Helpful ILARIS® Tools in the Information Pack

For You and Your Patients

This pack includes important information and resources to help you when prescribing ILARIS® for patients suffering from Cryopyrin-Associated Periodic Syndrome (CAPS) to help them manage their disease effectively.

It is important that you are familiar with the material to ensure the proper use of ILARIS®.

This ILARIS® Information Pack includes the following:

ILARIS® Preparation and Injection Guide

- Patient-friendly brochure demonstrating simple instructions for the successful administration of ILARIS®
- Dosing instructions and step-by-step visuals simplify preparation and injection
  - Treatment should be initiated and supervised by a specialist physician experienced in the diagnosis and treatment of CAPS[1]
  - After proper training, patients may self-inject ILARIS® if they are capable[1]

In the case of an administration error, contact:

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ILARIS® Patient Alert Card

- A wallet-sized card that patients must carry with them at all times
- Includes important safety information that all healthcare professionals involved in the patient's care should know in case of a medical emergency

It is required that you give your ILARIS® patients this card to carry with them at all times after initiating ILARIS® treatment.

ILARIS® Summary of Product Characteristics (SmPC)

- Detailed document featuring important properties of ILARIS®:
  - Safety and efficacy data, including results from clinical trials
  - Review of the targeted mechanism of action
  - Pharmacokinetic and pharmacodynamic data
  - Important safety information and precautions

Closely review the contents provided in the Information Pack prior to prescribing ILARIS®.

ILARIS®
(canakinumab)
150 mg subcutaneous injection

Reference: 1. Ilaris [summary of product characteristics]. West Sussex, United Kingdom: Novartis Europharm Limited; 2011.

Identification and Diagnosis of CAPS Patients—The ILARIS® Registry Is Open for CAPS Patients

Patient Identification and Diagnosis

CAPS is believed to occur in around 6500 patients worldwide[1] and 2500 in the European Union.[2] However, due to lack of diagnosis or misdiagnosis, fewer than 1000 cases have been officially reported worldwide.[3]

Undiagnosed CAPS patients are in great need of long-term symptom relief and prevention of progressive complications.[4]

The following methods may help in identifying CAPS patients:

Explore immediate family history and consider CAPS connections to other relatives

Consider patients who have reported symptoms resembling other conditions

Assess patients with periodic fever and skin reactions for a mutation of the *NLRP3* gene

Reach out to colleagues who may have undiagnosed CAPS patients within their practice

β CONFIDENT

Opportunity to Enroll ILARIS® Patients in the ILARIS® Registry

The ILARIS® -CONFIDENT registry is a worldwide database of CAPS patients that will assess long-term safety and treatment outcomes with ILARIS® under local care conditions.

By registering your ILARIS® patients, common characteristics between genotype and phenotype, potential disease modification may be established.

The long-term efficacy and safety data provided by the ILARIS® registry can help inform best practices in CAPS for successful treatment outcomes.

Collaboration with other established and planned autoinflammatory databases is expected. Visit the Novartis Registry Web site at www.ilarisregistry.com for more information.

References: 1. Durrant KLW, Goldbach-Mansky R, Hoffman H, Leslie K, Rubin B. CAPS: cryopyrin-associated periodic syndromes. San Francisco, CA: The NOMID Alliance; 2008. **2.** European Medicines Agency (EMEA). Committee for orphan medicinal products. Public summary of positive opinion for orphan designation of rilonacept for the treatment of cryopirin-associated periodic syndromes (familial cold urticaria syndrome (FCUS), Muckle-Wells syndrome (MWS), and neonatal onset multisystem inflammatory disease (NOMID), also known as chronic infantile neurological cutaneous articular syndrome (CINCA)). http://www.emea.europa.eu/pdfs/human/comp/opinion/17086808en.pdf. Published July 29, 2008. Accessed August 27, 2009. **3.** Data on file; Novartis Pharma AG. **4.** Hoffman HM. Hereditary immunologic disorders caused by pyrin and cryopyrin. *Curr Allergy Asthma Rep.* 2007;7:323-330.

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ILARIS®
(canakinumab)
150 mg subcutaneous injection

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A Healthcare Professional's Guide to Treatment of Patients with Cryopyrin-Associated Periodic Syndromes (CAPS) with ILARIS®

Indication

ILARIS® is indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) in adults, adolescents, and children aged 4 years and older with body weight above 15 kg, 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

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Important Safety Information

What You Should Know Before Treatment With ILARIS®

ILARIS® was well tolerated, as demonstrated by more than 100 CAPS patients in clinical trials and more than 800 patients in the overall database.[1] However, the following risks are associated with treatment:

Injection-Site Reactions

More than 90% of patients receiving ILARIS® did not experience any injection-site reactions after the first injection, and those that did occur were of a mild-to-moderate nature.[1,2]

Infections, Including Serious Infections[1]

- Monitor patients carefully for signs and symptoms of infections during and after treatment with ILARIS®
- Exercise caution when administering ILARIS® to patients with infections, a history of recurring infections, or underlying conditions which may predispose them to infections
- ILARIS® 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 ILARIS®; the causal relationship of ILARIS® to these events is unknown.

It is unknown if the use of IL-1 inhibitors such as ILARIS® 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. This evaluation should include a detailed medical history, particularly in adult patients. Appropriate screening tests (eg, tuberculin skin test, Interferon-Gamma-Release-Assay (IGRA), or chest X-ray) should be performed in all patients (local recommendations may apply). Patients must be monitored closely for signs and symptoms of tuberculosis during and after treatment with ILARIS®. All patients should be instructed to seek medical advice if signs or symptoms suggestive of tuberculosis (eg, persistent cough, weight loss, subfebrile temperature) appear during ILARIS® therapy. In the event of conversion from a negative to positive purified protein derivative (PPD) test, especially in high-risk patients, alternative means of screening for a tuberculosis infection should be considered.

References: 1. Ilaris [summary of product characteristics]. West Sussex, United Kingdom: Novartis Europharm Limited; 2011. **2.** Lachmann HJ, Kone-Paut I, Kuemmerle-Deschner JB, et al. Use of canakinumab in the cryopyrin-associated periodic syndrome. *N Engl J Med*. 2009;360:2416-2425.

Important Safety Information (cont'd)

What You Should Know Before Treatment With ILARIS®

Neutropenia[1]

Neutropenia (absolute neutrophil count <1.5 x 10^9/L) has been observed with medicinal products that inhibit IL-1, including ILARIS®. Treatment with ILARIS® should not be initiated in patients with neutropenia. It is recommended that neutrophil counts be assessed prior to initiating treatment and, for continuous treatment with ILARIS®, after 1 to 2 months, and periodically thereafter while receiving ILARIS®.

Potential Risk of Immunogenicity and Hypersensitivity Reactions[1]

- Cases suggestive of hypersensitivity reactions with ILARIS® have been reported
  - The majority of these events were mild in severity

No anaphylactoid or anaphylactic reactions have been reported. However, the risk of severe hypersensitivity reactions, which is not uncommon for injectable proteins, cannot be excluded.

No antibodies to ILARIS® have been detected in CAPS patients treated with ILARIS®. Antibodies against ILARIS® were observed in approximately 1% of gouty arthritis patients in clinical studies.

Unknown Safety in Pregnant and Lactating Women[1]

- Women should use effective contraceptives during treatment with ILARIS® and for up to 3 months after the last dose
- It is not known whether ILARIS® is excreted in human milk
- Formal studies of the potential effect of ILARIS® 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.

Frequency of Adverse Events[1]

≥ 10% of patients	<10% of patients
Nasopharyngitis	Urinary tract infection
Vertigo	Upper respiratory tract infection
Injection-site reactions	Viral infection

Reference: 1. Ilaris [summary of product characteristics]. West Sussex, United Kingdom: Novartis Europharm Limited; 2011.

Important Safety Information (cont'd)

Managing Treatment With ILARIS®

The following conditions should be evaluated regularly throughout treatment:

Malignancies[1]

- Perform annual assessments in ILARIS® patients regarding the presence of malignancies

Malignancy events have been reported in patients treated with ILARIS® during clinical development. The risk for the development of malignancies with anti-IL-1 therapy is unknown.

Neutropenia[1]

- Assess neutrophil counts in patients:
  - Before initiating treatment with ILARIS®
  - 1 to 2 months into treatment
  - Periodically thereafter
- If a patient becomes neutropenic:
  - Monitor the absolute neutrophil count (ANC) and consider discontinuation of treatment
- You should not initiate treatment in patients with neutropenia

Neutropenia (ANC <1.5 x 10^9/L) has been observed commonly with another IL-1 inhibitor used in rheumatoid arthritis patients, a condition in which ILARIS® is not approved for use.

Lipid Profile

- Monitor patients regularly during treatment for changes in their lipid profiles[2]

Patients treated with ILARIS® showed increased levels of triglycerides in comparative trials (>5 x ULN was 2.4% with ILARIS® and 0.7% with triamcinolone acetonide); the clinical significance of this observation is unknown. Increases in total cholesterol, HDL, and LDL levels as well as triglycerides have been observed in CAPS patients treated with another anti-IL-1 therapy.[2]

Vaccinations[1]

- No data are available on the risk of secondary transmission of infection by live (attenuated) vaccines in patients receiving ILARIS®. Therefore, live vaccines should not be given concurrently in patients receiving ILARIS® unless the benefits clearly outweigh the risks
- Prior to initiation of ILARIS® therapy, adult and paediatric patients should receive all recommended vaccinations, as appropriate, including pneumococcal and inactivated influenza vaccines
- For patients on ILARIS® therapy, wait at least 3 months after the last injection and before the next injection to administer any live vaccines
- In healthy adults, ILARIS® did not affect the induction and persistence of antibody responses after vaccination with influenza and glycosylated protein-based meningococcus vaccines.

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References: 1. Ilaris [summary of product characteristics]. West Sussex, United Kingdom: Novartis Europharm Limited; 2011. **2.** Arcalyst [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; 2009.