Novartis receives three new FDA approvals for the expanded use of Ilaris for patients with rare Periodic Fever Syndrome conditions

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- - Ilaris® (canakinumab) is the first and only FDA-approved biologic treatment for patients with TRAPS, HIDS/MKD and FMF(1)
- - These three simultaneous approvals conducted under FDA Priority Review follow Breakthrough Therapy Designations to address the unmet need of patients
- - Ilaris provides rapid and sustained disease control for patients with these rare and debilitating Periodic Fever Syndromes

EAST HANOVER, N.J., Sept. 23, 2016 /PRNewswire/ -- Novartis announced today that the US Food and Drug Administration (FDA) has granted three simultaneous approvals for the expanded use of Ilaris® (canakinumab) to treat three rare and distinct types of Periodic Fever Syndromes.

Ilaris is the first and only FDA-approved biologic treatment for patients with Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD) and Familial Mediterranean Fever (FMF).[1,2] All three conditions are part of a group of rare autoinflammatory diseases called Periodic Fever Syndromes, which are also referred to as Hereditary Periodic Fevers (HPF). The most common syndrome is FMF, which mainly affects people of Eastern Mediterranean ancestry. It affects 1 in 250 to 1 in 1,000 individuals in these populations, many of whom are children.[3]

"We are grateful to the scientists, clinical trial investigators and all associates who worked tirelessly in support of patients to gain three simultaneous FDA approvals of ILARIS," said Fabrice Chouraqui, President of Novartis Pharmaceuticals Corporation, "It is through their hard work that Novartis can offer a desperately needed new treatment option to the adults and children who suffer from these debilitating conditions and continue to serve the rare disease community."

The FDA approvals are based on results from the pivotal Phase III CLUSTER study which showed rapid (at Day 15) and sustained disease control with Ilaris compared to placebo through 16 weeks, in patients with either TRAPS, HIDS/MKD or FMF.[2] As a result of the positive data, the FDA granted Ilaris Breakthrough Therapy status and priority reviews for each of the three Periodic Fever Syndrome conditions.

Periodic Fever Syndromes are a group of rare autoinflammatory diseases that cause disabling and persistent fevers which may be accompanied by joint pain, swelling, muscle pain and skin rashes with complications that can be life-threatening.[1]

"Adults and children living with TRAPS, HIDS/MKD or FMF often experience extensive delays in diagnosis because the disorders are so rare that many physicians are unaware of them," said Hal M. Hoffman, M.D., chief of Pediatric Allergy, Immunology, and Rheumatology at Rady Children's Hospital-San Diego and University of California San Diego. "Following diagnosis, our goal is to get patients treated as soon as possible and that has been challenging due to the lack of available treatment options. That's what makes these three

approvals for ILARIS so important for patients."

Ilaris is already approved and marketed in the US as an effective and well-tolerated treatment for another Periodic Fever Syndrome condition – Cryopyrin-Associated Periodic Syndromes (CAPS), and another autoinflammatory condition – Systemic Juvenile Idiopathic Arthritis (SJIA).

About Periodic Fever Syndromes

Periodic Fever Syndromes are a group of diseases that cause serious recurrent fever and inflammation through non-infectious activation of the immune system. Most patients present with symptoms in infancy or childhood, but in some patients the condition only becomes apparent or diagnosed in adulthood.[1]

Previous treatments for these rare conditions consisted of oral anti-inflammatory drugs, such as corticosteroids, which were used only to help manage the symptoms. While other medicines, such as non-steroidal anti-inflammatory drugs, have also been used to help reduce symptoms, they do not prevent or change the overall course of a flare.[1]

About Ilaris

Ilaris is a selective, high-affinity, human monoclonal antibody that inhibits Interleukin-1 (IL-1) beta, which is an important part of the body's immune system defenses.[4] Excessive production of IL-1 beta plays a prominent role in certain inflammatory diseases.[5,6] Ilaris works by blocking the action of IL-1 beta for a sustained period of time, therefore inhibiting inflammation that is caused by its over-production.[4]

Ilaris is currently approved and marketed for the treatment of SJIA in the US and EU and for the treatment of Adult-Onset Still's Disease (AOSD) and the symptomatic treatment of refractory acute gouty arthritis in the EU. Ilaris is also approved in more than 70 countries, including in the EU, Switzerland, Canada, and Japan for the treatment of the Periodic Fever Syndrome CAPS: rare, lifelong, genetic disorders with debilitating symptoms. In the US, Ilaris is approved for two subtypes of CAPS: Muckle-Wells Syndrome (MWS) and Familial Cold Autoinflammatory Syndrome (FCAS). The approved indications may vary depending upon the individual country.

Important Safety Information

ILARIS can cause serious side effects, including increased risk of serious side infections. ILARIS can lower the ability of your immune system to fight infections. Your healthcare provider should: test you for tuberculosis (TB) before you receive ILARIS; monitor you closely for symptoms of TB during treatment with ILARIS; check you for symptoms of any type of infection before, during, and after treatment with ILARIS. Tell your healthcare provider right away if you have any symptoms of an infection such as fever, sweats or chills, cough, flu-like symptoms, weight loss, shortness of breath, blood in your phlegm, sores on your body, warm or painful areas on your body, diarrhea or stomach pain, or feeling very tired.

You should not receive ILARIS if you are allergic to canakinumab or any of the ingredients in ILARIS.

Before you receive ILARIS, tell your healthcare provider about all your medical conditions, including if you: think you have or are being treated for an active infection; have symptoms of an infection; have a history of infections that keep coming back; have a history of low white blood cells; have or have had HIV, Hepatitis B, or Hepatitis C; are scheduled to receive any immunizations (vaccines) as you should not get 'live vaccines' if you are receiving ILARIS; are pregnant or planning to become pregnant since it is not known if ILARIS will harm an unborn baby (patients who become pregnant while receiving ILARIS should tell their healthcare provider right away); are breastfeeding or planning to breastfeed as it is not known if ILARIS passes into your breast milk. You and your healthcare provider should decide if you will receive ILARIS or breastfeed. You should not do both.

ILARIS can cause serious side effects, including: serious infections; decreased ability of your body to fight infections (immunosuppression; for people treated with medicines that cause immunosuppression like ILARIS, the chances of getting cancer may increase); allergic reactions (call your healthcare provider right away if you have any of these symptoms of an allergic reaction: rash, itching and hives, difficulty breathing or swallowing, dizziness or feeling faint); risk of infection with live vaccines (you should not get live vaccines if you are receiving ILARIS; tell your healthcare provider if you are scheduled to receive any vaccines).

The most common side effects of ILARIS include:

When ILARIS is used for the treatment of CAPS: cold symptoms; diarrhea, flu (influenza), runny nose, headache, cough, body aches; nausea, vomiting, and diarrhea (gastroenteritis), feeling like you are spinning (vertigo), weight gain, injection site reactions (such as redness, swelling, warmth, or itching) and nausea.

When ILARIS is used for the treatment of TRAPS, HIDS/MKD, and FMF: cold symptoms, upper respiratory tract infection, runny nose, sore throat, nausea, vomiting, and diarrhea (gastroenteritis), and injection site reactions (such as redness, swelling, warmth, or itching).

When ILARIS is used for the treatment of SJIA: cold symptoms, upper respiratory tract infection, pneumonia, runny nose, sore throat, urinary tract infection, nausea, vomiting and diarrhea (gastroenteritis), stomach pain, and injection site reactions (such as redness, swelling, warmth, or itching).

What is Macrophage Activation Syndrome (MAS)?

MAS is a syndrome associated with SJIA and some other autoinflammatory diseases like HIDS/MKD that can lead to death. Tell your healthcare provider right away if your SJIA symptoms get worse or if you have any of these symptoms of an infection: a fever lasting longer than 3 days; a cough that does not go away; redness in one part of your body; warm feeling or swelling of your skin.

You are encouraged to report negative side effects of prescription drugs to FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088

Please see full Prescribing Information, including Medication Guide at https://www.pharma.us.novartis.com/sites/www.pharma.us.novartis.com/files/ilaris.pdf for additional Important Safety Information.

Disclaimer
The foregoing release contains forward-looking statements that can be identified by words such as "Breakthrough Therapy Designations," "Breakthrough Therapy," "goal," or similar terms, or by express or implied discussions regarding potential new indications or labeling for Ilaris, or regarding potential future revenues from Ilaris. You should not place undue reliance on these statements. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. There can be no guarantee that Ilaris will be submitted or approved for any additional indications or labeling in any market, or at any particular time. Nor can there be any guarantee that Ilaris will be commercially successful in the future. In particular, management's expectations regarding Ilaris could be affected by, among other things, the uncertainties inherent in research and development, including unexpected clinical trial results and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; the company's ability to obtain or maintain proprietary intellectual property protection; general economic and industry conditions; global trends toward health care cost containment, including ongoing pricing pressures; unexpected safety, quality or

manufacturing issues, and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis
Novartis Pharmaceuticals Corporation offers a broad range of medicines for cancer, cardiovascular disease, endocrine disease, inflammatory disease, infectious disease, neurological disease, organ transplantation, psychiatric disease, respiratory disease and skin conditions.

Located in East Hanover, NJ Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG, which provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. In 2015, the Group achieved net sales of USD 49.4 billion, while R&D throughout the Group amounted to approximately USD 8.9 billion (USD 8.7 billion excluding impairment and amortization charges). Novartis Group companies employ approximately 118,000 full-time-equivalent associates. Novartis products are available in more than 180 countries around the world. For more information, please visit http://www.novartis.com.

References

1. Cleveland Clinic. Periodic Fever Syndrome. Available at: https://my.clevelandclinic.org/services/orthopaedics-rheumatology/diseases-conditions/periodic-fever-syndrome. Accessed September 2016.https://my.clevelandclinic.org/services/orthopaedics-rheumatology/diseases-conditions/periodic-fever-syndrome. Accessed September 2016.
2. Novartis. Ilaris Prescribing Information. September 2016. Available at: www.pharma.us.novartis.com/product/pi/pdf/ilaris.pdf. Accessed September 2016.
3. National Amyloidosis Centre. Amyloidosis Patient Information Site: The inherited periodic fever syndromes – general information. Available at: www.amyloidosis.org.uk/fever-syndromes/inherited-fever-syndromes/. Accessed September 2016.
4. Dhimolea E. Canakinumab, MAbs. 2010 Jan-Feb;2(1):3-13.
5. Jesus AA, Goldbach-Mansky R. IL-1 blockade in autoinflammatory syndromes. Annu Rev Med. 2014;65:223-244.
6. Toker O, Hashkes PJ. Critical appraisal of canakinumab in the treatment of adults and children with cryopyrin-associated periodic syndrome (CAPS). Biologics. 2010;4:131-138.

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