Closely review the contents of this information pack before prescribing canakinumab.

A healthcare professional's guide

to the use of ILARIS® (canakinumab) in the treatment of patients with:
Periodic Fever Syndromes (CAPS), systemic juvenile idiopathic arthritis (SJIA)

EU RMP V11.2 May/2017

You can report any side effects or adverse events through:

Novartis Consulting AG.
Saudi Arabia: P.O. Box 16032, Riyadh 11464, Tel: +966114658882
DS&E
Phone: +996112658100
Fax: +966112658107
Email: adverse.events@novartis.com

National pharmacovigilance and drug safety center
Toll free phone: 8002490000
Fax: +966112057662
E-mail: npc.drug@sfda.gov.sa
Or by online: https://ade.sfda.gov.sa

NOVARTIS
PHARMACEUTICALS

Indications

Periodic fever syndromes

ILARIS® is indicated for the treatment of the following autoinflammatory periodic fever syndromes in adults, adolescents and children aged 2 years and older:

CAPS

ILARIS® is indicated for the treatment of cryopyrinassociated periodic syndromes (CAPS), including:

- Muckle-Wells syndrome (MWS)
- Neonatal-onset multisystem inflammatory disease (NOMID)/chronic infantile neurological, cutaneous, articular syndrome (CINCA)
- Severe forms of familial cold autoinflammatory syndrome (FCAS)/familial cold urticaria (FCU), presenting with signs and symptoms beyond cold-induced urticarial skin rash

SJIA

ILARIS® is indicated for the treatment of systemic juvenile idiopathic arthritis (SJIA) in patients aged 2 years and older who have responded inadequately to previous therapy with non-steroidal anti-inflammatory drugs (NSAIDs) and systemic corticosteroids. ILARIS® can be given as monotherapy or in combination with methotrexate.

Important safety information

What you should know before treatment with canakinumab

The following risks are associated with treatment:

Infections, including serious infections and opportunistic infections

- There is an increased risk of infections, including serious infections, in patients treated with canakinumab.
- Monitor patients carefully for signs and symptoms of infections during and after treatment with canakinumab.
- Exercise caution when administering canakinumab to patients with infections, a history of recurring infections, or underlying conditions which may predispose them to infections.
- In periodic fever syndromes and SJIA: Canakinumab should not be initiated or continued in patients during an active infection requiring medical intervention.
- Isolated cases of unusual or opportunistic infections were reported with canakinumab.
- It is unknown if the use of IL-1 inhibitors such as canakinumab increases the risk of reactivation of tuberculosis or opportunistic infections. Before initiation of therapy, all patients must be evaluated for both active and latent tuberculosis infection.

Macrophage activation syndrome In SJIA only:

- Macrophage activation syndrome (MAS) is a known, life-threatening disorder that may develop in rheumatic conditions, in particular SJIA patients. If MAS occurs, or is suspected, evaluation and treatment should be started as early as possible.
- Physicians should be attentive to symptoms of infection or worsening of SJIA, as these are known triggers for MAS.
- Based on the currently available clinical trial experience, canakinumab does not appear to increase the incidence of MAS in SJIA patients, but no definitive conclusions can be made.

Neutropenia

- Neutropenia (absolute neutrophil count <1.5x 109/L) has been observed with medicinal products that inhibit IL-1, including canakinu ab.
- Treatment with canakinumab should not be initiated in patients with neutropenia.
- It is recommended that neutrophil counts be assessed prior to initiating treatment, **after 1 to 2 months and periodically during treatment with canakinumab.**
- If a patient becomes neutropenic, monitor the absolute neutrophil count and consider discontinuation of treatment.

Vaccinations

- No data are available on the risk of secondary transmission of infection by live (attenuated) vaccines in patients receiving canakinumab. Therefore, live vaccines should not be given concurrently in patients receiving canakinumab unless the benefits clearly outweigh the risks.
- Prior to initiation of canakinumab therapy, adult and paediatric patients should receive all recommended vaccinations, as appropriate, including pneumococcal and inactivated influenza vaccines.
- For patients on canakinumab therapy, wait at least 3 months after the last injection and before the next injection to administer any live vaccines.

Important safety information continued

What you should know before treatment with canakinumab

The following risks are associated with treatment:

Potential risk of immunogenicity and hypersensitivity reactions

- Antibodies against canakinumab were observed in a small proportion of patients treated with canakinumab. This could lead to immune-mediated symptoms including hypersensitivity reactions.
- During clinical development, no anaphylactic or anaphylactoid reactions were observed
- No neutralizing antibodies were detected
- No apparent correlation of antibody development to clinical response or adverse events was observed Malignancies

Malignancies have been reported in patients treated with canakinumab during clinical development. The risk for the development of malignancies with anti- interleukin (IL)-1 therapy is unknown.
tA potential risk cannot be excluded in patients treated with canakinumab.

Malignancies

- Malignancies have been reported in patients treated with canakinumab during clinical development. The risk for the development of malignancies with anti-interleukin (IL)-1 therapy is unknown. A potential risk cannot be excluded in patients treated with canakinumab.
- In periodic fever syndromes and (SJIA): Perform annual assessments in canakinumab patients regarding the presence of malignancies.

Unknown safety in pregnant and lactating women

- It is not known whether canakinumab is excreted in human milk.
- Formal studies of the potential effect of canakinumab on human fertility have not been conducted.
- Women who are pregnant or desire to become pregnant should be treated only after a thorough benefit-risk evaluation.
- Physicians should discuss the risks regarding the unknown safety of canakinumab in pregnant and lactating women with patients if they become or plan to become pregnant.

Disorders of lipoprotein metabolism

- Monitor patients regularly during treatment for changes in their lipid profiles.
- In active-controlled gouty arthritis trials, patients treated with canakinumab showed changes in lipoprotein metabolism (increased levels of triglycerides and in cholesterol fractions); the clinical significance of this observation is unknown.

Dosing Recommendation for CAPS – Adults and larger children

The recommended starting dose of canakinumab in CAPS patients depends on the patient's age and body weight. Start by finding the right table for the patient's age, then choose the row for the patient's current body weight.

Adults and children ≥4 years of age with body weight ≥15 kg:

- 150 mg for body weight >40 kg
- 2 mg/kg for body weight ≥15 kg and ≤40 kg

See next table for body weight <15 kg

This is administered every 8 weeks as a single dose via subcutaneous injection. Increased doses, as described below, can be considered if a satisfactory clinical response (resolution of rash and other generalized inflammatory symptoms) is not achieved

Current Body Weight (kg)	Starting dose (2 mg/kg or 150 mg)		First Increased Dose [1] (4 mg/kg or 300 mg)		Second Increased Dose [2] (8 mg/kg or 600 mg)	
	Volume (mL)	Dose (mg)	Volume (mL)	Dose (mg)	Volume (mL)	Dose (mg)
15 – <17	0.2	30	0.4	60	0.8	120
17 – <21	0.25	37.5	0.5	75	1	150
21 – 24	0.3	45	0.6	90	1.2	180
>24 – 28	0.35	52.5	0.7	105	1.4	210
>28 – <32	0.4	60	0.8	120	1.6	240
32 – <36	0.45	67.5	0.9	135	1.8	270
36 – 40	0.5	75	1.0	150	2.0	300
>40	1.0	150	2.0	300	4.0	600

1 If a satisfactory clinical response has not been achieved 7 days after treatment start, a second dose (same as starting dose) of canakinumab can be considered. If a full treatment response is subsequently achieved, the intensified dosing regimen of 300 mg or 4 mg/kg (for children ≥15 kg and ≤40 kg) every 8 weeks should be maintained. For doses >150 mg (1 mL), more than 1 vial of ILARIS® is required. 2 If a satisfactory clinical response has not been achieved 7 days after the second dose, a third dose of canakinumab can be considered (another 300 mg or 4 mg/k g [for children ≥15 kg and ≤40 kg]).

If a full treatment response is subsequently achieved, maintaining the intensified dosing regimen of 600 mg or 8 mg/kg every 8 weeks should be considered, based on individual clinical judgement.

Dosing Recommendation for CAPS – Small children

The recommended starting dose of canakinumab in CAPS patients depends on the patient's age and body weight. Start by finding the right table for the patient's age, then choose the row for the patient's current body weight.

Children aged 2 to <4 years with body weight ≥7.5 kg, and Children aged ≥4 years with body weight ≥7.5 to <15 kg:

- **4 mg/kg**

See previous table for body weight ≥15 kg
This is administered every 8 weeks as a single dose via subcutaneous injection. An increased dose, as described below, can be considered if a satisfactory clinical response (resolution of rash and other generalized inflammatory symptoms) is not achieved.

Current Body Weight (kg)	Starting Dose (4 mg/kg)		Increased Dose [1] (8 mg/kg)	
	Volume (mL)	Dose (mg)	Volume (mL)	Dose (mg)
7.5-8.5	0.2	30	0.4	60
>8.5-10	0.25	37.5	0.5	75
>10-12	0.3	45	0.6	90
>12-14	0.35	52.5	0.7	105
>14-<16	0.4	60	0.8	120
16-<18	0.45	67.5	0.9	135
18-<20	0.5	75	1	150
20-<22	0.55	82.5	1.1	165
22-23	0.6	90	1.2	180
>23-25	0.65	97.5	1.3	195
>25-27	0.7	105	1.4	210
>27-29	0.75	112.5	1.5	225
29-<31	0.8	120	1.6	240
31-<33	0.85	127.5	1.7	255
33-<35	0.9	135	1.8	270
35-<37	0.95	142.5	1.9	285
37-40	1.0	150	2	300

1 If a satisfactory clinical response has not been achieved 7 days after treatment start, a second dose (same as starting dose, 4 mg/ kg) of canakinumab can be considered. If a full treatment response is subsequently achieved, maintaining the intensified dosing regimen of 8 mg/kg every 8 weeks should be considered, based on individual clinical judgement.
For doses >150 mg (1 mL), 2 vials of ILARIS® are required.

Dosing Recommendation for (SJIA)

The recommended dose of canakinumab for SJIA patients with body weight ≥7.5 kg is 4 mg/kg (up to a maximum of 300 mg) administered every 4 weeks via subcutaneous injection.

Current Body Weight (kg)	Canakinumab dose (4 mg/kg or 300 mg)	
	Volume (mL)	Dose (mg)
7.5 – 8.5	0.2	30
>8.5 – 10	0.25	37.5
>10 – 12	0.3	45
>12 – 14	0.35	52.5
>14 – <16	0.4	60
16 – <18	0.45	67.5
18 – <20	0.5	75
20 – <22	0.55	82.5
22 – 23	0.6	90
>23 – 25	0.65	97.5
>25 – 27	0.7	105
>27 – 29	0.75	112.5
>29 – <31	0.8	120
31 – <33	0.85	127.5
33 – <35	0.9	135
35 – <37	0.95	142.5
37 – <39	1.0	150
39 – <41	1.05	157.5
41 – 42	1.1	165
>42 – 44	1.15	172.5
>44 – 46	1.2	180
>46 – 48	1.25	187.5
>48 – 50	1.3	195
>50 – 52	1.35	202.5
>52 – <54	1.4	210
54 – 55	1.45	217.5
>55 – 57	1.5	225
>57 – 59	1.55	232.5

Dosing Recommendation for (SJIA) continued

Current Body Weight (kg)	Canakinumab dose (4 mg/kg or 300 mg)	
	Volume (mL)	Dose (mg)
>59 – 61	1.6	240
>61 – 63	1.65	247.5
>63 – 65	1.7	255
>65 – 67	1.75	262.5
>67 – <68	1.8	270
68 – <71	1.85	277.5
71 – <73	1.9	285
73 – 74	1.95	292.5
>74	2.0	300

For doses >150 mg (1 mL), 2 vials of ILARIS® are required.

Helpful tools in this information pack For you and your patients

In order to increase understanding of the safe and effective use of canakinumab, you are provided with these educational materials in addition to a copy of the national Prescribing Information.

The educational materials highlight the following aspects:
In this healthcare professionals' guide:

- Indications
- Important safety information
- Dosing recommendations

Patient reminder card

You should complete all the empty fields on the card (patient's name, date of first dose and actual dose administered, doctor's name and phone number) before you give the card to your patient. The card serves as a reminder of the dose used for the patient and includes important information that patients should know about their canakinumab treatment.

Self-administration

- When self-administration is planned, the healthcare provider must instruct the patient or caregiver on proper technique.
- There are diagrams and instructions in the package leaflet.