What is Ilaris® (canakinumab)?

Ilaris is a high-affinity human monoclonal antibody that selectively blocks the action of interleukin-1 beta (IL-1 beta)[1,2]. Excessive production of IL-1 beta plays a prominent role in certain inflammatory diseases[3,4].

Ilaris is approved for use in a number of rare diseases[1,2]:

- Periodic Fever Syndromes:
  - Cryopyrin-Associated Periodic Syndromes (CAPS)
  - Tumor Necrosis Factor-Receptor Associated Periodic Syndrome (TRAPS)
  - Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)
  - Familial Mediterranean Fever (FMF)
- Systemic Juvenile Idiopathic Arthritis (SJIA)
- Active Still's Disease including Adult-Onset Still's Disease (AOSD) – in the EU only
- Gouty arthritis – in the US only

What is IL-1 beta?

IL-1 beta is one of a group of proteins called cytokines that the body's immune system produces as part of its response to injury or pathogens. The body releases cytokines to help protect it from further injury. This release is part of the body's immune response and leads to changes in the surrounding area, known as inflammation, which may be accompanied by redness, warmth, swelling and pain. Sometimes this inflammation stays switched on and drives further inflammation, which causes problems. In certain diseases, known as autoinflammatory diseases, excessive production of IL-1 beta is responsible for abnormal prolonged and damaging inflammation[5]. Because of the association of IL-1 beta with an unwanted and elongated inflammatory response, scientists have investigated whether blocking its action could be a way of treating autoinflammatory diseases[5].

How does Ilaris work?

Excessive production of IL-1 beta plays a prominent role in certain inflammatory diseases[3]. Ilaris inhibits IL-1 beta by binding to it and stopping it from attaching to cells and causing further inflammation[1]. By blocking the activity of IL-1 beta, Ilaris can relieve symptoms associated with prolonged inflammation[1,4].

Why is there a need for new treatments for autoinflammatory diseases?

Ilaris is approved for use in a range of autoinflammatory diseases all of which previously had no or limited treatment options.

Before the approval of Ilaris for TRAPS, HIDS/MKD and CAPS, there was no treatment available to change the course of an episode of fever as related to these Periodic Fever Syndromes[1]. The mainstay of treatment was steroidal and non-steroidal anti-inflammatory agents, but these were only used to help manage the symptoms of disease[6]. Long-term steroid use leads to serious side effects[6].

Before the approval of Ilaris for FMF, colchicine was the only FDA-approved treatment for FMF. Colchicine is not effective in 5% of patients with FMF[6].

Treatment options for SJIA are limited and associated with potentially serious side effects, including growth suppression and osteoporosis[7].

Gouty arthritis, although an extremely common condition, is associated with under treatment or no treatment at all. It is at least five times more prevalent than rheumatoid arthritis[8,9] and is a serious, chronic and progressive disease, the incidence of which is rising[10,11].

Where is Ilaris currently licensed for use?

CAPS (a Period Fever Syndrome condition):

- Ilaris is approved in more than 70 countries, including in the EU, Switzerland, Canada and Japan, for the treatment of CAPS – a subset of Periodic Fever Syndromes that are rare, lifelong, genetic disorders with debilitating symptoms[1,2]
- In the US, Ilaris is approved for two of the three subtypes of CAPS: familial cold autoinflammatory syndrome (FCAS) and Muckle-Wells syndrome (MWS)[2]

TRAPS, HIDS/MKD and FMF:

- In the US, Ilaris is approved for three other Periodic Fever Syndromes: TRAPS, HIDS/MKD and FMF

AOSD and SJIA:

- In the EU, Ilaris is currently approved for Adult-Onset Still's Disease (AOSD) and Systemic Juvenile Idiopathic Arthritis (SJIA)
- In the US, Ilaris is currently approved for the treatment of SJIA

Gouty arthritis:

- In the EU, Ilaris is approved for the symptomatic treatment of refractory acute gouty arthritis

The approved indication may vary depending upon the individual country.

Ilaris in clinical trials

CAPS (a Period Fever Syndrome condition): For the 48-week pivotal trial, the primary endpoint was sustained response and the secondary endpoint was complete remission[1,12]. In the 24-week period, 100% of patients on Ilaris had sustained remission compared with 19% on placebo. Of patients on Ilaris 97% experienced complete remission[1,12,].

Ilaris was also investigated in the largest documented registry cohort for CAPS. Ilaris demonstrated a safety profile consistent with that observed in the clinical trial program and provided continued effectiveness in CAPS patients for up to 5 years[13].

TRAPS, HIDS/MKD and FMF*:* In the CLUSTER trial, patients with three other forms of Periodic Fever Syndromes; FMF, TRAPS and HIDS/MKD were studied. Ilaris was associated with a rapid reduction in disease activity and its effect lasted for the 16-week study duration. At the start of the trial, all patients had active disease; by the end of the trial 82%, 92% and 94% of TRAPS, HIDS/MKD and FMF patients had no active disease[14].

SJIA*:* In two Phase III studies, Ilaris demonstrated efficacy in systemic JIA with active systemic features[15].

Gouty arthritis: Two main trials investigated the efficacy of Ilaris and involved 454 gouty arthritis patients. Patients were given either Ilaris or the anti-inflammatory medicine triamcinolone acetonide for 12 weeks. In gouty arthritis, both studies showed that Ilaris was more effective at reducing pain intensity than triamcinolone acetonide[14].

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