

USING KINERET®

A GUIDE FOR HEALTHCARE PROFESSIONALS (HCPs)

Please communicate the information outlined in this booklet to the patient/caregiver, to ensure correct patient dosing and use of the graduated syringe including the correct injection technique when prescribing Kineret® (anakinra) in Still's disease—including Systemic Juvenile Idiopathic Arthritis (SJIA) and Adult-Onset Still's Disease (AOSD)—Cryopyrin-Associated Periodic Syndromes (CAPS) and Familial Mediterranean Fever (FMF).

This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA



What the Kineret® user will need

1.

Subcutaneous (s.c.) injection training by an appropriate healthcare professional

Although patients and caregivers can become confident in injecting at home, it can be daunting to begin with. The right education on s.c. injection technique when Kineret® (anakinra) is initiated may ensure correct use. It is important to tell the patient/caregiver that injecting Kineret can sometimes make the skin react (see page 13)..

2.

Specific instruction on the graduated syringe

To ensure the correct dose is administered, careful guidance will need to be communicated on the use of the graduated syringe (see page 10).

3.

Approved education material

Sobi has produced a comprehensive booklet, An Introduction to Kineret®, that should be given to all who use Kineret for Still's disease, CAPS, or FMF, to ensure appropriate use. This booklet, requested and approved by Saudi food and drug authority, should be handed to the patient or their caregiver when they start using Kineret®.



What patients and caregivers need to know

Once you have discussed Kineret® (anakinra) with the patient or caregiver and agreed that it should be prescribed, the following practical information should be covered.

How to inject Kineret

The patient or caregiver will need to receive appropriate instruction on how to give a subcutaneous injection, either to themselves or to the patient in their care.

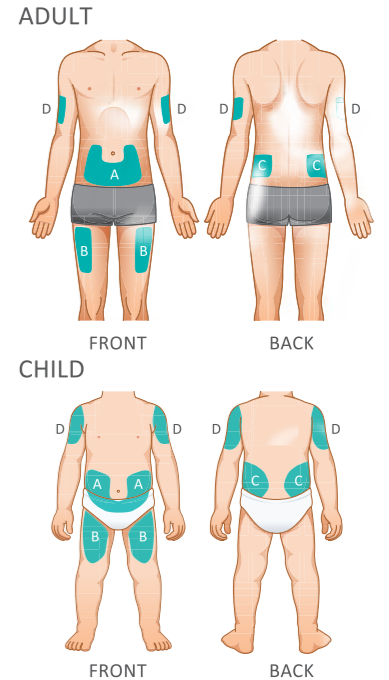
Where to inject Kineret

The most suitable places to inject:

- A** *the abdomen (except for the area around the navel)*
- B** *the top of the thighs (this is especially good for infants under a year if they have slightly chubby legs)*
- C** *the upper outer areas of the buttocks**
- D** *the outer area of the upper arms**

*Only suitable if a caregiver is giving the injection

- **Do not inject into skin that is tender, red, bruised, or hard**
- **Avoid scars or stretch marks**
- **Do not inject close to a vein**



It is helpful to advise the patient/caregiver to change the injection site each time so the area does not become sore.

Calculate your patient's dose

The dose of Kineret® (anakinra) should be calculated and adjusted in line with the recommended dosage in the Summary of Product Characteristics (SPC). It is vital that the patient or caregiver fully understands the dose in milligrams and graduations on the syringe.

CAPS: Adults, adolescents, children and infants aged 8 months and older with a body weight of 10 kg or above

Starting dose

The recommended starting dose in all CAPS subtypes is 1-2 mg/kg/day by subcutaneous injection. The therapeutic response is primarily reflected by reduction in clinical symptoms such as fever, rash, joint pain, and headache, but also in inflammatory serum markers (CRP/SAA levels), or occurrence of flares.

Maintenance dose in mild CAPS (FCAS, mild MWS)

Patients are usually well-controlled by maintaining the recommended starting dose (1-2 mg/kg/day).

Maintenance dose in severe CAPS (MWS and NOMID/CINCA)

Dose increases may become necessary within 1-2 months based on therapeutic response. The usual maintenance

dose in severe CAPS is 3-4 mg/kg/day, which can be adjusted to a maximum of 8 mg/kg/day.

In addition to the evaluation of clinical symptoms and inflammatory markers in severe CAPS, assessments of inflammation of the CNS, including the inner ear (MRI or CT, lumbar puncture, and audiology) and eyes (ophthalmological assessments) are recommended after an initial 3 months of treatment, and thereafter every 6 months, until effective treatment doses have been identified. When patients are clinically well-controlled, CNS and ophthalmological monitoring may be conducted yearly.

FMF

The recommended dose for patients weighing 50 kg or more is 100 mg/day by subcutaneous injection. Patients weighing less than 50 kg should be dosed by body weight with a recommended dose of 1-2 mg/kg/day.

Still's disease

The recommended dose for patients weighing 50 kg or more is 100 mg/day by subcutaneous injection. Patients weighing less than 50 kg should be dosed by body weight with a starting dose of 1-2 mg/kg/day.

Response to treatment should be evaluated after 1 month: In case of persistent systemic manifestations dose may be adjusted in children or continued treatment with Kineret should be reconsidered by the treating physician.

Paediatric population (< 18 years)

No data are available in children under the age of 8 months.

CAPS: Posology and administration in children and infants aged 8 months and older with a body weight of 10 kg or above are the same as for adult CAPS patients, based on body weight.

FMF: Children weighing less than 50 kg are dosed by

body weight with a recommended dose of 1-2 mg/kg/day, patients weighing 50 kg or more are dosed with 100 mg/day. In children with inadequate response the dose can be escalated up to 4 mg/kg/day.

The efficacy data of Kineret in children under 2 years of age with FMF are limited.

Still's disease: Children weighing less than 50 kg are dosed by body weight with a starting dose of 1-2 mg/kg/day, patients weighing 50 kg or more are dosed with 100 mg/day. In children with inadequate response the dose can be escalated up to 4 mg/kg/day.

For Still's disease, dose by weight

Starting dose for patients weighing 50 kg or more:

The recommended starting dose in patients who weigh 50 kg or more is 100 mg/day by subcutaneous injection.

Starting dose for patients weighing less than 50 kg:

Patients who are less than 50 kg should be dosed by body weight with a starting dose of 1-2 mg/kg/day by subcutaneous injection

Dose adjustment in children (<18 years):

Response to treatment should be evaluated after 1 month. In case of persistent systemic manifestations or inadequate response, dose can be escalated up to 4 mg/kg/day, or continued treatment with Kineret® (anakinra) should be reconsidered.

See the SPC for full dosage and follow-up details, including different patient populations. See below for further instructions on delivering the appropriate dose.

Dosing for Still's disease

Kineret Still's disease initiation dose	
Weighs 50 kg or more	Weighs less than 50 kg
100 mg/day	100 mg/day
Kineret Still's disease dose adjustment	
Can be increased up to 4 mg/kg/day for patients under 18 years	

Dosing for CAPS

The dose of Kineret® (anakinra) should be calculated and adjusted in line with the recommended dosage in the Summary of Product Characteristics (SPC). It is vital that the patient or caregiver fully understands the dose in milligrams and graduations on the syringe.

For CAPS, dose by severity

Starting dose:

The recommended starting dose in all CAPS subtypes is 1-2 mg/kg/day by subcutaneous injection.

Maintenance dose in mild CAPS (FCAS, mild MWS):

Patients are usually well-controlled by maintaining the recommended starting dose (1-2 mg/kg/day).

Maintenance dose in severe CAPS (MWS and NOMID/CINCA):

Dose increases may become necessary within 1-2 months based on therapeutic response. The usual maintenance dose in severe CAPS is 3-4 mg/kg/day, which can be adjusted to a maximum of 8 mg/kg/day.

In addition to the evaluation of clinical symptoms and inflammatory markers in severe CAPS, assessments of inflammation of the CNS, including the inner ear (by MRI or CT, lumbar puncture, and audiology) and eyes (ophthalmological assessments) are recommended after an initial 3 months of treatment, and thereafter every 6 months, until effective treatment doses have been identified. When patients are clinically well-controlled, CNS and ophthalmological monitoring may be conducted yearly.

See the SPC for full dosage and follow-up details, including different patient populations.

See page 8 for further instructions on delivering the appropriate dose.

Kineret CAPS initiation dose	
1-2 mg/kg/day	
Kineret CAPS maintenance dose	
FCAS/mild disease	Severe disease
1-2 mg/kg/day (often not necessary to increase the dose)	3-4 mg/kg/day up to 8 mg/kg/day

Dosing for FMF

The recommended dose for patients weighing 50 kg or more is 100 mg/day by subcutaneous injection. In patients weighing less than 50 kg, Kineret® should be dosed by body weight with a recommended dose of 1-2 mg/kg/day.

In children with inadequate response the dose can be escalated up to 4 mg/kg/day.

Dosing for FMF

Kineret® FMF initiation dose	
Weights 50 kg or more	Weights less than 50 kg
100 mg/day	1-2 mg/kg/day
Kineret® FMF dose adjustment	
Can be increased up to 4 mg/kg/day for patients under 18 years	

Ensure the appropriate dose is given

Kineret® (anakinra) is supplied ready for use in a graduated pre-filled syringe. The marks on the side of the syringe indicate the milligrams.

The syringe allows for doses between 20 and 100 mg. As the minimum dose is 20 mg, Kineret is not approved for use in paediatric patients with a body weight below 10 kg. If less than 100 mg is to be administered, some of the liquid will need to be discarded. Instructions for the patient on how to do this appear in the Kineret patient booklet.

As a healthcare professional, you will need to calculate the dose to be used, based initially on the weight of the patient and may later be adjusted based on therapeutic response.¹ In addition, the dose will need to be adjusted to the nearest dose, which can be delivered from one or more graduated syringes.

As Kineret can only be administered as 20 to 100 mg per injection in 10 mg increments, it is important that the prescribed dose allows for this administration.



Dose calculation examples

Still's disease and FMF	CAPS
<p>Julia is being treated for Still's disease and needs a dose of 1-2 mg/kg/day.</p> <p>Julia's weight is 13 kg.</p> <p>Daily dose = $13 \times 1-2 \text{ mg/kg/day} = 13-26 \text{ mg/day}$</p> <p>Here, it is most practical to prescribe 20 mg per day to be given at suitable times, approximately the same every day.</p>	<p>Harry suffers from severe Muckle-Wells Syndrome and needs a dose of 4-5 mg/kg/day.</p> <p>Harry's weight is 45 kg.</p> <p>Daily dose = $45 \text{ kg} \times 4-5 \text{ mg/kg/day} = 180-225 \text{ mg/day}$</p> <p>Here, it is most practical to prescribe 200 mg per day to be given at suitable times, approximately the same every day.</p>
<p>Andrei is being treated for FMF and has ceased responding to his initial dose of 1-2 mg/kg/day. He now needs a dose increase to 4 mg/kg/day.</p> <p>Andrei's weight is 17 kg.</p> <p>New daily dose = $17 \times 4 \text{ mg/kg/day} = 68 \text{ mg/day}$</p> <p>In this case, you will want to prescribe 70 mg per day to be given at suitable times, approximately the same every day.</p>	<p>Lucy is recently diagnosed with NOMID/CINCA syndrome and has ceased responding to her initial dose of 1-2 mg/kg/day. She now needs a dose increase to 2-3 mg/kg/day.</p> <p>Lucy's weight is 12 kg.</p> <p>New daily dose = $12 \text{ kg} \times 2-3 \text{ mg/kg/day} = 24-36 \text{ mg/day}$</p> <p>You could prescribe 30 mg of Kineret® (anakinra) once daily to be used around the same time each day (preferably in the morning to have the highest concentration during the daytime period).</p>

Safety considerations

Neutropenia

Kineret treatment should not be initiated in patients with neutropenia. As neutropenia may occur in patients treated with Kineret, it is important to monitor neutrophil counts prior to initiating Kineret treatment and monthly after initiation of therapy for the first six months and quarterly thereafter.

In patient develop neutropenia, Kineret treatment should be discontinued and neutrophil counts should be monitored closely.

Thrombocytopenia

In clinical studies in RA patients, thrombocytopenia has been reported in 1.9% of treated patients compared to 0.3% in the placebo group. The thrombocytopenias have been mild, i.e. platelet counts have been $>75 \times 10^9/\text{L}$. Mild thrombocytopenia has also been observed in CAPS patients

Managing injection site reactions

Explain that injecting Kineret® (anakinra) can sometimes make the skin react. Such reactions typically appear within 2 weeks of starting treatment and disappear within 4-6 weeks. The reactions are usually mild to moderate and take the form of redness, bruising, inflammation, pain, or discomfort. Skin reactions are unlikely to occur if they haven't happened in the first month of treatment.

Tips that might help alleviate the signs and symptoms of injection site reactions (ISRs) are included in the booklet, An Introduction to Kineret, for patients and caregivers. Feel free to discuss them together



The syringe should be left out of the fridge for approximately 30 minutes and allowed to warm to room temperature or be warmed in the hand before injecting



The patient should be clearly instructed NOT to heat the syringe in hot water, in a microwave oven, or by any other means



Be sure to rotate injection sites



Cool the injection site with an ice pack before and after injecting



You may recommend applying hydrocortisone or antihistamine cream to the injection site if patient's general health status allows. Prophylaxis with hydrocortisone cream, ideally 30-60 minutes before the injection, may be used in all patients for the first 3-6 months of treatment to reduce the frequency of ISRs

For optimal Kineret use by patients and caregivers, please make sure to provide them with the following:

- *Training on good subcutaneous injection technique and site rotation*
- *The approved patient booklet, An Introduction to Kineret*
- *Education on how to give the correct dose using the graduated syringe*
- *Information on safe disposal of medicine sharps in accordance with local requirements*
- *An HCP's contact number in case the patient/caregiver needs additional support using Kineret*

Adverse event reporting

Reporting suspected adverse events is important as it allows for continued monitoring of the benefit/risk balance of Kineret.

The National Pharmacovigilance Centre (NPC) Saudi Food and Drug Authority (SFDA):

- SFDA call center: 19999
- E-mail: npc.drug@sfd.a.gov.sa
- Website: <http://ade.sfda.gov.sa/>



Swedish Orphan Biovitrum AB (publ):

- Email: pv-ksa@sobi.com

More information

For more information about KINERET contact:

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References:

Kineret (anakinra) Summary of Product Characteristics for Saudi Arabia, date March 2023.



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NP-32067 | December 2023

