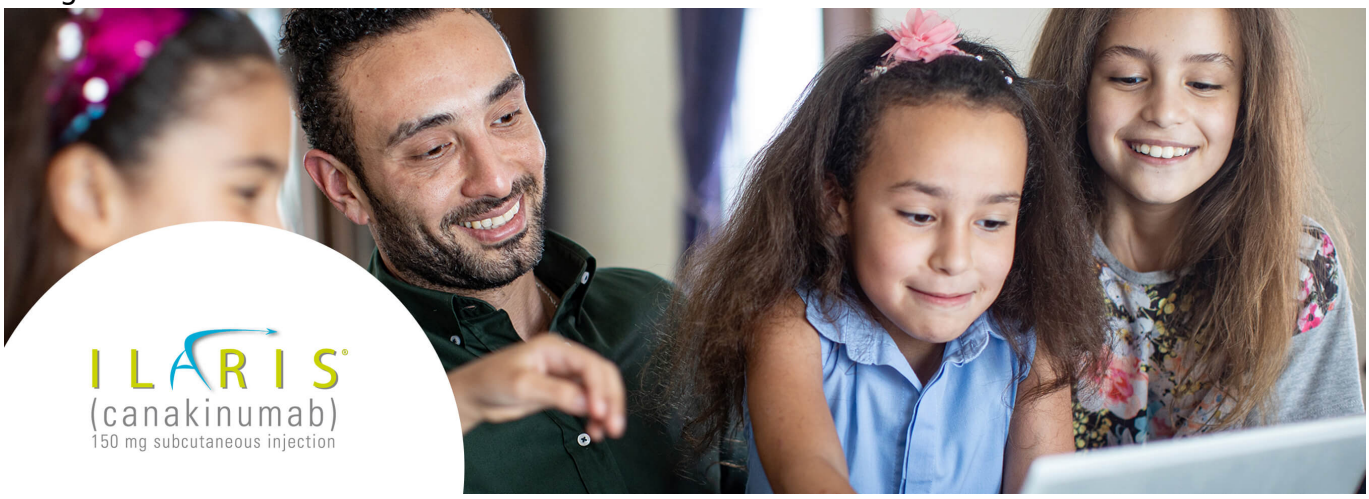
NOVARTIS

Ilaris - Safety profile - in PFS - HCP

Prescribing information

Image



Image

ILARIS® (canakinumab) safety profile in periodic fever syndromes (PFS)

Indications[1]

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:

- Cryopyrin-associated 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
- Tumour necrosis factor receptor associated periodic syndrome (TRAPS)
- Hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD)
- Familial Mediterranean Fever (FMF)
    - ILARIS should be given in combination with colchicine, if appropriate

Still’s disease
ILARIS is indicated in patients who have responded inadequately to previous therapy with non-steroidal anti-inflammatory drugs (NSAIDs) and systemic corticosteroids, for the treatment of active Still’s disease, including:

- Adult-onset Still’s disease (AOSD)
- Systemic juvenile idiopathic arthritis (SJIA) in patients aged 2 years and older
- ILARIS can be given as monotherapy or in combination with methotrexate

Gouty arthritis
ILARIS is indicated for the symptomatic treatment of adult patients with frequent gouty arthritis attacks (at least 3 attacks in the previous 12 months) in whom non-steroidal anti-inflammatory drugs (NSAIDs) and colchicine are contraindicated, are not tolerated, or do not provide an adequate response, and in whom repeated courses of corticosteroids are not appropriate.

Key safety profile data for ILARIS in the treatment of **FMF, HIDS/MKD, TRAPS** and **CAPS**.

Paediatric population
CAPS, TRAPS, HIDS/MKD and **FMF:** The safety and efficacy of canakinumab in CAPS, TRAPS, HIDS/MKD, and FMF patients under 2 years of age have not been established. Currently available data are described in the SmPC, but no recommendation on a posology can be made.

SJIA: The safety and efficacy of canakinumab in SJIA patients under 2 years of age have not been established. No data are available.

Please refer to the ILARIS Summary of Product Characteristics (SmPC) for full safety information.[1]

- The most frequent adverse drug reactions were infections predominantly of the upper respiratory tract. No impact on the type or frequency of adverse drug reactions was seen with longer-term treatment[1]

- Hypersensitivity reactions have been reported in patients treated with canakinumab[1]

- Opportunistic infections have been reported in patients treated with canakinumab (please see 'Special warnings and precautions for use' below)[1]

Tabulated list of adverse reactions

MedDRA System Organ Class	Indications: CAPS, TRAPS, HIDS/MKD, FMF, SJIA
Infections and infestations	
Very common	Respiratory tract infections (including pneumonia, bronchitis, influenza, viral infection, sinusitis, rhinitis, pharyngitis, tonsillitis, nasopharyngitis, upper respiratory tract infection) Ear infection Cellulitis Gastroenteritis Urinary tract infection
Common	Vulvovaginal candidiasis
Nervous system disorders	
Common	Dizziness/vertigo
Gastrointestinal disorders	
Very common	Upper abdominal pain*
Skin and subcutaneous tissue disorders	
Very common	Injection site reaction
Musculoskeletal and connective tissue disorders	
Very common	Arthralgia*
Common	Musculoskeletal pain*
Investigations	

MedDRA System Organ Class	Indications: CAPS, TRAPS, HIDS/MKD, FMF, SJIA
Very common	Creatinine renal clearance decreased*† Proteinuria*‡ Leukopenia* (see 'Laboratory anomalies' below)
Common	Neutropenia (see 'Laboratory anomalies' below)
Uncommon	Platelet count decreased (see 'Laboratory anomalies' below)

Frequency categories are defined using the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

*In SJIA.
†Based on estimated creatinine clearance, most were transient.
‡Most represented transient trace to 1+ positive urinary protein by dipstick.

Adapted from ILARIS® (canakinumab) Summary of Product Characteristics.[1]

Laboratory anomalies[1]

Long-term data and laboratory abnormalities in CAPS patients
During clinical trials with canakinumab in CAPS patients mean values for haemoglobin increased, and those for white blood cells, neutrophils and platelets decreased.

Elevations of transaminases have been observed rarely in CAPS patients.

Asymptomatic and mild elevations of serum bilirubin have been observed in CAPS patients treated with canakinumab without concomitant elevations of transaminases.

In the long-term, open-label studies with dose escalation, events of infections (gastroenteritis, respiratory tract infection, upper respiratory tract infection), vomiting and dizziness were more frequently reported in the 600 mg or 8 mg/kg dose group than in other dose groups.

Laboratory abnormalities in TRAPS, HIDS/MKD and FMF patients
Neutrophils: Although ≥ Grade 2 reductions in neutrophil count occurred in 6.5% of patients (common) and Grade 1 reductions occurred in 9.5% of patients, the reductions are generally transient and neutropenia-associated infection has not been identified as an adverse reaction.

Platelets: Although reductions in platelet count (≥ Grade 2) occurred in 0.6% of patients, bleeding has not been identified as an adverse reaction. Mild and transient Grade 1 reduction in platelets occurred in 15.9% of patients without any associated bleeding adverse events.

Special populations[1]

Canakinumab has not been studied in patients with hepatic impairment. No

recommendation on a posology can be made.

No dose adjustment is needed in patients with renal impairment. However, clinical experience in such patients is limited.

Contraindications[1]

- Hypersensitivity to the active substance or to any of the following excipients: mannitol, histidine, histidine hydrochloride monohydrate, polysorbate 80, water for injections.

- Active, severe infections

Special warnings and precautions for use[1]

Infections
Canakinumab is associated with an increased incidence of serious infections. Therefore patients should be monitored carefully for signs and symptoms of infections during and after treatment with canakinumab. Physicians should exercise caution when administering canakinumab to patients with infections, a history of recurring infections, or underlying conditions which may predispose them to infections.

Canakinumab should not be initiated or continued in patients during an active infection requiring medical intervention.

Tuberculosis screening
In approximately 12% of CAPS patients tested with a PPD (purified protein derivative) skin test in clinical trials, follow-up testing yielded a positive test result while treated with canakinumab without clinical evidence of a latent or active tuberculosis infection. It is unknown whether the use of interleukin-1 (IL-1) inhibitors such as canakinumab increases the risk of reactivation of tuberculosis. Before initiation of therapy, all patients must be evaluated for both active and latent tuberculosis infection.

Patients must be monitored closely for signs and symptoms of tuberculosis during and after treatment with canakinumab. All patients should be instructed to seek medical advice if signs or symptoms suggestive of tuberculosis (e.g. persistent cough, weight loss, subfebrile temperature) appear during canakinumab therapy.

Neutropenia and leukopenia
Neutropenia (absolute neutrophil count [ANC] $<1.5 \times 10^9$/l) and leukopenia have been observed with medicinal products that inhibit IL-1, including canakinumab. Treatment with canakinumab should not be initiated in patients with neutropenia or leukopenia. It is recommended that white blood cell (WBC) counts including neutrophil counts be assessed prior to initiating treatment and again after 1 to 2 months.

If a patient becomes neutropenic or leukopenic, the WBC counts should be monitored closely and treatment discontinuation should be considered.

Malignancies
Malignancy events have been reported in patients treated with canakinumab. The risk for

the development of malignancies with anti-interleukin (IL)-1 therapy is unknown.

Hypersensitivity reactions
Hypersensitivity reactions with canakinumab therapy have been reported. The majority of these events were mild in severity. During clinical development of canakinumab in over 2,600 patients, no anaphylactoid or anaphylactic reactions attributable to treatment with canakinumab were reported. However, the risk of severe hypersensitivity reactions, which is not uncommon for injectable proteins, cannot be excluded.

Hepatic function
Transient and asymptomatic cases of elevations of serum transaminases or bilirubin have been reported in clinical trials.

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 with canakinumab unless the benefits clearly outweigh the risks. Prior to initiation of canakinumab therapy it is recommended that adult and paediatric patients receive all vaccinations, as appropriate, including pneumococcal vaccine and inactivated influenza vaccine.

Mutation in NLRP3 gene in CAPS patients
Clinical experience in CAPS patients without a confirmed mutation in the NLRP3 gene is limited.

Macrophage activation syndrome in patients with Still's disease (SJIA and AOSD)
Macrophage activation syndrome (MAS) is a known, life-threatening disorder that may develop in patients with rheumatic conditions, in particular Still's disease. 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 Still's disease, as these are known triggers for MAS. Based on clinical trial experience, canakinumab does not appear to increase the incidence of MAS in Still's disease patients, but no definitive conclusion can be made.

Drug reaction with eosinophilia and systemic symptoms (DRESS)
DRESS has rarely been reported in patients treated with ILARIS, predominantly in patients with sJIA. Patients with DRESS may require hospitalisation, as this condition may be fatal. If signs and symptoms of DRESS are present and an alternative aetiology cannot be established, canakinumab should not be re-administered and a different treatment considered.

Fertility, pregnancy and lactation[1]

Women should use effective contraceptives during treatment with canakinumab and for up to 3 months after the last dose.

The risk for the foetus/mother is unknown. Women who are pregnant or who desire to become pregnant should therefore only be treated after a thorough benefit–risk evaluation. Women who received canakinumab during pregnancy should be instructed to inform the baby's healthcare professional before any vaccinations are given to their newborn infant.

The decision whether to breastfeed during canakinumab therapy should therefore only be

taken after a thorough benefit–risk evaluation.

Interactions between canakinumab and other medicinal products have not been investigated in formal studies. Please see the SmPC for full details on interactions.

Please refer to the SmPC for more information and the full list of special warnings and precautions for use.[1]

ANC, absolute neutrophil count; CAPS, cryopyrin-associated periodic syndromes; CINCA, chronic infantile neurological, cutaneous, articular syndrome; FCAS, familial cold autoinflammatory syndrome; FCU, familial cold urticaria; FMF, familial Mediterranean fever; HIDS, hyperimmunoglobulin D syndrome; IR, incidence rate; MAS, macrophage activation syndrome; MKD, mevalonate kinase deficiency; MWS, Muckle-Wells syndrome; NOMID, neonatal-onset multisystem inflammatory disease; NSAID, non-steroidal anti-inflammatory drug; SJIA, systemic juvenile idiopathic arthritis; SmPC; summary of product characteristics; TRAPS, tumour necrosis factor receptor-associated periodic syndrome; WBC, white blood cell count.

Reference

1. ILARIS® (canakinumab) Summary of Product Characteristics.

Safety profile in Still’s disease

Safety profile in Still’s disease

See more details

Hide details

Resources for HCPs

Resources for HCPs

See more details

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis online through the pharmacovigilance intake (PVI) tool at www.novartis.com/report, or alternatively email medinfo.uk@novartis.com or call 01276 698370.
