A CHANCE AT RELIEF ISN'T LUCK. **IT'S ILARIS®.**

With ILARIS, relief from periodic fever syndromes may be within reach.

ILARIS is indicated for 8 autoinflammatory diseases across Still's disease, periodic fever syndromes (PFS), and gout flares[1]

- **Still's disease:** SJIA and AOSD
- **PFS:** FMF, HIDS/MKD, TRAPS, and CAPS (FCAS and MWS)

Not an actual patient. Individual results will vary.

AOSD, adult-onset Still's disease; CAPS, cryopyrin-associated periodic syndromes; FCAS, familial cold autoinflammatory syndrome; FMF, familial Mediterranean fever; HIDS, hyperimmunoglobulin D syndrome; MKD, mevalonate kinase deficiency; MWS, Muckle-Wells syndrome; SJIA, systemic juvenile idiopathic arthritis; TRAPS, tumor necrosis factor receptor–associated periodic syndrome.

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.

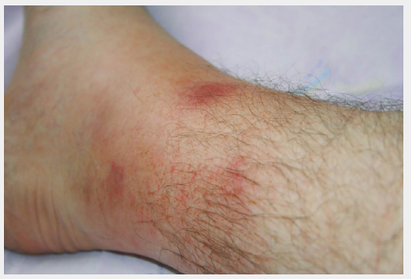
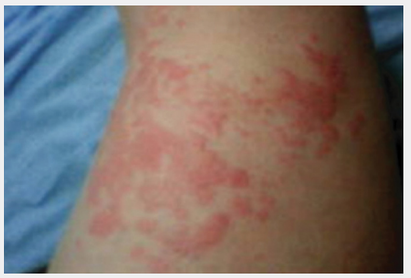
Please see additional Important Safety Information throughout and full Prescribing Information, including Medication Guide, for ILARIS.

ILARIS® (canakinumab)
150 mg subcutaneous injection

Periodic fever syndromes are characterized by[2,3]:

- Fever with temperatures peaking at >39 °C (>102.2 °F)
- Rash in varying forms
- Systemic inflammation often with arthralgia/arthritis
- Elevated inflammatory markers

FMF[2,4-6]	
Predominant ethnic distribution	Turkish, Armenian, Arab, Jewish, Italian
Worldwide prevalence or number of cases	1 to 5 in 10,000
Typical age at onset	<20 years
Duration of attacks	≤3 days
Frequency of attacks	Irregular; once per week to once every 5 to 10 years
Gene mutation	*MEFV*
Inheritance	Autosomal recessive

FMF[2-4,6,7]	
Cutaneous findings	  • Erysipelas-like erythema • Characterized by red, warm, and swollen areas • Lesions are tender to the touch, can be 10 cm to 15 cm in diameter, and usually occur below the knee on the anterior leg or top of foot
Other select clinical features	• Abdominal pain • Chest pain • Arthritis/monoarthritis
High serology	Increase in CRP, ESR, and SAA

Rash images credits: Top Image: Reproduced with permission from Emedmd.com (FMF).

Bottom Image: Reproduced with permission from Hayato Tsuruma et al. An adult case of atypical familial Mediterranean fever (pyrin-associated autoinflammatory disease) similar to adult-onset Still's disease, *Clin Case Rep.* 2019;7(4):2. Figure 1A.

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; SAA, serum amyloid A.

IMPORTANT SAFETY INFORMATION
WARNINGS AND PRECAUTIONS

Serious Infections

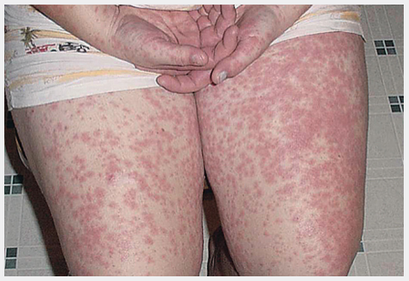
ILARIS has been associated with an increased risk of serious infections. Exercise caution when administering ILARIS to patients with infections, a history of recurring infections or underlying conditions, which may predispose them to infections. Avoid administering ILARIS to patients during an active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

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

ILARIS® (canakinumab) 150 mg subcutaneous injection

Periodic fever syndromes (cont)

HIDS/MKD[2,4,8,9]	
Predominant ethnic distribution	Dutch or Northern European
Worldwide prevalence or number of cases	>180
Typical age at onset	<1 year
Duration of attacks	3 to 7 days
Frequency of attacks	Irregular; 2- to 8-week intervals
Gene mutation	*MVK*
Inheritance	Autosomal recessive

HIDS/MKD[2-4]	
Cutaneous findings	 • Diffuse maculopapular eruption extending to the palms and soles, or nodular, urticarial, or morbilliform • Erythematous macules that are sometimes painful can occur
Other select clinical features	• Abdominal pain • Lymphadenopathy • Aphthous ulcers
High serology	Increase in CRP, ESR, IgD, and SAA

Rash image credit: Reprinted from *Textbook of Pediatric Rheumatology*, 7th ed, Petty RE et al. Periodic Fever Syndromes and Other Inherited Autoinflammatory Diseases, page 617, 2016, with permission from Elsevier.

IMPORTANT SAFETY INFORMATION (cont)
WARNINGS AND PRECAUTIONS (cont)

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.

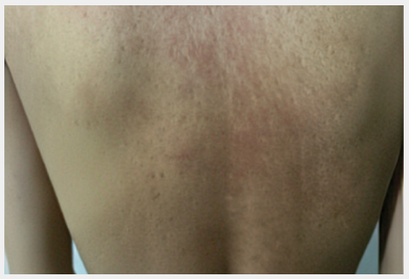
IgD, immunoglobulin D.

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

ILARIS® (canakinumab) 150 mg subcutaneous injection

Periodic fever syndromes (cont)

TRAPS[2-4,10-13]	
Predominant ethnic distribution	All ethnicities
Worldwide prevalence or number of cases	>1000
Typical age at onset	Varies; <3 years to <20 years
Duration of attacks	7 to 28 days; nearly continuous in one-third of patients
Frequency of attacks	Irregular; 5 weeks to months or years
Gene mutation	TNFRSF1A
Inheritance	Autosomal dominant

TRAPS[2-5,14]	
Cutaneous findings	 • Erythematous, migratory patch • Often overlies an area of myalgia and migrates together in a centrifugal pattern • Often found on the torso or extremity
Other select clinical features	• Abdominal pain • Musculoskeletal pain • Eye manifestations, such as periorbital edema
High serology	Increase in CRP, ESR, and SAA

Rash image credit: Reproduced with permission from Kosar Asnaashari and Nima Rezaei, Chapter 28 - Rheumatologic manifestations of autoinflammatory diseases, 2023, page 575, figure 3.

IMPORTANT SAFETY INFORMATION (cont)
WARNINGS AND PRECAUTIONS (cont)

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.

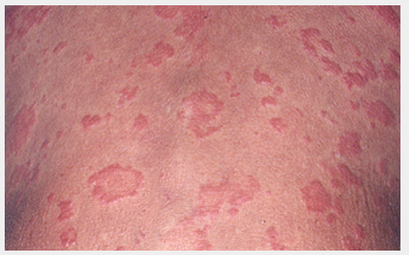
Please see additional Important Safety Information throughout and full Prescribing Information, including Medication Guide, for ILARIS.

ILARIS® (canakinumab) 150 mg subcutaneous injection

Periodic fever syndromes (cont)

	CAPS: FCAS	CAPS: MWS[2,4,5]
Predominant ethnic distribution	Mostly European	
Worldwide prevalence or number of cases	<1 in 1,000,000*	
Typical age at onset	<1 year	<20 years
Duration of attacks	12 to 24 hours	2 to 3 days
Frequency of attacks	Variable; triggered by generalized cold exposure	Variable; triggered by cold, stress, and exercise
Gene mutation	NLRP3	
Inheritance	Autosomal dominant	

*Prevalence includes patients with FCAS, MWS, and neonatal-onset multisystem inflammatory disease.

	CAPS: FCAS	CAPS: MWS[2-4,14,15]
Cutaneous findings	 • Urticaria-like appearance • Typically raised, erythematous, maculopapular, usually nonpruritic • Described by patients as feeling painful, tight, and/or warm • Severity worsening in the evening • Usually appears on the trunk and limb with individual migratory lesions	
Other select clinical features	• Headache • Arthralgia • Fatigue • Myalgia • Conjunctivitis	• Headache • Arthralgia • Fatigue • Conjunctivitis
High serology	Increase in CRP, ESR, and SAA	

Rash image credit: Reprinted from *Textbook of Pediatric Rheumatology*, 7th ed, Petty RE et al. Periodic Fever Syndromes and Other Inherited Autoinflammatory Diseases, page 617, 2016, with permission from Elsevier.

IMPORTANT SAFETY INFORMATION (cont)
WARNINGS AND PRECAUTIONS (cont)

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.

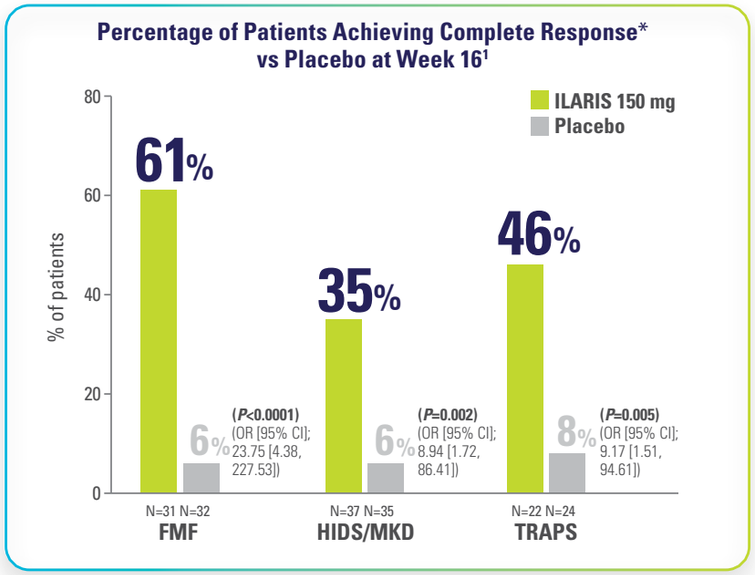
Hypersensitivity Reactions

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.

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

ILARIS® (canakinumab) 150 mg subcutaneous injection

Rapid resolution of index flare at Day 15—with no new flares through Week 16—was achieved by significantly more patients receiving ILARIS[1]



***Complete response defined as resolution of index flare (PGA <2 and CRP ≤10 mg/L or a ≥70% reduction from baseline) at Day 15 and no new flare (PGA ≥2 and CRP ≥30 mg/L) throughout the 16-week treatment period.[1]**

- At Day 15, the majority of patients with FMF (81%, n/N=25/31), HIDS/MKD (65%, n/N=24/37), and TRAPS (64%, n/N=14/22) who received ILARIS achieved resolution of index disease flare vs placebo: FMF (31%, n/N=10/32), HIDS/MKD (37%, n/N=13/35), and TRAPS (21%, n/N=5/24)[1]

FMF, TRAPS, and HIDS/MKD Study Design[1]

The efficacy of ILARIS was assessed in patients with PFS across 3 disease cohorts: FMF, HIDS/MKD, and TRAPS. In the 16-week, double-blind, placebo-controlled treatment period, patients were randomized to receive ILARIS 150 mg (2 mg/kg for a body weight ≤40 kg) or placebo every 4 weeks for 16 weeks and were allowed uptitration to ILARIS 300 mg (or 4 mg/kg) every 4 weeks for patients whose disease flare did not resolve or who had persistent disease or active treatment.[1]

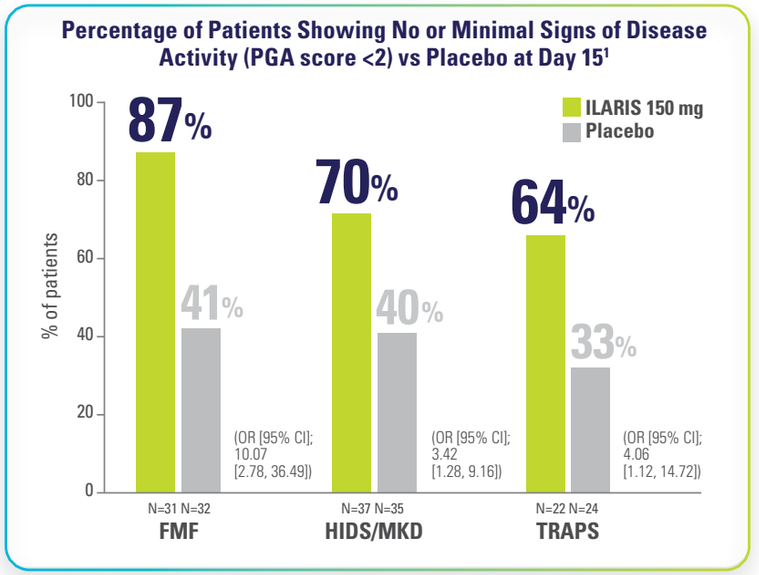
The primary endpoint was the proportion of complete responders within each cohort as defined by patients who had resolution of their index disease flare at Day 15 and did not experience a new disease flare during the remainder of the 16-week treatment period.[1]

A 5-point PGA scale was used by physicians to assess overall disease severity, where 0=no disease-associated signs and symptoms, 1=minimal, 2=mild, 3=moderate, and 4=severe. The key signs and symptoms assessed in the PGA for each condition were the following: FMF: abdominal pain, skin rash, chest pain, arthralgia/arthritis; HIDS/MKD: abdominal pain, lymphadenopathy, aphthous ulcers; TRAPS: abdominal pain, skin rash, musculoskeletal pain, eye manifestations.[1,16]

PGA, Physician's Global Assessment.

In the same study,

After the initial dose, at Day 15 ILARIS improved disease activity as measured by PGA[1]



PGA scores at baseline[17]:

- **10% of patients with FMF in the ILARIS group had mild disease vs 19% in the placebo group[17]**
  - In the ILARIS group, 55% had moderate disease and 36% had severe disease compared with 59% and 22%, respectively, in the placebo group
- **27% of patients with HIDS/MKD in the ILARIS group had mild disease vs 20% in the placebo group[17]**
  - In the ILARIS group, 60% had moderate disease and 14% had severe disease compared with 60% and 20%, respectively, in the placebo group
- **41% of patients with TRAPS in the ILARIS group had mild disease vs 46% in the placebo group[17]**
  - In the ILARIS group, 50% had moderate disease and 9% had severe disease compared with 46% and 8%, respectively, in the placebo group

IMPORTANT SAFETY INFORMATION (cont)
WARNINGS AND PRECAUTIONS (cont)

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.

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

ILARIS® (canakinumab) 150 mg subcutaneous injection

After the initial dose, at Day 15 ILARIS improved disease activity as measured by CRP levels[1]

At Day 15, CRP ≤10 mg/L achieved by:

FMF
90% of patients receiving ILARIS (n/N=28/31) vs **28% receiving placebo** (n/N=9/32)

HIDS/MKD
68% of patients receiving ILARIS (n/N=25/37) vs **26% receiving placebo** (n/N=9/35)

TRAPS
59% of patients receiving ILARIS (n/N=13/22) vs **33% receiving placebo** (n/N=8/24)

CRP treatment comparisons (OR [95% CI]): FMF (22.51 [5.41, 93.62]), HIDS/MKD (6.05 [2.14, 17.12]), TRAPS (3.88 [1.05, 14.26]).[1]

IMPORTANT SAFETY INFORMATION (cont)
WARNINGS AND PRECAUTIONS (cont)

Immunizations (cont)

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.

IMPORTANT SAFETY INFORMATION (cont)
WARNINGS AND PRECAUTIONS (cont)

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.

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

ILARIS® (canakinumab) 150 mg subcutaneous injection

In Part 1:

The majority of patients achieved complete clinical response at Weeks 1 and 8 after the first dose of ILARIS[1,18]

Percentage of Patients Achieving Complete Clinical Response With ILARIS[1,18]:

WEEK 1	WEEK 8
71%	97%
(n/N=25/35)	(n/N=34/35)

Complete clinical response was defined as meeting all of the following criteria[18]:

- Physician's assessment of disease activity ≤ minimal (rated on a 5-point scale consisting of absent, minimal, mild, moderate, and severe)
- Assessment of skin disease ≤ minimal (rated on a 5-point scale consisting of absent, minimal, mild, moderate, and severe)
- Normal serum values of CRP and SAA (<10 mg/L)

Assessment of disease activity included a composite of the following symptoms: urticarial skin rash, headache/migraine, fatigue/malaise, conjunctivitis, arthralgia, myalgia, and other symptoms related or unrelated to CAPS.

CAPS Study Design[1,18,19]

A 3-part study in patients with CAPS (MWS) treated with a subcutaneous dose of ILARIS 150 mg (in patients weighing >40 kg) or ILARIS 2 mg/kg (in patients weighing ≥15 kg and ≤40 kg) every 8 weeks.

PART 1 An 8-week open-label treatment period in which 35 patients were treated with a single injection of ILARIS 150 mg.

PART 2 A double-blind, randomized withdrawal phase in which patients who achieved a complete clinical response and did not relapse by Week 8 in Part 1 were randomized to ILARIS 150 mg or 2 mg/kg in patients weighing ≥15 kg and ≤40 kg (n=15) or placebo (n=16) every 8 weeks for 24 weeks. During Part 2, patients continued with blinded treatment unless a relapse occurred to prompt early entry into Part 3.

PART 3 An open-label treatment period in which patients received ILARIS 150 mg (n=31) every 8 weeks. Patients entered Part 3 at the end of Part 2 or at the time of relapse, whichever occurred first. For patients who completed Part 2 without disease flare, Part 3 had a duration of 16 weeks. For patients who had disease relapse in Part 2, Part 3 had a duration of up to 40 weeks. The total study duration was 48 weeks.

The primary endpoint was the proportion of patients experiencing relapse in Part 2.

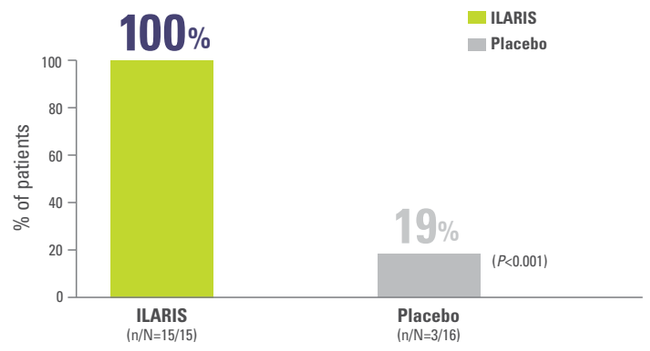
IMPORTANT SAFETY INFORMATION (cont)
ADVERSE REACTIONS

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.

In Part 2:

After 3 doses* of ILARIS, 100% of patients remained flare free through 24 weeks[18†]

Percentage of Patients Who Were Flare Free vs Placebo at Week 32[18]



None of the patients treated with ILARIS had a disease relapse‡ over 24 weeks[18]

- For patients taking placebo, median time to flare was 100 days

- During the open-label treatment period (Part 3), 97% (n/N=30/31) of patients were without disease relapse[19§]

Physician's Global Assessment of Disease Activity and Assessment of Skin Disease[1,18]:

At the end of Study Part 2

- 93% (n/N=14/15) had no rash and 7% (n/N=1/15) had minimal rash after treatment with ILARIS vs 31% (n/N=5/16) and 19% (n/N=3/16), respectively, with placebo
- 100% (n/N=15/15) had no or minimal disease activity after treatment with ILARIS vs 25% (n/N=4/16) with placebo

At the end of Study Part 3

- 94% (n/N=29/31) had no rash and 6% (n/N=2/31) had minimal rash after treatment with ILARIS
- 97% (n/N=30/31) had no or minimal disease activity after treatment with ILARIS

- Analysis has not been adjusted for multiple comparisons. No conclusions of statistical or clinical significance can be drawn

*For patients with CAPS, ILARIS is dosed once every 8 weeks.[1]

†Ten patients in the placebo group met the criteria for clinical relapse, and 3 patients discontinued Part 2 due to unsatisfactory therapeutic effect.[19]

‡**Disease relapse:** Defined as CRP and/or SAA value >30 mg/L and either a score of mild or worse for physician's assessment of disease activity or a score of minimal or worse for physician's assessment of disease activity and assessment of skin disease.[1]

§Includes all 15 patients randomized to ILARIS in Part 2 and 15 of 16 patients randomized to placebo in Part 2. Disease relapse was defined as CRP and/or SAA value >30 mg/L and either a score of mild or worse for physician's assessment of disease activity or a score of minimal or worse for physician's assessment of disease activity and assessment of skin disease.[1,19]

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

ILARIS® (canakinumab) 150 mg subcutaneous injection

Safety profile of ILARIS from FMF, HIDS/MKD, and TRAPS clinical trials[1]

- In Part 2, 90 patients were initially randomized to ILARIS 150 mg and 91 patients were randomized to placebo every 4 weeks[1]
  - ILARIS group: 55.6% of patients remained on the initial dose through Week 16, with 6.7% receiving an additional ILARIS dose between Day 7 and Day 15
  - Placebo group: 9.9% of patients remained on placebo through Week 16, with 28.6% switching to ILARIS treatment by Day 15
- Overall, there were 58 patients with FMF, 68 patients with HIDS/MKD, and 43 patients with TRAPS in the safety set with a cumulative exposure of 47.61 patient-years. The cumulative exposure in the placebo group was 8.03 patient-years[1]

Most Common Adverse Drug Reactions (≥3%) in Patients Treated With ILARIS[1]

Adverse reactions by preferred term in ≥3% of patients with FMF, HIDS/MKD, and TRAPS	ILARIS %
Injection site reactions	10.1
Infections, including nasopharyngitis	10.7
Upper respiratory tract infection	7.1
Rhinitis	5.3
Gastroenteritis	3.0
Pharyngitis	3.0

- The most common adverse reactions (≥10%) were injection site reactions and nasopharyngitis[1]
- Serious infections (eg, conjunctivitis, pneumonia, pharyngitis, pharyngotonsillitis) were observed in approximately 2.4% (0.03 per 100 patient-days) of patients receiving ILARIS[1]

No new or unexpected safety findings of ILARIS emerged in the PFS clinical trial[1,17]

Among all 3 patient cohorts in the ILARIS group:

- No deaths were reported
- No anti-canakinumab antibodies were detected in any patient
- No patients with FMF, 2 patients with HIDS/MKD, and 1 patient with TRAPS discontinued treatment due to AEs

AE, adverse event.

IMPORTANT SAFETY INFORMATION (cont)
ADVERSE REACTIONS (cont)

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.

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

ILARIS® (canakinumab) 150 mg subcutaneous injection

Safety profile of ILARIS from CAPS clinical trials[1]

Most Common Adverse Drug Reactions (≥10%) in Patients Treated With ILARIS[1]	
Preferred term	**ILARIS** (N=35), n (%)
Number of patients with AEs	35 (100)
Nasopharyngitis	12 (34)
Diarrhea	7 (20)
Influenza	6 (17)
Rhinitis	6 (17)
Nausea	5 (14)
Headache	5 (14)
Bronchitis	4 (11)
Gastroenteritis	4 (11)
Pharyngitis	4 (11)
Weight increased	4 (11)
Musculoskeletal pain	4 (11)
Vertigo	4 (11)

- A total of 9 serious adverse reactions were reported with ILARIS in CAPS clinical trials, including infections and vertigo*
  - 1 patient discontinued treatment due to potential infection
- 9% of patients experienced injection site reactions in Part 1[1]
  - Injection site reactions occurred in 1 patient in each arm (7%) of Part 2 and in 1 patient in Part 3
  - No severe injection site reactions were reported
- Infections, predominantly of the upper respiratory tract, in some instances serious, were reported with ILARIS[1]
  - 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

*These data reflect exposure to ILARIS in 104 adult and pediatric patients with CAPS in placebo-controlled (35 patients) and uncontrolled trials. Sixty-two patients were exposed to ILARIS for at least 6 months, 56 for at least 1 year, and 4 for at least 3 years.[1]

ILARIS dosing

ILARIS Is Given Subcutaneously by a Health Care Professional[1]		
Dosed according to body weight	**Recommended dose**	**Recommended titration**
1x PER MONTH IN STILL'S DISEASE: SJIA and AOSD[1]		
≥7.5 kg	4 mg/kg (with a maximum of 300 mg) every 4 weeks	–
1x PER MONTH IN PFS: FMF, HIDS/MKD, and TRAPS[1]		
≤40 kg	2 mg/kg every 4 weeks	Dose can be increased to 4 mg/kg every 4 weeks*
>40 kg	150 mg every 4 weeks	Dose can be increased to 300 mg every 4 weeks*
1x EVERY 2 MONTHS IN PFS: CAPS (FCAS and MWS)[1]		
≥15 kg to ≤40 kg	2 mg/kg every 8 weeks	For pediatric patients, dose can be increased to 3 mg/kg every 8 weeks*
>40 kg	150 mg every 8 weeks	–
FOR A GOUT FLARE[1]		
Dosing for gout flares is not based on body weight	For adult patients, the recommended dose is 150 mg as a single dose at the time of a gout flare	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

*If clinical response is inadequate.

Refer to the full Prescribing Information for detailed preparation and administration instructions.

1x PER MONTH in Still's disease, FMF, HIDS/MKD, and TRAPS

1x EVERY 2 MONTHS in CAPS (including FCAS and MWS)

For a gout flare in adult patients, administer a single dose at the time of the flare.[1]
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.

IMPORTANT SAFETY INFORMATION
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.

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

ILARIS® (canakinumab) 150 mg subcutaneous injection

Dedicated and dependable support with ILARIS Companion

ILARIS companion
Dedicated and dependable support

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

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

ILARIS Free Trial Offer (FTO) Program§

- Free Trial Offer for ILARIS® (canakinumab) is good for one (1) starter dose of ILARIS at no cost for new patients with valid prescription regardless of insurance. For one-time use only
- Sign up using the Free Trial Offer request form to start ILARIS if the patient has an urgent medical need

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**

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.

§ See Program Terms and Conditions on ILARIS Free Trial Offer Form available at [www.ilarishcp.com/access]. This offer is only valid to new patients starting on ILARIS for an FDA approved indication. Novartis reserves the right to rescind revoke or amend this program without notice.

IMPORTANT SAFETY INFORMATION (cont)
WARNINGS AND PRECAUTIONS (cont)

Serious Infections (cont)

Avoid administering ILARIS to patients during an active infection requiring medical intervention. Discontinue ILARIS if a patient develops a serious infection.

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ILARIS® (canakinumab)
150 mg subcutaneous injection

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.

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.

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.

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.

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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ILARIS® (canakinumab) 150 mg subcutaneous injection

ILARIS Companion provides dedicated and dependable support. Contact a program representative at **1-866-972-8315**. For more information, visit **www.ILARISHCP.com**

IMPORTANT SAFETY INFORMATION

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