Drug Coverage Policy

Effective Date……11/01/2025
Coverage Policy Number…… DQM008
Policy Title…..Kineret Drug Quantity Management Policy – Per Days

Inflammatory Conditions – Kineret Drug Quantity Management Policy – Per Days

- Kineret® (anakinra subcutaneous injection – Biovitrim)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Indication
Kineret, an interleukin-1 (IL-1) receptor antagonist, indicated for the following uses:[1]

- **Cryopyrin-associated periodic syndromes** (CAPS) for treatment of neonatal-onset multisystem inflammatory disease (NOMID).
- **Deficiency of interleukin-1 receptor antagonist** (DIRA).
- **Rheumatoid arthritis**, to reduce the signs and symptoms and slow the progression of structural damage in adults with moderately to severely active disease who have failed one or more disease-modifying antirheumatic drugs (DMARDs) given ± DMARDs other than tumor necrosis factor inhibitors (TNFis).

Dosing
Kineret is administered by subcutaneous (SC) injection.[1] A new syringe must be used for each dose. The graduated syringes allow for partial doses between 20 mg and 100 mg to be given. Any unused portion after each dose should be discarded. Regardless of indication, consider administration of the prescribed dose every other day for patients who have severe renal insufficiency or end stage renal disease (defined as creatinine clearance < 30 mL/min, as estimated from serum creatinine levels).

    - CAPS: 1 to 2 mg per kg once daily (QD) for patients with NOMID. The dose may be individually adjusted to a maximum of 8 mg per kg daily to control active inflammation. Adjust doses in 0.5 to 1 mg per kg increments. QD dosing is generally recommended, but dose may be split into twice daily administration.
    - **DIRA:** 1 to 2 mg per kg QD. The dose may be individually adjusted to a maximum of 8 mg per kg QD to control active inflammation. Adjust doses in 0.5 to 1 mg per kg increments.
- **Rheumatoid arthritis:** 100 mg QD at approximately the same time every day. Higher doses did not result in a higher response.

Off-Label Use
In addition to the FDA-approved uses, guidelines support the use of Kineret for the treatment of other conditions as well:

- **Castleman Disease:** the National Comprehensive Cancer Network (NCCN) guidelines (version 2.2025 – January 28, 2025) list Kineret as an alternative regimen for subsequent therapy as a single agent for multicentric Castleman disease that is relapsed or refractory disease.[3] For this condition, the dose of Kineret is 100 mg SC QD.
- **Histiocytic Neoplasms:** NCCN guidelines (version 1.2025 – June 20, 2025) provide recommendations for Kineret as first-line or subsequent treatment for Erdheim-Chester disease regardless of mutation.[4] For this condition, the dose of Kineret is 100 mg SC QD.
- **Immunotherapy-Related Toxicities:** NCCN guidelines (version 1.2025 – December 20, 2024) provide recommendations for use of Kineret as a treatment option in the management of immune checkpoint inhibitor-related hemophagocytic lymphohistiocytosis (HLH-like syndrome), chimeric antigen receptor (CAR) T-cell-related toxicities, including prophylaxis of immune effector cell-associated neurotoxicity syndrome (ICANS), and for the management of cytokine release syndrome.[5] Dosing for these indications varies across case reports/series, but NCCN recommends dosing of up to 100mg SC every 6 hours for a minimum of 7-10 days (with the duration extending up to 27 days in one trial).
- **Still's disease [including Systemic Juvenile Idiopathic Arthritis (SJIA) and Still's Disease, Adult Onset (AOSD)]):** The European Alliance of Associations for Rheumatology (EULAR) and Pediatric Rheumatology European Society (PReS) joint clinical guidelines for management of Still's disease (2024) indicate SJIA and AOSD are the same disease, differing in age of onset, and can be referred to collectively as Still's disease.[2] Guidelines recommend an IL-1 or IL-6 inhibitor be initiated as early as possible after diagnosis. No preferred agent is provided. Macrophage activation syndrome (MAS), which is a life-threatening complication of Still's disease, should be treated with high dose

steroids and if needed, other treatments which include Kineret. Dosing of Kineret for the treatment of SJIA and Still's disease varies based on reference, but guidelines support a dose of 4 mg per kg per day in children or up to 200 mg per day in 1 or 2 divided doses in adults.

Availability
Kineret is available as a 100 mg/0.67 mL prefilled syringes.[1]

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POLICY STATEMENT
This Drug Quantity Management program has been developed to promote the safe, effective, and economic use of Kineret and to manage potential premature dose escalation. If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. All approvals are provided for 1 year in duration, unless otherwise noted below. "One-time" approvals are provided for 30 days in duration.

Drug Quantity Limits

Product	Strength and Form	Retail Maximum Quantity per 28 Days	Home Delivery Maximum Quantity per 84 Days
Kineret® (anakinra subcutaneous injection)	100 mg/0.67 mL prefilled syringe	28 syringes	84 syringes

Exceptions to the quantity limits listed above are covered as medically necessary when ONE of the following criteria is met (1, 2, or 3). Any other exception is considered not medically necessary.

CRITERIA

1. If the patient has cryopyrin-associated periodic syndromes (CAPS) or deficiency of interleukin-1 receptor antagonist (DIRA), approve a quantity sufficient to allow for a dose of up to 8 mg per kg per day for 28 days at retail or for 84 days at home delivery.
Note: CAPS encompasses three rare genetic syndromes: familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and neonatal-onset multisystem inflammatory disease (NOMID) or chronic infantile neurological cutaneous and articular syndrome (CINCA). Refer to the table below for the maximum quantities that may be approved based on the patient's weight. When the patient is in between two weights provided, use the higher weight to ensure an adequate quantity is approved.

Table 1. Kineret Syringe Approval Quantity for CAPS or DIRA.

Patient Weight	Maximum Dose per Day (8 mg/kg/day)	# of syringes per day	Approve the requested quantity, not to exceed the following number of syringes	
			Retail	Home Delivery
≤ 10 kg	≤ 80 mg	1	No override needed. Base limits provide a quantity sufficient.	

15 kg	120 mg	2	56 syringes per 28 days	168 syringes per 84 days
20 kg	160 mg	2	56 syringes per 28 days	168 syringes per 84 days
25 kg	200 mg	2	56 syringes per 28 days	168 syringes per 84 days
30 kg	240 mg	3	84 syringes per 28 days	252 syringes per 84 days
35 kg	280 mg	3	84 syringes per 28 days	252 syringes per 84 days
40 kg	320 mg	4	112 syringes per 28 days	336 syringes per 84 days
45 kg	360 mg	4	112 syringes per 28 days	336 syringes per 84 days
50 kg	400 mg	4	112 syringes per 28 days	336 syringes per 84 days
55 kg	440 mg	5	140 syringes per 28 days	420 syringes per 84 days
60 kg	480 mg	5	140 syringes per 28 days	420 syringes per 84 days
65 kg	520 mg	6	168 syringes per 28 days	504 syringes per 84 days
70 kg	560 mg	6	168 syringes per 28 days	504 syringes per 84 days
75 kg	600 mg	6	168 syringes per 28 days	504 syringes per 84 days
80 kg	640 mg	7	196 syringes per 28 days	588 syringes per 84 days
85 kg	680 mg	7	196 syringes per 28 days	588 syringes per 84 days
90 kg	720 mg	8	224 syringes per 28 days	672 syringes per 84 days
95 kg	760 mg	8	224 syringes per 28 days	672 syringes per 84 days
100 kg	800 mg	8	224 syringes per 28 days	672 syringes per 84 days
> 100 kg	Consult Utilization Management Pharmacist to assist with quantity calculation.			

CAPS – Cryopyrin-associated periodic syndromes; DIRA – Deficiency of interleukin-1 receptor antagonist.

2. If the patient has systemic juvenile idiopathic arthritis (SJIA) or Still's disease, approve the requested quantity, not to exceed 56 syringes per 28 days at retail or 168 syringes per 84 days at home delivery.
Note: This is a quantity sufficient for a dose up to 200 mg per day.

3. If the patient has been or will be treated with a Chimeric Antigen Receptor (CAR) T-cell therapy, approve a one-time override for the requested quantity, not to exceed 112 syringes.
Note: Examples of CAR T-cell therapy include Abecma (idecabtagene vicleucel intravenous infusion), Aucatzyl (obecabtagene autoleucel intravenous infusion), Breyanzi (lisocabtagene maraleucel intravenous infusion), Carvykti (ciltacabtagene autoleucel intravenous infusion), Kymriah (tisagenlecleucel intravenous infusion), Tecartus (brexucabtagene intravenous infusion), and Yescarta (axicabtagene ciloleucel intravenous infusion).

References

1. Kineret® subcutaneous injection [prescribing information]. Stockholm, Sweden: Biovitrum; September 2024.
2. Fautrel B, Mitrovic S, De Matteis A, et al. EULAR/PReS recommendations for the diagnosis and management of Still's disease, comprising systemic juvenile idiopathic arthritis and adult-onset Still's disease. *Ann Rheum Dis*. 2024;83(12):1614-1627.
3. The NCCN Castleman Disease Clinical Practice Guidelines in Oncology (version 2.2025 – January 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 14, 2025.
4. The NCCN Histiocytic Neoplasms Clinical Practice Guidelines in Oncology (version 1.2025 – June 20, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 14, 2025.
5. The NCCN Management of Immunotherapy-Related Toxicities Clinical Practice Guidelines in Oncology (version 1.2025 – December 20, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on July 14, 2025.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy.	11/01/2025

The policy effective date is in force until updated or retired.