 – 2 mg/kg/day SC QD or divided BID</td>
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<td></td>
<td>Maintenance dose:</td>
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<td></td>
<td>8 mg/kg/day SC QD or divided BID</td>
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VI. Product Availability

- Single-use prefilled syringe: 100 mg/0.67 mL

VII. References


Reviews, Revisions, and Approvals

| Policy split from USS.SPMN.09 Cryopyrin-Associated Periodic Syndromes (CAPS) Treatments and Rheumatoid Arthritis and Ankylosing Spondylitis Treatments. Converted to new template. Removed all safety criteria. Modified approval duration to 6 months for initial and 12 months for re-auth. CAPS: Added route of administration and dosing frequency per PI. RA: Added age requirement per PI; modified criteria to require trial of methotrexate, unless contraindicated; added sulfasalazine and hydroxychloroquine as an alternative to methotrexate if methotrexate is contraindicated; added requirement for trial and failure of PDL Enbrel and Humira, unless contraindicated; removed requirement for attestation of compliance for re-auth. Converted to new template. Added therapeutic alternatives table. Revised criteria for confirmation of RA diagnosis per 2010 ACR Criteria. | 08.16 | 09.16 |
| 4Q17 Annual Review RA: removed requirement for submission of diagnostic lab since a specialist is required to prescribe or be consulted | 09.29.17 | 11.17 |
| 2Q 2018 annual review: no significant changes; modified trial and failure of preferred agents for RA; references reviewed and updated. | 02.27.18 | 05.18 |
| 4Q 2018 annual review: no significant changes; references reviewed and updated. | 09.04.18 | 11.18 |
| 2Q 2019 annual review: no significant changes; added Xeljanz/Xeljanz XR to list of trial options for RA; references reviewed and updated. | 02.26.19 | 05.19 |
Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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