DISCOVER

ILARIS®
(canakinumab)
150 mg subcutaneous injection

FOR GOUT FLARES

INDICATIONS

ILARIS® (canakinumab) is an interleukin-1β blocker indicated for the treatment of the following autoinflammatory Periodic Fever Syndromes:

- Cryopyrin-Associated Periodic Syndromes (CAPS), in adults and pediatric patients 4 years of age and older, including:
  - Familial Cold Autoinflammatory Syndrome (FCAS)
  - Muckle-Wells Syndrome (MWS)
- Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS) in adult and pediatric patients
- Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD) in adult and pediatric patients
- Familial Mediterranean Fever (FMF) in adult and pediatric patients

ILARIS is indicated for the treatment of active Still's disease, including Adult-Onset Still's Disease (AOSD) and Systemic Juvenile Idiopathic Arthritis (SJIA) in patients 2 years of age and older.

ILARIS is indicated for the symptomatic treatment of adult patients with gout flares in whom nonsteroidal 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.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ILARIS is contraindicated in patients with confirmed hypersensitivity to canakinumab or to any of the excipients.

WARNINGS AND PRECAUTIONS

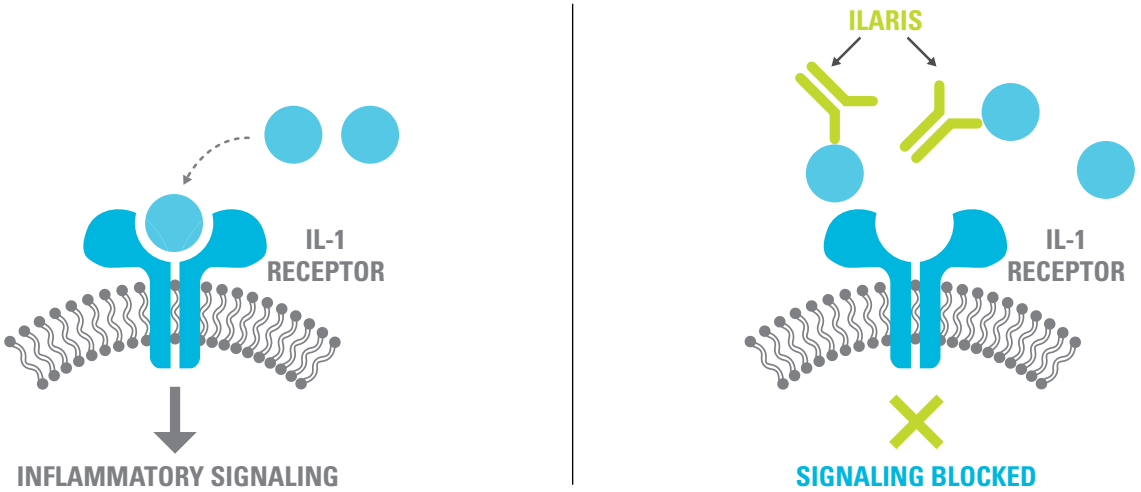
Serious Infections

ILARIS has been associated with an increased risk of serious infections. Exercise caution when administering ILARIS to patients with infections, a history of recurring infections or underlying conditions, which may predispose them to infections. Avoid administering ILARIS to patients during an active infection requiring medical intervention. Discontinue ILARIS if a patient develops a serious infection.

ILARIS SELECTIVELY TARGETS IL-1β TO BLOCK INFLAMMATORY SIGNALING[1]

ILARIS binds to human IL-1β and neutralizes its activity by blocking its interaction with IL-1 receptors, but it does not bind IL-1α or IL-1 receptor antagonist (IL-1ra)

- ILARIS is a human monoclonal anti-human IL-1β antibody



Mechanism of Action

Gout flares are characterized by activation of resident macrophages and infiltrating neutrophils in the joint, and concomitant overproduction of IL-1β resulting in an acute painful inflammatory response. IL-1β production by macrophages is triggered by uric acid (monosodium urate monohydrate) crystals in the joint and surrounding tissue through activation of the NLRP3 inflammasome complex.

IL, interleukin; NLR family, pyrin domain-containing 3.

IMPORTANT SAFETY INFORMATION (cont)
WARNINGS AND PRECAUTIONS

Serious Infections (cont)

Infections, predominantly of the upper respiratory tract, in some instances serious, have been reported with ILARIS. Generally, the observed infections responded to standard therapy. Isolated cases of unusual or opportunistic infections (eg, aspergillosis, atypical mycobacterial infections, cytomegalovirus, herpes zoster) were reported during ILARIS treatment. A causal relationship of ILARIS to these events cannot be excluded. In clinical trials, ILARIS has not been administered concomitantly with tumor necrosis factor (TNF) inhibitors. An increased incidence of serious infections has been associated with administration of another interleukin-1 (IL-1) blocker in combination with TNF inhibitors. Coadministration of ILARIS with TNF inhibitors is not recommended because this may increase the risk of serious infections.

Please see Important Safety Information throughout brochure and full Prescribing Information, including Medication Guide, for ILARIS.

ILARIS®
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150 mg subcutaneous injection

CLINICAL STUDIES FOR TREATMENT OF GOUT FLARES[1]

Study Designs

The efficacy of ILARIS was demonstrated in two 12-week, randomized, double-blind, active-controlled studies in patients with gout flares for whom NSAIDs and/or colchicine were contraindicated, not tolerated or ineffective, and who had experienced at least three gout flares in the previous year (Studies 1 and 2). The studies continued in (1) two 12-week, double-blind, active-controlled extensions, followed by; (2) two open-label extensions and continued; (3) in a third open-label extension (combined for both studies) up to a maximum of 36 months where all patients were treated with ILARIS upon a new flare.

In Study 1 (NCT01029652), patients were randomized to receive ILARIS 150 mg subcutaneous (N=115) or triamcinolone acetonide 40 mg intramuscular (N=115) at baseline and thereafter treated upon a new flare. Two patients randomized to canakinumab were not included in the analysis as they did not receive any study medication. In Study 2 (NCT01080131), patients were randomized to receive ILARIS 150 mg subcutaneous (N=112) or triamcinolone acetonide 40 mg intramuscular (N=114) at baseline and thereafter treated upon a new flare.

In Studies 1 and 2, over 85% of patients had at least one comorbidity, including hypertension (60%), obesity (53%), diabetes (15%), and ischemic heart disease (12%). Twenty-five percent of patients had chronic kidney disease (stage ≥3), based on eGFR. Concomitant treatment with allopurinol or other uric acid-lowering therapies was reported by 42% of patients at entry.

The majority of patients (73%) reported between 3 to 6 flares in the year prior to study entry and the remainder reported 7 or more flares. Approximately one-third of the patients enrolled (76 in the ILARIS group [33.5%] and 84 in the triamcinolone acetonide [36.7%] group) had documented inability (intolerance, contraindication, or lack of response) to use both, NSAIDs and colchicine. The remainder had intolerance, contraindication, or lack of response to either NSAIDs or colchicine.

In both studies, the co-primary endpoints were: (i) patient's assessment of gout flare pain intensity at the most affected joint at 72 hours post-dose measured on a 0 to 100 mm visual analogue scale (VAS) and; (ii) the time to first new gout flare. The studies aimed to determine whether ILARIS 150 mg would be superior to triamcinolone acetonide 40 mg.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS

Serious Infections (cont)

Drugs that affect the immune system by blocking TNF have been associated with an increased risk of new tuberculosis (TB) and reactivation of latent TB. It is possible that use of IL-1 inhibitors, such as ILARIS, increases the risk of reactivation of TB or of opportunistic infections.

Prior to initiating immunomodulatory therapies, including ILARIS, evaluate patients for active and latent TB infection. Appropriate screening tests should be performed in all patients. ILARIS has not been studied in patients with a positive TB screen, and the safety of ILARIS in individuals with latent TB infection is unknown. Treat patients testing positive in TB screening according to standard medical practice prior to therapy with ILARIS. Instruct patients to seek medical advice if signs, symptoms, or high risk exposure suggestive of TB (eg, persistent cough, weight loss, subfebrile temperature) appear during or after ILARIS therapy. Healthcare providers should follow current CDC guidelines both to evaluate for and to treat possible latent TB infections before initiating therapy with ILARIS.

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ILARIS® (canakinumab) 150 mg subcutaneous injection

CLINICAL STUDIES FOR TREATMENT OF GOUT FLARES[1] (cont)

Study Designs

Study 3 (NCT01356602), an additional 12-week, randomized, double-blind, active-controlled study, enrolled 397 patients with ILARIS 150 mg subcutaneous (Pre-Filled Syringe [PFS], N=133, Lyophilizate [LYO], N=132) or triamcinolone acetonide 40 mg intramuscular (N=132). Eight patients (2 ILARIS PFS, 3 ILARIS LYO, 3 triamcinolone) were not included for efficacy assessment as they did not receive study medication. Pain intensity at the most affected joint, assessed on a 0 to 100 mm VAS at 72 hours post-dose was the primary endpoint, and time to first new gout flare was a secondary endpoint. Approximately 44% of patients (45.9% ILARIS PFS group, 47.4%, ILARIS LYO group, and 40.6% in the triamcinolone acetonide group) were unable to use NSAIDs and colchicine (due to contraindications, intolerance, or inadequate response) in this study.

Analyses of both endpoints were conducted for Studies 1, 2, and 3 for the subpopulation of patients unable to use NSAIDs and colchicine (due to contraindications, intolerance, or inadequate response) and overall population of patients unable to use NSAIDs and/or colchicine.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS

Immunosuppression

The impact of treatment with anti-IL-1 therapy on the development of malignancies is not known. However, treatment with immunosuppressants, including ILARIS, may result in an increase in the risk of malignancies.

Hypersensitivity Reactions

Hypersensitivity reactions have been reported with ILARIS. During clinical trials, no anaphylactic reactions attributable to treatment with canakinumab have been reported. It should be recognized that symptoms of the underlying disease being treated may be similar to symptoms of hypersensitivity. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), characterized by serious skin eruptions, has been reported in patients with autoinflammatory conditions treated with ILARIS. If a severe hypersensitivity reaction occurs, immediately discontinue ILARIS; treat promptly and monitor until signs and symptoms resolve.

Immunizations

Avoid administration of live vaccines concurrently with ILARIS. Update all recommended vaccinations prior to initiation of therapy with ILARIS. In addition, because ILARIS may interfere with normal immune response to new antigens, vaccinations may not be effective in patients receiving ILARIS.

Canakinumab, like other monoclonal antibodies, is actively transported across the placenta mainly during the third trimester of pregnancy and may cause immunosuppression in the *in utero* exposed infant. The risks and benefits should be considered prior to administering live vaccines to infants who were exposed to ILARIS *in utero* for at least 4 to 12 months following the mother's last dose of ILARIS.

Macrophage Activation Syndrome

Macrophage Activation Syndrome (MAS) is a known, life-threatening disorder that may develop in patients with rheumatic conditions, in particular Still's disease, and should be aggressively treated. Physicians should be attentive to symptoms of infection or worsening of Still's disease as these are known triggers for MAS. Eleven cases of MAS were observed in 201 SJIA patients treated with canakinumab in clinical trials. Based on the clinical trial experience, ILARIS does not appear to increase the incidence of MAS in Still's disease patients, but no definitive conclusion can be made.

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CLINICAL STUDIES FOR TREATMENT OF GOUT FLARES[1] (cont)

Gout Flares Efficacy on Pain

In all studies (Study 1, 2, and 3), pain intensity of the most affected joint (0-100 mm VAS) at 72 hours post-dose was consistently lower for patients treated with ILARIS compared with triamcinolone acetonide in the subpopulation of patients unable to use NSAIDs and colchicine. This benefit of ILARIS on pain intensity was comparable to the overall patient populations, ie, patients unable to use NSAIDs and/or colchicine in all three studies.

Pain Intensity of the Most Affected Joint at 72-h post treatment					STUDY 1
POPULATION	ILARIS 150 mg		Triamcinolone acetonide 40 mg		Difference (95% CI)* in Pain Intensity 72 Hours Post-dose VAS (0-100 mm): ILARIS vs Triamcinolone acetonide
	N	Mean (SE)*	N	Mean (SE)*	
Patients unable to use NSAIDs and colchicine	22	21.4 (6.05)	37	38.4 (4.65)	–17.0 mm (–32.3, –1.6)
Patients unable to use NSAIDs and/or colchicine	113	27.9 (2.42)	115	39.7 (2.40)	–11.8 mm (–18.5, –5.1)

*Adjusted mean, standard error for mean and difference between treatment groups are estimated based on analysis of covariance (ANCOVA) model with treatment, baseline VAS score and baseline BMI as covariates. For Study 3, the use of urate lowering therapy (Yes/No) at baseline is also included in the model as additional covariate.
N=number of patients randomized and received at least one dose of study treatment.

IMPORTANT SAFETY INFORMATION (cont)

ADVERSE REACTIONS

Serious adverse reactions reported with ILARIS in the CAPS clinical trials included infections and vertigo. The most common adverse reactions greater than 10% associated with ILARIS treatment in CAPS patients were nasopharyngitis, diarrhea, influenza, rhinitis, headache, nausea, bronchitis, gastroenteritis, pharyngitis, weight increased, musculoskeletal pain, and vertigo.

The most common adverse reactions greater than or equal to 10% reported by patients with TRAPS, HIDS/MKD, and FMF treated with ILARIS were injection site reactions and nasopharyngitis.

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ILARIS® (canakinumab) 150 mg subcutaneous injection

CLINICAL STUDIES FOR TREATMENT OF GOUT FLARES[1] (cont)

Pain Intensity of the Most Affected Joint at 72-h post treatment				STUDY 2
POPULATION	**ILARIS 150 mg**		**Triamcinolone acetonide 40 mg**		**Difference (95% CI)* in Pain Intensity 72 Hours Post-dose VAS (0-100 mm): ILARIS vs Triamcinolone acetonide**
	N	**Mean (SE)***	**N**	**Mean (SE)***	
Patients unable to use NSAIDs and colchicine	53	24.1 (3.32)	44	33.1 (3.65)	–9.1 mm (–18.9, 0.8)
Patients unable to use NSAIDs and/or colchicine	112	21.9 (2.31)	114	31.7 (2.29)	–9.8 mm (–16.2, –3.4)

*Adjusted mean, standard error for mean and difference between treatment groups are estimated based on analysis of covariance (ANCOVA) model with treatment, baseline VAS score and baseline BMI as covariates. For Study 3, the use of urate lowering therapy (Yes/No) at baseline is also included in the model as additional covariate.
N=number of patients randomized and received at least one dose of study treatment.

IMPORTANT SAFETY INFORMATION (cont)
ADVERSE REACTIONS

The most common adverse drug reactions greater than 10% associated with ILARIS treatment in SJIA patients were infections (nasopharyngitis and upper respiratory tract infections), abdominal pain, and injection site reactions.

The most common adverse reactions greater than 2% reported by adult patients with gout flares treated with ILARIS in clinical trials were nasopharyngitis, upper respiratory tract infections, urinary tract infections, hypertriglyceridemia, and back pain.

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CLINICAL STUDIES FOR TREATMENT OF GOUT FLARES[1] (cont)

Pain Intensity of the Most Affected Joint at 72-h post treatment					STUDY 3
POPULATION	ILARIS 150 mg		Triamcinolone acetonide 40 mg		Difference (95% CI)* in Pain Intensity 72 Hours Post-dose VAS (0-100 mm): ILARIS vs Triamcinolone acetonide
	N	Mean (SE)*	N	Mean (SE)*	
Patients unable to use NSAIDs and colchicine	62	20.8 (3.11)	51	40.3 (3.42)	–19.5 mm (–28.6, –10.3)
	60†	18.5 (3.16)			–21.8 mm (–31.0, –12.6)
Patients unable to use NSAIDs and/or colchicine	129	19.7 (2.05)	129	32.4 (2.05)	–12.7 mm (–18.4, –7.0)
	131†	17.0 (2.04)			–15.4 mm (–21.1, –9.8)

*Adjusted mean, standard error for mean and difference between treatment groups are estimated based on analysis of covariance (ANCOVA) model with treatment, baseline VAS score and baseline BMI as covariates. For Study 3, the use of urate lowering therapy (Yes/No) at baseline is also included in the model as additional covariate.
†Prefilled Syringe (PFS) formulation.
N=number of patients randomized and received at least one dose of study treatment.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ILARIS is contraindicated in patients with confirmed hypersensitivity to canakinumab or to any of the excipients.

WARNINGS AND PRECAUTIONS

Serious Infections

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Infections, predominantly of the upper respiratory tract, in some instances serious, have been reported with ILARIS. Generally, the observed infections responded to standard therapy. Isolated cases of unusual or opportunistic infections (eg, aspergillosis, atypical mycobacterial infections, cytomegalovirus, herpes zoster) were reported during ILARIS treatment.

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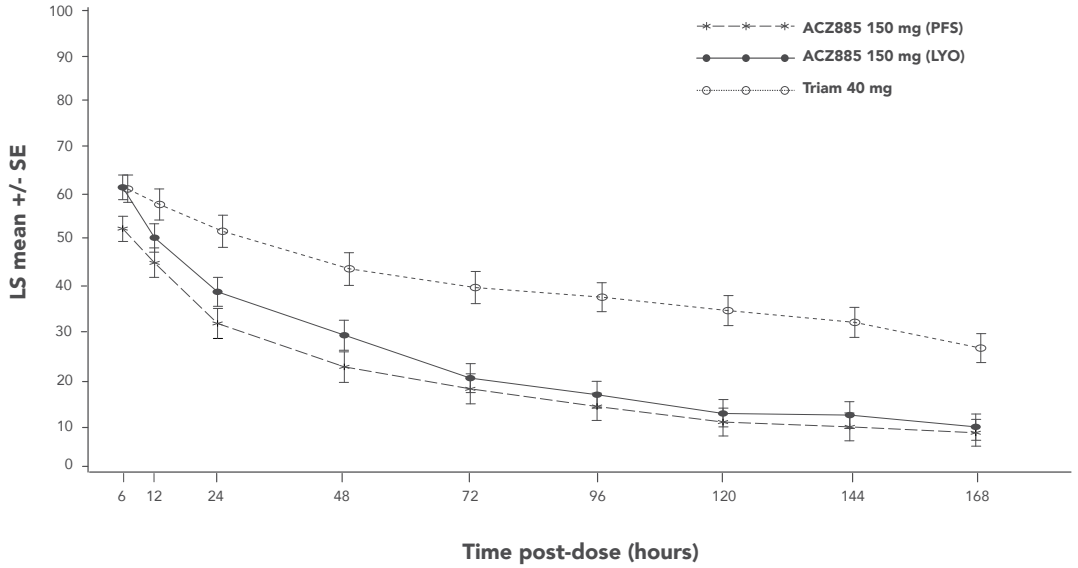
CLINICAL STUDIES FOR TREATMENT OF GOUT FLARES[1] (cont)

Pain Intensity Over Time in the Subpopulation of Patients Unable to Use NSAIDs and Colchicine (Study 3, ILARIS [ACZ885] 150 mg)



IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS

Serious Infections (cont)

A causal relationship of ILARIS to these events cannot be excluded. In clinical trials, ILARIS has not been administered concomitantly with tumor necrosis factor (TNF) inhibitors. An increased incidence of serious infections has been associated with administration of another interleukin-1 (IL-1) blocker in combination with TNF inhibitors. Coadministration of ILARIS with TNF inhibitors is not recommended because this may increase the risk of serious infections.

Drugs that affect the immune system by blocking TNF have been associated with an increased risk of new tuberculosis (TB) and reactivation of latent TB. It is possible that use of IL-1 inhibitors, such as ILARIS, increases the risk of reactivation of TB or of opportunistic infections.

Prior to initiating immunomodulatory therapies, including ILARIS, evaluate patients for active and latent TB infection. Appropriate screening tests should be performed in all patients. ILARIS has not been studied in patients with a positive TB screen, and the safety of ILARIS in individuals with latent TB infection is unknown.

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CLINICAL STUDIES FOR TREATMENT OF GOUT FLARES[1] (cont)

Time to New Flare

In the subpopulation of patients in Studies 1, 2 and 3 unable to use NSAIDs and colchicine, time to new flare over 12 weeks from randomization showed a reduction in the risk of a new flare when treated with ILARIS compared with triamcinolone acetonide 40 mg. This risk reduction for a new flare after ILARIS treatment versus triamcinolone acetonide was comparable to the overall patient population over 12 weeks in all 3 studies.

Time to New Flare Over the 12 Weeks From Randomization					STUDY 1
POPULATION	**ILARIS 150 mg**		**Triamcinolone acetonide 40 mg**		**Risk reduction for a new flare ILARIS vs Triamcinolone acetonide Hazard ratio* (95% CI)**
	N	**Flare rate†(n)**	**N**	**Flare rate†(n)**	
Patients unable to use NSAIDs and colchicine	22	14% (3)	38	46% (17)	75% 0.25 (0.07, 0.85)
Patients unable to use NSAIDs and/or colchicine	113	19% (21)	115	37% (40)	55 % 0.45 (0.26 to 0.76)

*Prefilled Syringe (PFS) formulation.
†Flare rates up to 12 weeks are estimated using Kaplan-Meier method; n=number of patients with new flares. The risk reduction and hazard ratio between treatment groups are estimated using Cox proportional hazard (Cox-PH) model with treatment and baseline BMI as covariates. For Study 3, the use of urate lowering therapy (Yes/No) at baseline is also included in the model as additional covariate.
N=number of patients randomized and received at least one dose of study treatment.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS

Serious Infections (cont)

Treat patients testing positive in TB screening according to standard medical practice prior to therapy with ILARIS. Instruct patients to seek medical advice if signs, symptoms, or high risk exposure suggestive of TB (eg, persistent cough, weight loss, subfebrile temperature) appear during or after ILARIS therapy. Healthcare providers should follow current CDC guidelines both to evaluate for and to treat possible latent TB infections before initiating therapy with ILARIS.

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CLINICAL STUDIES FOR TREATMENT OF GOUT FLARES[1] (cont)

Time to New Flare Over the 12 Weeks From Randomization					STUDY 2
POPULATION	ILARIS 150 mg		Triamcinolone acetonide 40 mg		Risk reduction for a new flare ILARIS vs Triamcinolone acetonide Hazard ratio* (95% CI)
	N	Flare rate†(n)	N	Flare rate†(n)	
Patients unable to use NSAIDs and colchicine	54	16% (8)	46	43% (19)	72% 0.28 (0.12, 0.65)
Patients unable to use NSAIDs and/or colchicine	112	14% (15)	114	38% (42)	68% 0.32 (0.18 to 0.58)

*Prefilled Syringe (PFS) formulation.
†Flare rates up to 12 weeks are estimated using Kaplan-Meier method; n=number of patients with new flares. The risk reduction and hazard ratio between treatment groups are estimated using Cox proportional hazard (Cox-PH) model with treatment and baseline BMI as covariates. For Study 3, the use of urate lowering therapy (Yes/No) at baseline is also included in the model as additional covariate.
N=number of patients randomized and received at least one dose of study treatment.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS

Immunosuppression

The impact of treatment with anti-IL-1 therapy on the development of malignancies is not known. However, treatment with immunosuppressants, including ILARIS, may result in an increase in the risk of malignancies.

Hypersensitivity Reactions

Hypersensitivity reactions have been reported with ILARIS. During clinical trials, no anaphylactic reactions attributable to treatment with canakinumab have been reported. It should be recognized that symptoms of the underlying disease being treated may be similar to symptoms of hypersensitivity. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), characterized by serious skin eruptions, has been reported in patients with autoinflammatory conditions treated with ILARIS. If a severe hypersensitivity reaction occurs, immediately discontinue ILARIS; treat promptly and monitor until signs and symptoms resolve.

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CLINICAL STUDIES FOR TREATMENT OF GOUT FLARES[1] (cont)

Time to New Flare Over the 12 Weeks From Randomization					STUDY 3
POPULATION	ILARIS 150 mg		Triamcinolone acetonide 40 mg		Risk reduction for a new flare ILARIS vs Triamcinolone acetonide Hazard ratio* (95% CI)
	N	Flare rate†(n)	N	Flare rate†(n)	
Patients unable to use NSAIDs and colchicine	62	10% (6)	51	32% (15)	71% 0.29 (0.11, 0.74)
	60*	3% (2)			91% 0.09 (0.02, 0.41)
Patients unable to use NSAIDs and/or colchicine	129	10% (12)	129	44% (52)	82% 0.18 (0.10, 0.34)
	131*	9% (12)			83% 0.17 (0.09, 0.33)

*Prefilled Syringe (PFS) formulation.
†Flare rates up to 12 weeks are estimated using Kaplan-Meier method; n=number of patients with new flares. The risk reduction and hazard ratio between treatment groups are estimated using Cox proportional hazard (Cox-PH) model with treatment and baseline BMI as covariates. For Study 3, the use of urate lowering therapy (Yes/No) at baseline is also included in the model as additional covariate.
N=number of patients randomized and received at least one dose of study treatment.

IMPORTANT SAFETY INFORMATION (cont)
WARNINGS AND PRECAUTIONS

Immunizations

Avoid administration of live vaccines concurrently with ILARIS. Update all recommended vaccinations prior to initiation of therapy with ILARIS. In addition, because ILARIS may interfere with normal immune response to new antigens, vaccinations may not be effective in patients receiving ILARIS.

Canakinumab, like other monoclonal antibodies, is actively transported across the placenta mainly during the third trimester of pregnancy and may cause immunosuppression in the *in utero* exposed infant. The risks and benefits should be considered prior to administering live vaccines to infants who were exposed to ILARIS *in utero* for at least 4 to 12 months following the mother's last dose of ILARIS.

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ADVERSE REACTIONS FROM CLINICAL TRIALS FOR TREATMENT OF GOUT FLARES[1]

The safety of ILARIS compared to triamcinolone acetonide in patients with gout flares was assessed in four 12-week, randomized, double-blind, active-controlled phase 3 studies and in two 12-week, double-blind, active-controlled extension studies. In the ILARIS treatment groups, 512 patients were treated up to 12 weeks and 165 of these patients up to 24 weeks. In the triamcinolone acetonide groups, 381 patients were treated up to 12 weeks and 152 of these patients up to 24 weeks. Patients received a single dose of ILARIS 150 mg (n=467) via subcutaneous injection or triamcinolone acetonide 40 mg (n=279) via intramuscular injection. Upon a new flare, 85 and 152 patients received at least one additional dose of ILARIS and triamcinolone acetonide, respectively.

The most commonly reported adverse drug reactions were infections and infestations. The most common infections reported in more than 2% of patients in the ILARIS treatment groups were nasopharyngitis, upper respiratory tract infections, and urinary tract infections. The trends observed in all infections are aligned with the overall known safety profile of canakinumab. Serious adverse events were reported in 1.4% of the ILARIS-treated patients, all of which were single events. No serious adverse events were reported in the triamcinolone acetonide-treated group.

Of the ILARIS-treated patients, 17% were 65 years of age and older, including 3% who were 75 years of age and older. No new safety findings were observed between these patients compared to patients under 65 years of age.

Tabulated Summary of Adverse Drug Reactions From Pivotal Gout Flare Clinical Trials

System Organ Class Adverse reaction	**ILARIS 150 mg** *N=552 n (%) (IR-w)	**Triamcinolone acetonide 40 mg** *N=431 n (%) (IR-w)
Infections and infestations		
All infections (eg, nasopharyngitis, upper respiratory tract infection, urinary tract infections)	90 (16.3%) (59.0)	40 (9.3%) (32.1)
Investigations		
Blood triglycerides increased	7 (1.3%) (3.8)	2 (0.5%) (1.3)
Platelet count decreased	4 (0.7%) (2.5)	1 (0.2%) (1.0)

*N=Number of patients at study entry.
IR-w=Study size weighted incidence rate (ie, number of patients with an event per 100 patient-years).

IMPORTANT SAFETY INFORMATION (cont)
WARNINGS AND PRECAUTIONS

Macrophage Activation Syndrome

Macrophage Activation Syndrome (MAS) is a known, life-threatening disorder that may develop in patients with rheumatic conditions, in particular Still's disease, and should be aggressively treated. Physicians should be attentive to symptoms of infection or worsening of Still's disease as these are known triggers for MAS. Eleven cases of MAS were observed in 201 SJIA patients treated with canakinumab in clinical trials. Based on the clinical trial experience, ILARIS does not appear to increase the incidence of MAS in Still's disease patients, but no definitive conclusion can be made.

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ADVERSE REACTIONS FROM CLINICAL TRIALS FOR TREATMENT OF GOUT FLARES[1] (cont)

Tabulated Summary of Adverse Drug Reactions From Pivotal Gout Flare Clinical Trials (cont)

System Organ Class Adverse reaction	**ILARIS 150 mg** *N=552 n (%) (IR-w)	**Triamcinolone acetonide 40 mg** *N=431 n (%) (IR-w)
Metabolism and nutrition disorders		
Hypertriglyceridemia	15 (2.7%) (9.5)	4 (0.9%) (3)
Musculoskeletal and connective tissue disorders		
Back pain	17 (3.1%) (10.9)	7 (1.6%) (6.2)
Nervous system disorders		
Dizziness	9 (1.6%) (5.8)	2 (0.5%) (1.7)

*N=Number of patients at study entry.
IR-w=Study size weighted incidence rate (ie, number of patients with an event per 100 patient-years).

IMPORTANT SAFETY INFORMATION (cont)
ADVERSE REACTIONS

Serious adverse reactions reported with ILARIS in the CAPS clinical trials included infections and vertigo. The most common adverse reactions greater than 10% associated with ILARIS treatment in CAPS patients were nasopharyngitis, diarrhea, influenza, rhinitis, headache, nausea, bronchitis, gastroenteritis, pharyngitis, weight increased, musculoskeletal pain, and vertigo.

The most common adverse reactions greater than or equal to 10% reported by patients with TRAPS, HIDS/MKD, and FMF treated with ILARIS were injection site reactions and nasopharyngitis.

The most common adverse drug reactions greater than 10% associated with ILARIS treatment in SJIA patients were infections (nasopharyngitis and upper respiratory tract infections), abdominal pain, and injection site reactions.

The most common adverse reactions greater than 2% reported by adult patients with gout flares treated with ILARIS in clinical trials were nasopharyngitis, upper respiratory tract infections, urinary tract infections, hypertriglyceridemia, and back pain.

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DOSAGE AND ADMINISTRATION[1]

Recommended Dosage for Gout Flares

The recommended dose of ILARIS for adult patients with a gout flare is 150 mg administered subcutaneously. In patients who require re-treatment, there should be an interval of at least 12 weeks before a new dose of ILARIS may be administered.

ILARIS IS FOR SUBCUTANEOUS USE ONLY

Administration Instructions for ILARIS Injection

1. ILARIS injection has a concentration of 150 mg/mL. Do not shake. The solution should be essentially free from particulates, clear to opalescent, colorless to slightly brownish-yellow tint. If the solution has a distinctly brown discoloration, is highly opalescent or contains visible particles, do not use.
2. Using a sterile 1-mL syringe and 18-gauge x 2" needle, carefully withdraw the required volume depending on the dose to be administered and subcutaneously inject using a 27-gauge x 0.5" needle.

Avoid injection into scar tissue as this may result in insufficient exposure to ILARIS.

Discard unused product or waste material in accordance with the local requirements.

Dosage Forms and Strengths

Injection: 150 mg/mL, clear to slightly opalescent, colorless to a slightly brownish yellow tint solution, in single-dose vials.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ILARIS is contraindicated in patients with confirmed hypersensitivity to canakinumab or to any of the excipients.

WARNINGS AND PRECAUTIONS

Serious Infections

ILARIS has been associated with an increased risk of serious infections. Exercise caution when administering ILARIS to patients with infections, a history of recurring infections or underlying conditions, which may predispose them to infections. Avoid administering ILARIS to patients during an active infection requiring medical intervention. Discontinue ILARIS if a patient develops a serious infection.

Please see Important Safety Information throughout brochure and full Prescribing Information, including Medication Guide, for ILARIS.

ILARIS® (canakinumab) 150 mg subcutaneous injection

OVERVIEW OF ILARIS COMPANION

ILARIS START FORM
Physician submits form to initiate treatment and patient support services.

BENEFITS INVESTIGATION*
Verifies health care plan benefits and provides reimbursement policies for ILARIS.

COVERAGE REVIEW AND SUPPORT
Identifies financial support programs for uninsured and underinsured patients.

PRIOR AUTHORIZATION (PA) SUPPORT†
Assists in identifying plan-specific PA criteria, if required.

APPEALS SUPPORT†
Provides support with insurance appeals.

HIGH PA APPROVAL RATE	ILARIS SHIPMENT TIME
≈90% of PA requests are approved[2]	12 days is the median time to ship ILARIS to patients[2]

Program services are available after the clinical decision to prescribe ILARIS has been made.

*Allows patients to learn about the coverage and cost of ILARIS.

†Information provided in support of a PA must be based on the physician's clinical judgment and forms must be completed by the physician/office staff.

‡Limitations apply. See Program Terms and Conditions on the ILARIS Start Form available at www.ilarishcp.com/access. This offer is not valid under Medicare, Medicaid, or any other federal or state program. Novartis reserves the right to rescind, revoke, or amend this program without notice.

CO-PAY SAVINGS OFFER‡
Designed to make ILARIS more affordable for commercially insured patients.

- Eligible patients pay no more than $30 per month, subject to annual cap
- Patients who are insured through federal or state programs are not eligible

FIRST DOSE PROGRAM‡
- If a payer approval decision is delayed, physicians will be contacted to discuss program enrollment for the patient
- Ships the initial dose of ILARIS to eligible patients free of charge if a payer approval is not received within 2 weeks

SPECIALTY PHARMACY OUTREACH
Works with a patient's specialty pharmacy on patient follow-up.

PRODUCT DELIVERY SUPPORT
Works with a health care plan's preferred specialty pharmacy to support coordination and delivery of ILARIS to the patient's home or physician's office.

HOME HEALTH NURSE SERVICE
Patients can have their injections administered in their homes or at a location other than the physician's office.

- Available in all 50 US states and Puerto Rico
- Requesting physician will receive a visit confirmation

Please see Important Safety Information throughout brochure and full Prescribing Information, including Medication Guide, for ILARIS.

ILARIS® (canakinumab) 150 mg subcutaneous injection

TREATMENT BEGINS WITH THE ILARIS START FORM

A missing patient signature will delay the start of program services. If patients are unavailable to sign the Start Form, they can provide consent at www.hipaaconsent.com.

ILARIS companion
Dedicated and dependable support

Submit a Start Form in 2 Steps

1. Download and fill out the Start Form, available at www.ilarishcp.com/access or from your Account Manager or Access & Reimbursement Manager

2. Print and fax the completed Start Form, signed by you AND your patient, to 1-866-972-8316

Purpose of the Start Form

- Enrolls the patient in ILARIS Companion
- Serves as the prescription for treatment with ILARIS and provides the option for enrollment into select services
- Identifies patient eligibility for patient assistance programs to reduce out-of-pocket costs

Required Information for the Start Form

- Physician AND patient signatures
- ICD-10-CM code
- Number of ILARIS vials
- Number of refills
- Patient's insurance information
- Dosage and administration instructions
- Place of administration (at home or at a physician's office)

All sections of this form must be completed by the physician, patient, and/or appropriate office staff member only.

If you have questions about services, contact a program representative at **1-866-972-8315** Monday to Friday, **9 AM to 6 PM ET**

References: 1. Ilaris. Prescribing information. Novartis Pharmaceuticals Corp. **2.** Data on file. ILARIS Companion CRM Statistics Updates 2023. Novartis Pharmaceuticals Corporation; 2023.

Please see Important Safety Information throughout brochure and full Prescribing Information, including Medication Guide, for ILARIS.

NOVARTIS

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ILARIS® (canakinumab) 150 mg subcutaneous injection