Clinical Policy Title:	anakinra
Policy Number:	RxA.739
Drug(s) Applied:	Kineret®
Original Policy Date:	04/18/2022
Last Review Date:	04/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Anakinra (Kineret®) is an interleukin-1 receptor antagonist. It is indicated for:

- 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).
- Cryopyrin-Associated Periodic Syndromes (CAPS): Treatment of Neonatal-Onset Multisystem Inflammatory Disease (NOMID).
- Deficiency of Interleukin-1 Receptor Antagonist (DIRA): Treatment of Deficiency of Interleukin-1 Receptor Antagonist (DIRA).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
anakinra (Kineret®)	RA	100 mg/day subcutaneously once daily Renal impairment (creatinine clearance < 30 mL/min): Administered every other day.	100 mg/day
	NOMID	1-2 mg/kg subcutaneously once daily The dose can be individually adjusted to a maximum of 8 mg/kg daily to control active inflammation. Adjust doses in 0.5 to 1 mg/kg increments Once daily administration is recommended but the dose may be split into twice daily administrations. Renal impairment (creatinine clearance < 30 mL/min): Administered every other day.	8 mg/kg/day

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
	DIRA	The recommended starting dose of Kineret® is 1-2 mg/kg daily The dose can be individually adjusted to a maximum of 8 mg/kg daily to control active inflammation. Adjust doses in 0.5 to 1 mg/kg increments. Renal impairment (creatinine clearance < 30 mL/min): Administered every other day.	8 mg/kg/day

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Rheumatoid Arthritis (must meet all):

1. Diagnosis of Rheumatoid Arthritis (RA);
2. Prescribed by or in consultation with a rheumatologist;
3. Member is ≥ 18 years;
4. Trial and failure of a ≥ 3 months of at least one conventional systemic therapy (methotrexate [MTX], sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   *Exception: If one biologic DMARD that is FDA-approved for rheumatoid arthritis has been previously tried, then trial of a conventional systemic agent is not required;
5. Members meets both (a AND b):
   a. Trial and failure of at least two (2) of the follwoing agents: Humira®, Cimzia®, Rinvoq®, Simponi® or Xeljanz®/ XR unless contraindicated or clinically significant adverse effects are experienced;
   *Exception: If a total of two TNF inhibitors (Humira®, Cimzia®, Simponi®/ Simponi Aria®, Enbrel®) has previously been tried and failed, trial of a third TNF inhibitor is not required;
   b. Trial and failure of both Actemra® & Orencia® unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 100 mg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

B. Neonatal-Onset Multisystem Inflammatory Disease (must meet all)**:**

1. Diagnosis of neonatal- onset multisystem inflammatory disease (NOMID) or chronic infantile neurological, cutaneous and articular syndrome (CINCA);
2. Prescribed by or in consultation with a rheumatologist;
3. Dose does not exceed 8 mg/kg/day.

Approval duration
Commercial: 12 months
Medicaid: 12 months

C. Deficiency of Interleukin-1 Receptor Antagonist (DIRA) (must meet all):
1. Diagnosis of Deficiency of Interleukin-1 Receptor Antagonist;
2. Member is ≥ 1 month;
3. Dose does not exceed 8 mg/kg/day.

Approval duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed;
   a. RA: 100 mg / day
   b. DIRA and NOMID: 8 mg/kg/day

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
DMARDs: Disease-Modifying Antirheumatic Drugs
FDA: Food and Drug Administration
CAPS: Cryopyrin-Associated Periodic Syndromes
NOMID: Neonatal-Onset Multisystem Inflammatory Disease
DIRA: Deficiency of Interleukin-1 Receptor Antagonist
MTX: Methotrexate
RA: Rheumatoid Arthritis

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
azathioprine (Azasan®, Imuran®)	**RA:** 1 mg/kg/day orally once daily or divided twice daily	2.5 mg/kg/day
d-penicillamine (Cuprimine®)	**RA:** Initial dose: 125 or 250 mg orally once daily	1,500 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Maintenance dose: 500 – 750 mg/day orally once daily	
cyclosporine (Sandimmune®, Neoral®)	**RA:** 2.5 – 4 mg/kg/day orally divided twice daily	4 mg/kg/day
hydroxychloroquine (Plaquenil®)	**RA:** Initial dose: 400 – 600 mg/day orally once daily Maintenance dose: 200 – 400 mg/day orally once daily	600 mg/day
leflunomide (Arava®)	**RA:** 100 mg orally once daily for 3 days, then 20 mg orally once daily	20 mg/day
methotrexate	**RA:** 7.5 mg/week orally, subcutaneously, or intramuscularly or 2.5 mg orally every 12 hr for 3 doses/week	30 mg/week
Ridaura®	**RA:** 6 mg orally once daily or 3 mg orally twice daily	9 mg/day (3 mg Three times daily)
sulfasalazine (Azulfidine®)	**RA:** 2 g/day orally in divided doses	3 g/day
Biologic DMARDs		
infliximab (Remicade®), Renflexis®, Inflectra®, Avsola®	**RA:** In conjunction with MTX Initial dose: 3 mg/kg intravenously at weeks 0, 2 and 6 Maintenance dose: 3 mg/kg intravenously every 8 weeks Some patients may benefit from increasing the dose up to 10 mg/kg or treating as often as every 4 weeks	10 mg/kg every 4 weeks
Simponi Aria®	**RA:** Initial dose: 2 mg/kg intravenously at weeks 0 and 4 Maintenance dose: 2 mg/kg intravenously every 8 weeks	2 mg/kg every 8 weeks
Xeljanz®, Xeljanz® XR	**RA:** Xeljanz®: 5 mg orally twice daily, as monotherapy or use in combination with nonbiologic disease-modifying antirheumatic drugs. Xeljanz® XR: 11 mg orally once daily	Xeljanz®: 10 mg/day Xeljanz® XR: 11 mg/day
Olumiant®	**RA:** 2 mg orally once daily	2 mg/day
Humira®	**RA:** Some patients with RA not receiving concomitant methotrexate may benefit from increasing the frequency to 40 mg every Week or 80 mg every other week	40 mg every other week
Actemra®	**RA**: Intravenous: 4 mg/kg every 4 weeks followed by an increase to 8 mg/kg every 4 weeks based on clinical response. Subcutaneous:	Intravenous: 800 mg every 4 weeks

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Weight < 100 kg: 162 mg every other week, followed by an increase to every week based on clinical response. Weight ≥ 100 kg: 162 mg every week.	Subcutaneous: 162 mg every week
Cimzia®	**RA:** Initial dose: 400 mg subcutaneously at 0, 2, and 4 weeks. Maintenance dose: 200 mg subcutaneously every other week (or 400 mg subcutaneously every 4 weeks)	400 mg every 4 weeks
Enbrel®	**RA:** 25 mg subcutaneously twice weekly or 50 mg subcutaneously once weekly	**RA:** Adults 50 mg/week subcutaneously. Induction therapy for psoriatic arthritis should not exceed 100 mg/week with no more than 50 mg/dose subcutaneously.
Kevzara®	**RA:** 200 mg subcutaneously once every two weeks	200 mg/2 Weeks
Orencia®	**RA:** Intravenous: weight-based dose at weeks 0, 2, and 4, followed by every 4 weeks Weight < 60 kg: 500 mg per dose Weight 60 to 100 kg: 750 mg per dose Weight > 100 kg: 1,000 mg per dose Subcutaneous: 125 mg once weekly RA: Patients switching from intravenous use to subcutaneous use, administer first subcutaneous dose instead of next scheduled intravenous dose. (For RA: Prior to the first subcutaneously dose, may administer an optional loading dose as a single intravenous infusion as per body weight categories above.)	**RA:** Intravenous: 1,000 mg every 4 weeks Subcutaneous: 125 mg/week
Rinvoq®	**RA:** 15 mg orally once daily Can be used as monotherapy or in combination with methotrexate or other non-biologic DMARDs. *For use in adults who have had an inadequate response or intolerance to one or more TNF blockers	RA: 15 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Simponi®	**RA:** 50 mg subcutaneously once monthly	RA :50 mg/month

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Known hypersensitivity to *E coli*-derived proteins, Kineret®, or to any component of the product.

  *Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Safety:
  - These agents are immunosuppressives and have the potential to increase the risk of infection and reactivate latent, chronic infections. They should not be administered to patients with a clinically important infection. Caution should be used in patients with chronic infections or history of recurrent infection. If patient develops a serious infection these agents should be discontinued.
- Neonatal-Onset Multisystem Inflammatory Disease:
  - Other names used for NOMID are as follows: chronic infantile neurological, CINCA, chronic neurologic, cutaneous, and articular syndrome, infantile onset multisystem inflammatory disease, IOMID syndrome, and Prieur-Griscelli syndrome.
- MTX is a pregnancy category X and is absolutely contraindicated in pregnancy and is not recommended for female patients attempting to conceive.

References

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3. Lexi-Drug. Lexicomp. Wolters Kluwer. Hudson, OH. Available at: http://online.lexi.com. Accessed February 14, 2022.
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Review/Revision History	Review/Revision Date	P&T Approval Date
RxA.592.Biologic_DMARDs was last reviewed and updated on 01/05/2022 and archived on	01/05/2022	04/18/2022

04/18/2022. For details, please refer to RxA.592.Biologic_DMARDs		
Drug specific policy for Kineret® was created based on RxA.592.Biologic_DMARDs: 1. Initial Approval Criteria, I.A.5: Updated to remove prior trial and failure criteria "Failure of two (2) of the following, each used for ≥ 3 months, unless contraindicated or clinically significant adverse effects are experienced: Humira®, Cimzia®, Inflectra®, Rinvoq™, Renflexis™, Simponi®, Simponi Aria®, or Xeljanz®/ Xeljanz XR®". 2. Initial Approval Criteria, I.A.5: Updated to include new trial and failure criteria Members meets both (a AND b): a. Trial and failure of at least two (2) of the follwoing agents: Humira®, Cimzia®, Rinvoq®, Simponi® or Xeljanz®/ XR unless contraindicated or clinically significant adverse effects are experienced; *Exception: If a total of two TNF inhibitors (Humira®, Cimzia®, Simponi®/ Simponi Aria®, Enbrel®) has previously been tried and failed, trial of a third TNF inhibitor is not required; b. Trial and failure of both Actemra® & Orencia® unless contraindicated or clinically significant adverse effects are experienced; 3. Appendix B, Drug Name: Updated to include brand-name therapeutic alternative of other biological DMARDs. 4. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C. 5. Appendix D, General Information: Updated to remove information regarding: (a, b and c) a. Rheumatoid Arthritis; b. Definition of failure of MTX or DMARDs; c. Examples of positive response to therapy. 6. References were reviewed and updated.	02/14/2022	04/18/2022