

ILARIS® (canakinumab)
**A NOVEL BIOLOGICAL TREATMENT FOR CHILDREN AND ADULTS WITH CAPS, A
SERIOUS LIFE-LONG AUTO-INFLAMMATORY DISEASE**

What is ILARIS?

ILARIS® (canakinumab), a human monoclonal antibody, is approved in the US for the treatment of patients with cryopyrin-associated periodic syndrome (CAPS), which includes a number of rare, life-long, auto-inflammatory disorders with debilitating symptoms and limited treatment options. ILARIS is the first approved treatment for patients who are four years of age and older suffering from two forms of CAPS: familial cold auto-inflammatory syndrome (FCAS) and Muckle-Wells syndrome (MWS).

The dosing schedule for ILARIS is one subcutaneous injection every eight weeks, which is less frequent than the only other approved therapy for CAPS.

ILARIS has orphan drug designation in CAPS in the US, as well as in the EU, Switzerland, Canada and Australia, where it is currently under review for approval. Priority review has been granted in Canada and Switzerland. ILARIS has been granted orphan drug designation for SJIA in the US, Switzerland and in the EU, and also has Fast Track status for SJIA in the US.

What are orphan drugs?

Orphan drugs are those developed to treat diseases affecting fewer than 200,000 people (in the US) or fewer than five out of 10,000 people (in the EU).

How does ILARIS work?

ILARIS is a fully human monoclonal antibody that provides potent and selective blockade of interleukin-1 beta (IL-1 β), which is part of the body's immune system defenses. Excessive production of IL-1 β is believed to play a major role in many inflammatory diseases.

ILARIS works by attaching itself to IL-1 β for a sustained period of time, neutralizing it and, therefore, blocking inflammation and its related symptoms.

Due to its highly targeted mode of action, ILARIS has the potential to treat a wide range of inflammatory diseases where overproduction of IL-1 β may play a key role. ILARIS is currently being studied as a potential treatment for systemic juvenile idiopathic arthritis (SJIA), some forms of gout, chronic obstructive pulmonary disorder (COPD) and type II diabetes.

What is an antibody?

Antibodies (also known as immunoglobulins) are proteins that are found in blood or other bodily fluids. The role of an antibody in the immune system is to identify and neutralize foreign objects, such as bacteria and viruses, directing the appropriate immune response for each foreign object they encounter.

Monoclonal antibodies are antibodies that are produced in a lab and designed to identify and neutralize a specific target (in this case IL-1 β).

ILARIS as a treatment for CAPS and other IL-1 β -driven auto-inflammatory diseases

In CAPS, a gene mutation leads to overproduction of IL-1 β and data demonstrate that in CAPS, production of IL-1 β is over five times higher than in healthy subjects. This leads to inflammation and results in the symptoms seen in CAPS diseases.

Clinical data has demonstrated that ILARIS was associated with rapid and complete remission in patients with CAPS, with a single dose providing relief from symptoms in as little as 24 hours in the majority of patients. ILARIS was generally well tolerated. The most common adverse events reported by patients treated with ILARIS in the study were nasopharyngitis, diarrhea, influenza, headache and nausea. No impact on the type or frequency of adverse events was seen with longer term treatment.

ILARIS: Illuminating the role of IL-1 β in inflammatory disease

The pivotal role of IL-1 β in inflammatory diseases and the importance of the selective mechanism of action of ILARIS in inhibiting the inflammatory process were described in the May 11, 2009 issue of the *Journal of Experimental Medicine*. Clinical and biomarker data generated in ILARIS' Proof-of-Concept (investigational) study were subjected to state-of-the-art modelling and simulation to yield new insights into the regulation of IL-1 β in patients.

Until now, the study of IL-1 β has been a challenge as it is virtually undetectable in human blood serum. However, when ILARIS specifically binds to IL-1 β , these newly formed ILARIS/IL-1 β complexes are detectable in serum, allowing study of the production of IL-1 β in the human body. Mathematical modelling of the clinical and biomarker data allowed the rate of IL-1 β production in patients to be calculated for the first time. Predictions made in this work were subsequently confirmed by Phase III study data.

Important Safety Information

Ilaris may affect the immune system and may lower the ability to fight infections. Infections, in some instances serious, have been reported after treatment. Ilaris should be used with caution in patients with an infection and discontinued if a serious infection develops. Patients should receive all recommended vaccinations prior to initiation of treatment and live vaccines should not be used in treated patients. Vertigo has been reported in patients treated with Ilaris. The most common side effects are inflammation of the upper airways, diarrhea, flu-like symptoms, headache and nausea. There are no studies in pregnant women with Ilaris and it should be used during pregnancy only if clearly needed.

For full Ilaris prescribing information, go to www.pharma.us.novartis.com.