EMA/770315/2021
EMEA/H/C/000363

Kineret (*anakinra*)

An overview of Kineret and why it is authorised in the EU

What is Kineret and what is it used for?

Kineret is a medicine that is used to treat:

- signs and symptoms of rheumatoid arthritis (an immune system disease causing inflammation of the joints) in adults. It is used in combination with methotrexate (a medicine used to reduce inflammation) in patients who have not responded adequately to methotrexate alone;
- cryopyrin-associated periodic syndromes (CAPS). CAPS are an example of a group of recurring inflammatory conditions known as periodic fever syndromes. Patients with CAPS have an alteration in the gene that produces a protein called cryopyrin which makes it overactive and leads to inflammation in many parts of the body, with symptoms such as fever, rash, joint pain and tiredness. Severe disabilities such as deafness and loss of vision may also occur;
- familial Mediterranean fever, another inherited periodic fever syndrome, which leads to repeated attacks of fever, inflammation and pain affecting various parts of the body including the abdomen (belly), joints, and chest. It may be associated with build-up of harmful protein deposits (amyloidosis) in organs such as the kidney. Kineret should be given with another medicine, colchicine, if appropriate;
- Still's disease, a disease causing inflammation of joints as well as rash and fever;
- COVID-19 in adults with pneumonia requiring supplemental oxygen (low or high flow oxygen) and who are at risk of developing severe respiratory failure, as determined by blood levels of a protein called suPAR (soluble urokinase plasminogen activator receptor) of at least 6 ng per ml.

For CAPS, familial Mediterranean fever and Still's disease, Kineret is used in patients from 8 months of age and weighing at least 10 kg.

Kineret contains the active substance anakinra.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

How is Kineret used?

Kineret can only be obtained with a prescription and treatment should be started and supervised by a doctor who has experience in the diagnosis and treatment of the conditions for which it is used.

Kineret is available as a solution for injection under the skin. The recommended dose of Kineret for rheumatoid arthritis is 100 mg once a day, given at around the same time each day. For CAPS, familial Mediterranean fever and Still's disease, the dose depends on body weight and for CAPS, on the severity of the condition. For COVID-19, the dose is 100 mg once a day for 10 days.

The injection site should be varied with each dose to avoid discomfort. Kineret should be used with caution in patients who have severely reduced liver function or moderately reduced kidney function. In patients with severely reduced kidney function the doctor should consider giving Kineret every other day.

For more information about using Kineret, see the package leaflet or contact your doctor or pharmacist.

How does Kineret work?

The active substance in Kineret, anakinra, is an immunosuppressive medicine (a medicine that reduces the activity of the immune system). It is a copy of a natural human protein called 'human interleukin 1 receptor antagonist' that blocks the receptors for a chemical messenger in the body called interleukin 1. This messenger is produced in high levels in patients with rheumatoid arthritis, causing inflammation of the joints and joint damage, and is also involved in the inflammation associated with CAPS, familial Mediterranean fever and Still's disease. By attaching to the receptors that interleukin 1 would normally attach itself to, anakinra blocks the activity of interleukin 1, helping to relieve the symptoms of these diseases.

What benefits of Kineret have been shown in studies?

Rheumatoid arthritis

Kineret has been studied in three main studies involving a total of 1,388 patients with rheumatoid arthritis. All three studies compared the effectiveness of Kineret with that of placebo (a dummy treatment). The first study included 468 patients, some of whom had taken other medicines for their disease in the past, and who were given either Kineret on its own or placebo. Results showed that certain doses of Kineret were more effective than placebo in reducing the symptoms of the disease, measured by the doctor and the patient using the 'American College of Rheumatology' score, which includes measurements of the number of painful or tender joints, disease activity, pain, disability and levels of C reactive protein in the blood (a marker of inflammation). However, because of the way the study was designed, the results were considered insufficient to support the use of the medicine on its own.

In the other two studies, Kineret was used as an add-on to existing treatment including methotrexate: one study, which involved 419 patients, used a range of doses of Kineret that depended on the patient's weight, and the other study, which involved 501 patients, used Kineret at a fixed dose of 100 mg once a day. Results showed that Kineret was more effective than placebo when used as an add-on to methotrexate. In the study using a fixed dose of Kineret, 38% of the patients adding Kineret had at least a 20% reduction in symptoms after six months, compared with 22% of those adding placebo.

Periodic fever syndromes

For *CAPS*, Kineret has been shown to produce a significant and rapid improvement in symptoms in one main study involving 43 patients with neonatal-onset multisystem inflammatory disease (NOMID/CINCA syndrome, the most severe form of CAPS). Average symptom scores fell from 4.5 to 0.8 within 3 days of starting treatment. The improvement was maintained over a follow-up period of up to 60 months. In addition, levels of amyloid A, a marker of inflammation, were also reduced.

In *familial Mediterranean fever*, Kineret 100 mg daily as an add-on to colchicine was more effective than placebo in reducing the number of attacks in a main study involving 25 patients whose condition had not responded to previous treatment with colchicine alone. Patients given Kineret had on average 1.7 attacks per month versus 3.5 per month in those given placebo; 6 out of 12 given Kineret had less than one attack per month, compared with none of the 13 given placebo.

Still's disease

In the first of 3 small studies, 11 of 15 children with Still's disease (73%) had at least a 30% reduction in symptoms after three months' treatment with Kineret. A second study in 24 children showed similar results: 67% had at least a 30% reduction in symptoms after one month compared with 8% given placebo. The third study was carried out in 22 adults who also received corticosteroids for their disease. Patients either received Kineret or another type of medicine, called a DMARD. After one month of treatment, more patients on Kineret (6 out of 12 patients) achieved remission compared with those taking a DMARD (3 out of 10 patients).

COVID-19

A study involving 606 hospitalised adults with moderate or severe COVID-19 pneumonia and who had suPAR levels of at least 6 ng per ml showed that Kineret was effective at treating COVID-19.

These patients received Kineret or placebo in addition to standard of care. Standard of care for most patients included low or high flow oxygen and the corticosteroid medicine dexamethasone, and some also received remdesivir (an antiviral medicine for COVID-19).

The study showed greater clinical symptom improvements in patients treated with Kineret plus standard of care compared with those who received placebo plus standard of care. Kineret reduced the risk of a patient's condition worsening to more severe disease or death during the 28-day study period compared with placebo. The treatment benefit of Kineret compared to placebo was supported by an increase in the number of patients who fully recovered and a reduction in the number of patients whose condition worsened to severe respiratory failure or death.

What are the risks associated with Kineret?

The most common side effects with Kineret (which may affect more than 1 in 10 patients) are headache, injection site reactions (redness, bruising, pain and inflammation), and increase in blood cholesterol. For the full list of side effects of Kineret, see the package leaflet.

Kineret must not be used in people who are hypersensitive (allergic) to anakinra, to any of the other ingredients, or to proteins produced by *Escherichia coli* (a type of bacterium). Kineret must not be started in patients who have neutropenia (low levels neutrophils, a type of blood cell that fights infection).

Why is Kineret authorised in the EU?

The European Medicines Agency decided that Kineret's benefits are greater than its risks for the treatment of the signs and symptoms of rheumatoid arthritis in combination with methotrexate, in patients with an inadequate response to methotrexate alone. The Agency recommended that Kineret be given marketing authorisation. Given the beneficial effect and the fact that there were no new safety concerns, the Agency also considered that the benefits outweighed the risks in patients with CAPS, familial Mediterranean fever, Still's disease and COVID-19. Although patients with Still's disease had a higher risk of liver problems, this risk was considered to be outweighed by the medicine's benefits.

What measures are being taken to ensure the safe use of Kineret?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Kineret have been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Kineret are continuously monitored. Side effects reported with Kineret are carefully evaluated and any necessary action is taken to protect patients.

Other information about Kineret

Kineret received a marketing authorisation valid throughout the European Union on 8 March 2002.

Further information on Kineret can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/kineret.

This overview was last updated in 12-2021.