AN INTERLEUKIN-1 TYPE 1 RECEPTOR (IL-1R1) ANTAGONIST*

Pr Kineret® (anakinra)

MAY NOT BE FOR EVERY PATIENT WITH RA OR NOMID,

but it could be the appropriate choice for her.

PrKINERET® (anakinra) is indicated for[1]:

RHEUMATOID ARTHRITIS

- Reducing the signs and symptoms of active rheumatoid arthritis (RA) in patients 18 years of age or older
- Inhibiting the progression of structural damage by reducing erosions and cartilage degradation in patients with active RA despite treatment with stable doses of methotrexate (MTX)

KINERET can be used alone or in combination with other disease-modifying antirheumatic drugs (DMARDs), particularly MTX.

CRYOPYRIN-ASSOCIATED PERIODIC SYNDROMES (CAPS)

- Treatment of neonatal-onset multisystem inflammatory disease (NOMID) in adults, adolescents, children and infants aged 8 months and older with a body weight of 10 kg or above

*Clinical significance is unknown.

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IL-1 is implicated in both RA and NOMID*

IL-1 in rheumatoid arthritis (RA)[1–3]

The spectrum of RA is composed of both autoimmune and autoinflammatory components.

- RA is thought to be mediated by antigen-driven T-cells and macrophages which in turn produce proinflammatory cytokines, such as IL-1 and tumour necrosis factor-alpha (TNF-α)

AUTOIMMUNE

RA is mainly thought of as an autoimmune disease

AUTOINFLAMMATORY

Difficult-to-treat patients could have RA with more autoinflammatory components than those who fit the standard profile.[1,2]

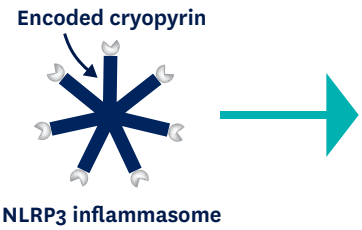
- IL-1 has proinflammatory effects and activates effector molecules responsible for joint destruction
- Both IL-1 and IL-1Ra have been identified in the synovial fluid and synovial sub-lining of RA and osteoarthritis (OA) patients

IL-1 in neonatal-onset multisystem inflammatory disease (NOMID)[1]

Mutated CIAS1/NLRP3 gene

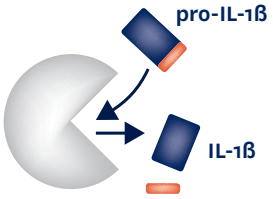
Mutations in the CIAS1/NLRP3 gene have been identified in a majority of patients with CAPS such as NOMID

Activated CIAS1/NLRP3 inflammasome



CIAS1/NLRP3 encodes cryopyrin, which is a component of the inflammasome

IL-1ß maturation and secretion



The activated inflammasome results in proteolytic maturation and secretion of IL-1ß, which has a broad range of effects

Adapted from the KINERET Product Monograph.

KINERET blocks the biological activity of IL-1α and IL-1β and inhibits their binding to the IL-1R1 receptor.

*Clinical significance is unknown.
CAPS: Cryopyrin-associated periodic syndromes.
CIAS1: Cold-induced autoinflammatory syndrome 1.
IL-1: Human interleukin-1.
IL-1Ra: Human interleukin-1 receptor antagonist.
NLRP3: NLR family pyrin domain containing 3.

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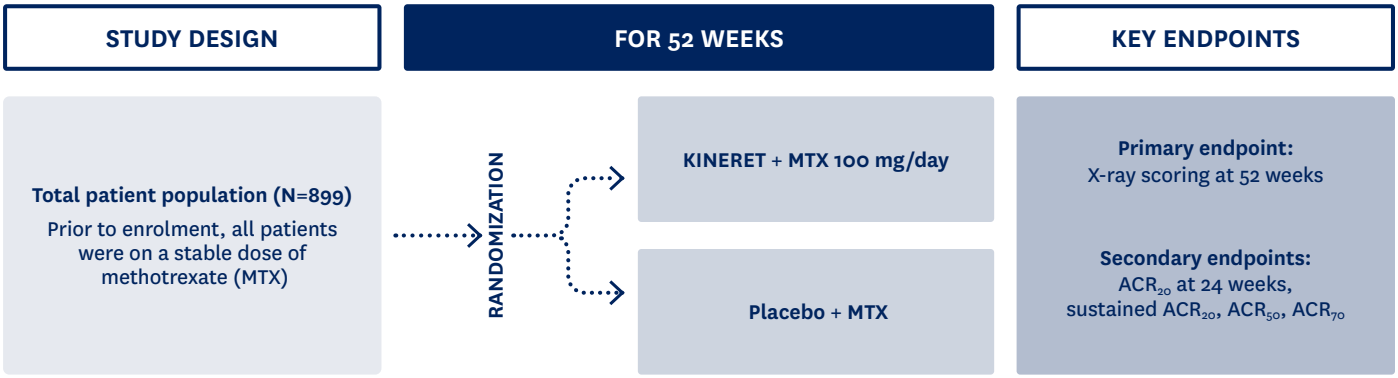
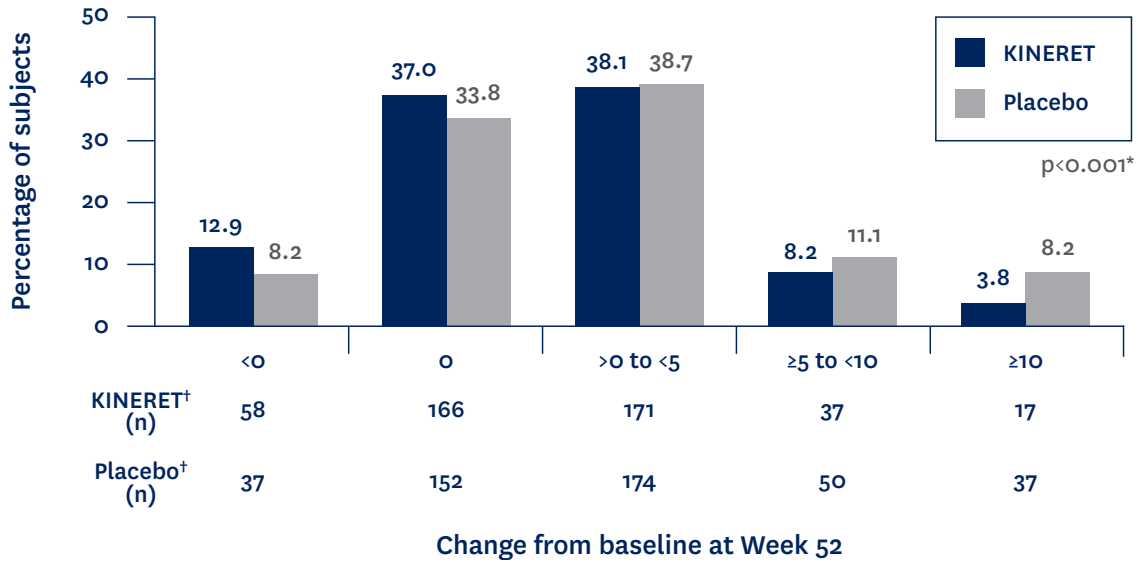
The efficacy of KINERET has been demonstrated in a confirmatory, double-blind, randomized, placebo-controlled study **in patients with active RA on MTX (N=899)**[1]



Adapted from the KINERET Product Monograph.

PRIMARY ENDPOINT

At Week 52, patients taking KINERET + MTX experienced a highly significant reduction in radiographically measured disease progression (TMSS) vs placebo[1]

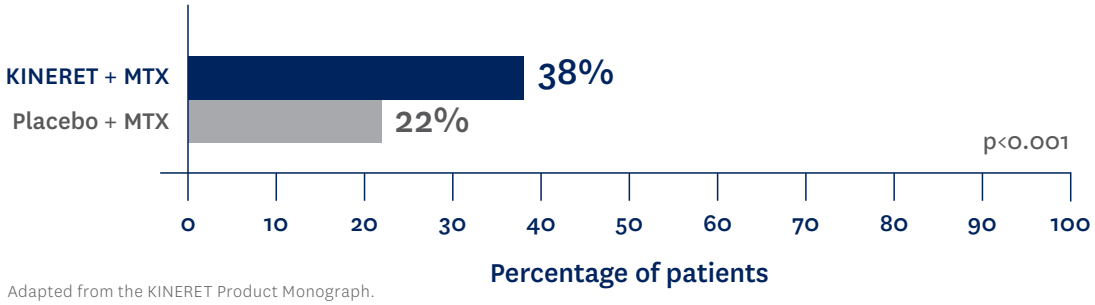


Adapted from the KINERET Product Monograph.

*p-value by Wilcoxon rank-sum test.
†n is the number of subjects who were randomized and received at least 1 dose of study drug.
ACR: American College of Rheumatology.
MTX: Methotrexate.
TMSS: Total Modified Sharp Score.

SECONDARY ENDPOINT

At Month 6, significantly more patients improved in signs and symptoms based on their ACR_{20} response with KINERET + MTX vs placebo + MTX[1]



Adapted from the KINERET Product Monograph.

KINERET has been shown to be generally well tolerated in patients with RA[1]

Serious infections

- KINERET was associated with an increased incidence of serious infections (1.7%) vs placebo (1.0%) in patients with RA across the pivotal trials
- A small subset of patients with RA and asthma had a higher incidence of serious infections after treatment with KINERET (4.5%) vs placebo (0.0%)

Summary of adverse events reported in ≥5% of KINERET-treated patients in pivotal placebo-controlled clinical trials conducted at the 100 mg/day dose

	KINERET-treated patients (n=1,565)	Placebo-treated patients (n=733)
Injection site reactions	70.8	28.5
Influenza-like symptoms	5.9	5.5
Arthralgia	5.9	6.4
Exacerbation of RA	19.3	28.9
Upper respiratory infection	13.8	16.6
Sinusitis	6.9	6.7
Headache	11.6	9.0
Abdominal pain	5.2	4.8
Nausea	8.4	6.7
Diarrhea	6.9	5.2

Adapted from the KINERET Product Monograph.

With the exception of ISRs, there appears to be no difference in the proportion of patients who discontinued treatment because of adverse events in the KINERET groups and the placebo group.[1]

- Most ISRs were typically described as mild to moderate, occurred during the first 4 weeks of therapy and lasted for 14–28 days
- The overall withdrawal rate due to ISRs across pivotal studies was 6%

ACR: American College of Rheumatology.
ISR: Injection site reactions.
MTX: Methotrexate.

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In a long-term, open-label and uncontrolled study, KINERET demonstrated efficacy and established a well-tolerated safety profile in **patients with NOMID**[1]

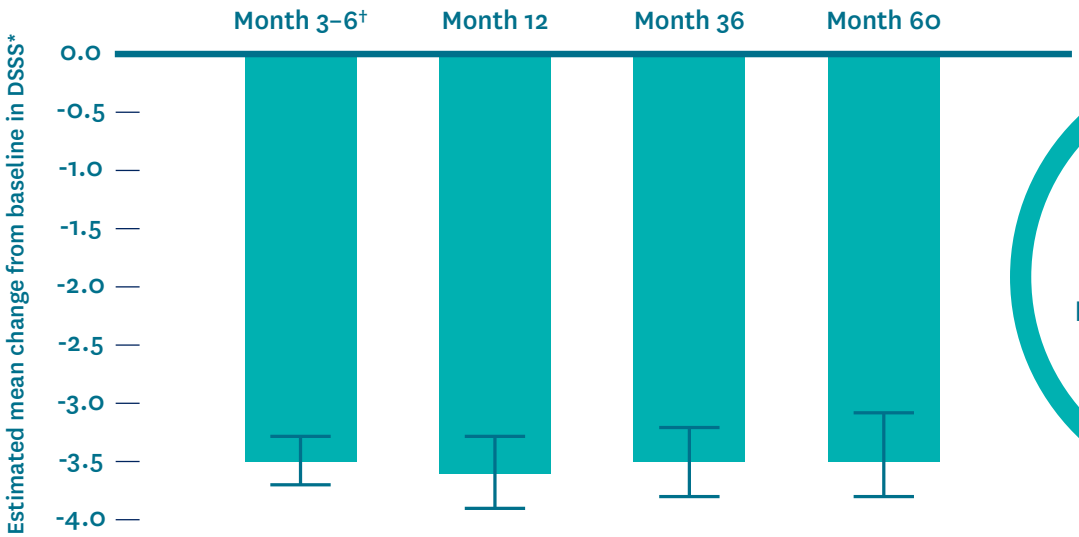
STUDY DESIGN	FOR UP TO 5 YEARS	PRIMARY ENDPOINT
Total patient population (N=43) Included pediatric and adult patients (age range: 0.7–46 years)	**KINERET dosing regimen** • Patients received an initial dose of 1–2.4 mg/kg body weight • Dose was adjusted by 0.5 to 1 mg/kg increments to help control signs and symptoms of disease, with a maximum dose of 8.2 mg/kg/day	NOMID symptoms as measured by the Diary Symptom Sum Score (DSSS)

Adapted from the KINERET Product Monograph.

Patients with NOMID taking KINERET showed improvements in DSSS from baseline over 60 months of treatment[1]

The Diary Symptom Sum Score (DSSS) ranged from 0 to 20 for prominent disease symptoms of fever, rash, joint pain, vomiting and headache.

Estimated change from baseline in overall DSSS in patients with severe NOMID (ITT diary population)

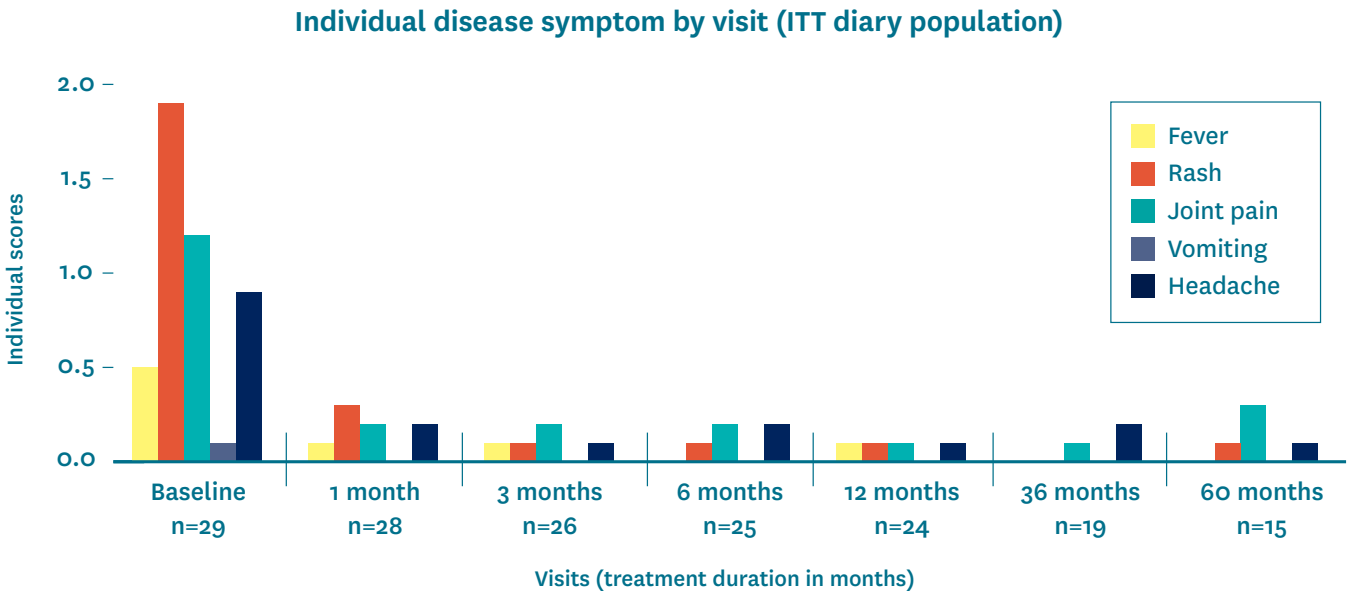


Results were consistent across all subgroups, including age, gender, presence of CIAS1-NLRP3 mutation, and disease phenotype.[1]

*Mean (SD) baseline value was 4.5 (3.2).
†Month 3–6 is the estimated average of the Month 3 and Month 6 visits.
CI: Confidence interval.
CIAS1: Cold-induced autoinflammatory syndrome 1.
ITT: Intent-to-treat.
NLRP3: NLR family pyrin domain containing 3.
NOMID: Neonatal-onset multisystem inflammatory disease.

Adapted from the KINERET Product Monograph.
Estimates of change from baseline and 95% CIs are based on a repeated measures analysis of covariance model including visit as a fixed factor and baseline value as a covariate. ITT diary observed cases (N=29).

Changes in individual disease symptoms were observed in all patients within 10 days of initiating KINERET and were sustained for up to 5 years with continued treatment[1]



Adapted from the KINERET Product Monograph.
Diary Symptom Scores, key symptoms: 0 = no symptoms, 1 = mild, 2 = moderate, 3 = more severe, 4 = severe.

KINERET: Safety and tolerability profile[1]

Safety profile in NOMID (based on uncontrolled open-label study)

- During the 5-year study, 14 patients (32.6%) reported 24 serious adverse events (SAEs)
  - The most common type of SAEs were infections
- 17 injection site reactions (ISRs) were reported in 10 patients during the 5-year study period
- The majority of ISRs were mild (76%) to moderate (24%)
- No ISR was reported after Year 2 of treatment, and no patient permanently or temporarily discontinued KINERET treatment due to injection site reactions
- The reporting frequency of adverse events (AEs), including infections, was higher during the first 6 months of treatment

ITT: Intent-to-treat.
NOMID: Neonatal-onset multisystem inflammatory disease.

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KINERET: Safety and tolerability profile[1]

Select treatment-emergent AEs (≥15% of patients) during the 60-month study with KINERET

	Study population	
System organ class Preferred term	Subject count (N=43) n (%)	Event count (PYRS=159.8) F (events/patient year)
Any AE	**38 (88.4)**	**979 (6.1)**
Infections and infestations	**36 (83.7)**	**218 (1.4)**
Upper respiratory tract infection	17 (39.5)	48 (0.3)
Nasopharyngitis	15 (34.9)	40 (0.3)
Sinusitis	12 (27.9)	28 (0.2)
Ear infection	11 (25.6)	23 (0.1)
Otitis media	11 (25.6)	20 (0.1)
Gastroenteritis	7 (16.3)	8 (0.1)
General disorders and administration site conditions	**27 (62.8)**	**136 (0.9)**
Pyrexia	17 (39.5)	51 (0.3)
Fatigue	10 (23.3)	27 (0.2)
Injection site reaction	8 (18.6)	12 (0.1)
Nervous system disorders	**21 (48.8)**	**125 (0.8)**
Headache	21 (48.8)	115 (0.7)
Musculoskeletal and connective tissue disorders	**20 (46.5)**	**200 (1.3)**
Arthralgia	18 (41.9)	133 (0.8)
Pain in extremity	9 (20.9)	27 (0.2)
Neck pain	8 (18.6)	11 (0.1)
Back pain	7 (16.3)	22 (0.1)
Respiratory, thoracic and mediastinal disorders	**18 (41.9)**	**83 (0.5)**
Oropharyngeal pain	9 (20.9)	27 (0.2)
Cough	9 (20.9)	19 (0.1)
Gastrointestinal disorders	**17 (39.5)**	**79 (0.5)**
Diarrhea	10 (23.3)	16 (0.1)
Vomiting	7 (16.3)	25 (0.2)
Skin and subcutaneous tissue disorders	**15 (34.9)**	**56 (0.4)**
Rash	14 (32.6)	51 (0.3)
Eye disorders	**14 (32.6)**	**44 (0.3)**
Ocular hyperemia	12 (27.9)	35 (0.2)
Injury, poisoning and procedural complications	**11 (25.6)**	**15 (0.1)**
Ear and labyrinth disorders	**7 (16.3)**	**10 (0.1)**

See Product Monograph for the complete list of adverse events.

Adapted from the KINERET Product Monograph.

AE: Adverse event.
F: Total number of events.
NOMID: Neonatal-onset multisystem inflammatory disease.
PYRS: Total patient years.

Recommended dosing in RA[1]

STARTING AND MAINTENANCE DOSE – ADULTS

100 MG/DAILY BY SUBCUTANEOUS INJECTION

Dose should be administered at approximately the same time of day, every day.
Rotating the injection sites is recommended.

RENALLY IMPAIRED PATIENTS
Physicians may consider an alternate dose of 100 mg of KINERET every other day for patients with RA with severely reduced renal function such as end stage renal disease (ESRD).

Recommended dosing in NOMID[1]

STARTING DOSE

1–2 MG/KG DAILY BY SUBCUTANEOUS INJECTION

DOSE ADJUSTMENTS

0.5–1.0 MG/KG INCREMENTS

Dose increases may become necessary within 1–2 months based on therapeutic response.

USUAL MAINTENANCE DOSE

3–4 MG/KG DAILY

Can be adjusted to a maximum of 8 mg/kg/day to control active inflammation.
Very limited data is available for doses higher than 5 mg/kg/day.
The dose should be administered at approximately the same time of day every day.
Rotating the injection sites is recommended.

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NOMID: Neonatal-onset multisystem inflammatory disease.

Clinical use:

Geriatrics (>65 years of age): No differences in safety or efficacy were observed between geriatric and younger patients in the RA trials. No patients ≥65 years of age were enrolled in the pivotal NOMID trial.

Pediatrics (<18 years of age): The efficacy of KINERET in children with RA (Juvenile Idiopathic Arthritis [JIA]) aged 0 to 18 years has not been established. KINERET is not recommended for children with NOMID who are <8 months of age.

Most serious warnings and precautions:

Serious infections: In patients with RA, an increased incidence of serious infections has been observed; discontinue KINERET if serious infection develops. In patients with NOMID, the risk of a disease flare when discontinuing KINERET treatment should be weighed against the potential risk of continued treatment. Treatment with KINERET should not be initiated in patients with active infections. The safety and efficacy of KINERET in immunosuppressed patients or in patients with chronic infections have not been evaluated.

Anaphylactic reactions: Allergic reactions, including anaphylactic reactions, angioedema, urticaria, rash and pruritus, have been reported; if these conditions are observed, discontinue KINERET and initiate appropriate therapy.

Other relevant warnings and precautions:

- To limit injection site amyloid deposits, rotate injection sites regularly, and do not inject into swollen or red areas
- If signs and symptoms of drug reaction with eosinophilia and systemic symptoms (DRESS) are present and an alternative etiology cannot be established, KINERET must not be readministered and a different treatment should be considered. Patients, predominantly pediatric patients, with DRESS may need hospitalization, as the condition may be fatal
- Prior to initiating immunomodulatory therapies, including KINERET, test patients for latent tuberculosis infection; the safety of KINERET in individuals with latent tuberculosis is unknown
- Use of KINERET in combination with TNF-blocking agents is not recommended
- Live vaccines should not be given concurrently with KINERET
- Evaluate patients with renal impairment before initiating therapy; consider a dose schedule change for those with severe renal insufficiency or end-stage renal disease
- Known or suspected underlying airway inflammation in patients with asthma should be brought under control prior to initiating KINERET. Exercise caution in patients with underlying airway inflammation
- Use during pregnancy only if the potential benefit justifies the potential risk to the fetus
- Exercise caution in nursing women
- Higher incidence of infections in the elderly population; exercise caution
- Assess neutrophil counts prior to initiating KINERET, and quarterly while receiving KINERET for a period up to 1 year; do not initiate if ANC $<1 \times 10^9$/L

For more information:

Please consult the Product Monograph at **sobi.ca/KINERET_PM_EN** for important information relating to adverse reactions, drug interactions, and dosing information, which has not been discussed in this piece.

The Product Monograph is also available through our medical department at 1-866-773-5274.

REFERENCES: 1. KINERET (anakinra) Product Monograph, Sobi Canada, Inc. Aug. 29, 2025. **2.** Savic S, Mistry A, Wilson AG, *et al.* Autoimmune-autoinflammatory rheumatoid arthritis overlaps: A rare but potentially important subgroup of diseases. *RMD Open* 2017;3(2):e000550.**3.** Isaacs JD and Moreland LW. (2nd Ed). 2011. Fast facts: Rheumatoid arthritis. Health Press Limited.

Starting on KINERET

Kineret ON TRACK™

To get a patient started on KINERET, enrol them in the KINERET ON TRACK™ Patient Support Program by contacting one of our representatives by phone (1-866-204-3546, 8 am–8 pm [ET] Monday–Friday) or email (kineret@innomar-strategies.com) and complete the enrolment form.

Single-use prefilled syringe

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Pr Kineret® NEXT (anakinra)

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- **Access** the **Patient Injection Site Reaction Brochure**

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