HELP TAKE THE FIRE OUT OF AUTOINFLAMMATORY DISEASE

ILARIS is indicated for 7 autoinflammatory diseases across Still's disease and a range of Periodic Fever Syndromes

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

NOW FDA APPROVED FOR ADULT-ONSET STILL'S DISEASE*

*ILARIS is approved for the treatment of active Still's disease including AOSD and SJIA in patients ≥2 years old.

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; PFS=periodic fever syndromes; 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 children aged 4 years and older, including:
  - Familial Cold Autoinflammatory Syndrome (FCAS)
  - Muckle-Wells Syndrome (MWS)
- Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS) in adults and pediatric patients
- Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD) in adults and pediatric patients
- Familial Mediterranean Fever (FMF) in adults and pediatric patients

ILARIS® (canakinumab) 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 aged 2 years and older.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

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

WARNINGS AND PRECAUTIONS

Serious Infections

ILARIS has been associated with an increased risk of serious infections. Physicians should 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 Important Safety Information on pages 26 and 27 and click here for the full Prescribing Information, including Medication Guide, for ILARIS.

ILARIS® (canakinumab)
150 mg subcutaneous injection

IL-1β is a critical driver of autoinflammatory disease[1-4]

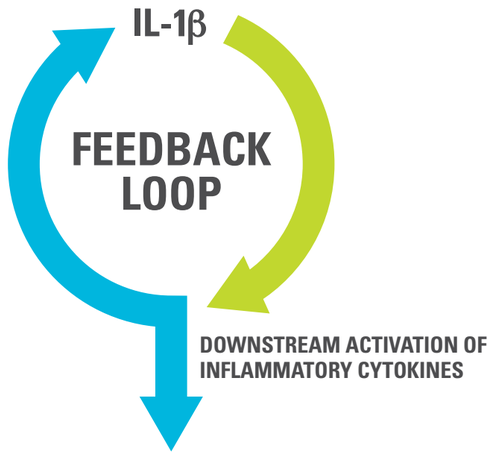
Autoinflammatory and autoimmune diseases have different pathogenic profiles[1-6]

- **IL-1β, IN ADDITION TO IL-6, IL-18, AND TNF**, is a critical driver of autoinflammatory diseases
  - IL-1β is primarily induced and actively produced by immune cells under disease conditions[7,8]
- **IFN-γ AND IL-17** are drivers of autoimmune diseases

In certain autoinflammatory diseases, there is an excessive release of activated IL-1β[2,4,9]

This overabundance can[4,7,10,11]:

- Cause an **inflammatory cascade**
- Trigger a **feedback loop**, inducing the production of even more IL-1β



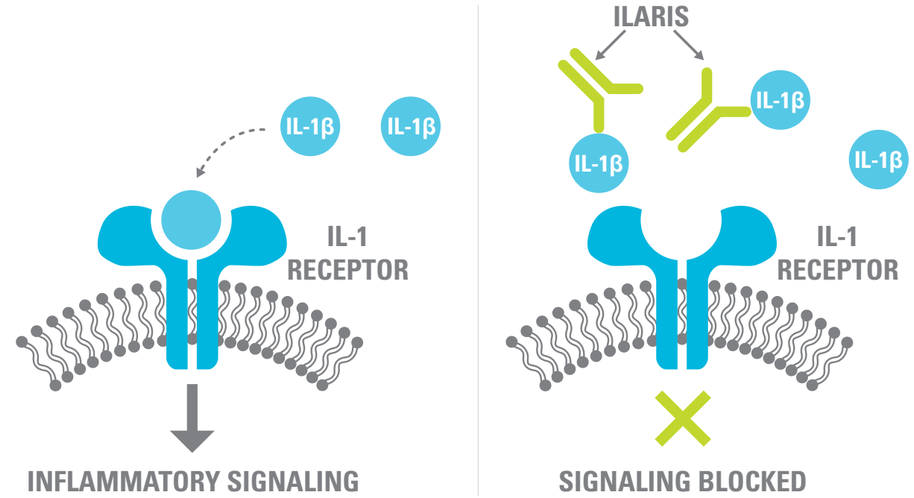
Examples:
IL-6, TNF

The inflammatory cascade in Still's disease and PFS can drive **fever and systemic inflammation**.[4,9,12-15]

ILARIS selectively targets IL-1β to block inflammatory signaling[16]

ILARIS neutralizes IL-1β activity, a critical driver of the autoinflammatory diseases Still's disease and PFS[1-5,16,17]

ILARIS Mechanism of Action[16]



- ILARIS is a recombinant, human anti-human–IL-1ββ monoclonal antibody[16]
- ILARIS binds to human IL-1β and neutralizes its activity by blocking its interaction with the IL-1 receptor[16]
- ILARIS does not bind to IL-1α or the IL-1 receptor antagonist[16]

IFN=interferon; IL=interleukin; MOA=mechanism of action; MOD=mechanism of disease; PFS=periodic fever syndromes; TNF=tumor necrosis factor.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Serious Infections (continued)

ILARIS should not be administered to patients during an active infection requiring medical intervention. Administration of ILARIS should be discontinued 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.

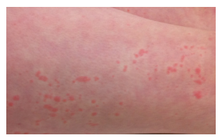
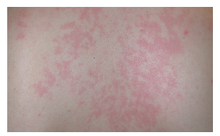
Please see Important Safety Information on pages 26 and 27 and click here for the full Prescribing Information, including Medication Guide, for ILARIS.

ILARIS® (canakinumab) 150 mg subcutaneous injection

SJIA and AOSD, which often present similarly, are the juvenile and adult forms of Still's disease[14,17-19]

- In patients **less than 16 years of age**, Still's disease is called SJIA (typical age of onset is 1 to 5 years old)
- In patients **16 years of age and older**, Still's disease is called AOSD (typical age of onset is 16 to 35 years old)

The most common signs and symptoms of Still's disease are a triad of fever, rash, and arthritis/arthralgia[18,19]

	SJIA[18]	AOSD[19]
Fever	• Occurs daily or twice daily • Temperature can spike to ≥39 °C (≥102.2 °F) with a return to normal or to below baseline temperature	• Occurs daily or twice daily, lasting <4 hours • Temperature can spike to ≥39 °C (≥102.2 °F)
Rash	 • Transient, salmon colored, macular or maculopapular • Typically found on the trunk, neck, and proximal extremities	 • Evanescent, salmon-pink colored, maculopapular • Typically found on the trunk and proximal extremities
Arthritis/ Arthralgia	• Can range from oligoarticular to polyarticular patterns • Primarily affects wrists, knees, and ankles	• Arthritis may be symmetrical with most developing polyarthritis with fever spikes • Primarily affects wrists, knees, and ankles

Rash images credits: Reproduced with permission from Isabelle Koné-Paut, MD (SJIA), DermNetNZ.org (AOSD).

Overlapping features and symptoms with other conditions, such as autoimmune diseases, may lead to a **delay in diagnosis or a misdiagnosis**.[18,19]

Detailed classification criteria: SJIA and AOSD

Diagnosing SJIA Based on the ILAR Classification Criteria[20,21]

ARTHRITIS AFFECTING ≥1 JOINTS FOR ≥6 WEEKS

With or preceded by +

FEVER FOR ≥2 WEEKS OCCURRING DAILY FOR ≥3 DAYS

Plus 1 or more of the following +

1. **Evanescent (nonfixed) erythematous rash**
2. **Generalized lymphadenopathy**
3. **Hepatomegaly and/or splenomegaly**
4. **Serositis**

Exclusion criteria for ILAR[20]:

- Psoriasis or a history of psoriasis in the patient or first-degree relative
- Arthritis in male aged >6 years who is HLA-B27 positive
- Ankylosing spondylitis, enthesitis-related arthritis, sacroiliitis with inflammatory bowel disease, Reiter's syndrome, or acute anterior uveitis, or a history of one of these disorders in a first-degree relative
- The presence of IgM rheumatoid factor on at least 2 occasions at least 3 months apart

Common laboratory abnormalities[18]:

- Highly elevated inflammatory markers such as ESR and CRP are usually present in patients with SJIA

Diagnosing AOSD Based on the Yamaguchi Criteria[22]

(Requires ≥5 Criteria, Including ≥2 Major Criteria)

Major criteria[22]:

1. Fever ≥39 °C (≥102.2 °F) lasting for ≥1 week
2. Arthralgia for ≥2 weeks
3. Macular or maculopapular, nonpruritic salmon-pink–colored rash
4. Leukocytosis (≥10,000/microL), including 80% more of granulocytes

Minor criteria[22]:

1. Sore throat
2. Lymphadenopathy and/or splenomegaly
3. Abnormal liver function tests
4. Negative tests for rheumatoid factor and antinuclear antibody

Exclusions[22]:

- Infections
- Malignancies
- Rheumatic diseases

Several common laboratory abnormalities include[19,23]:

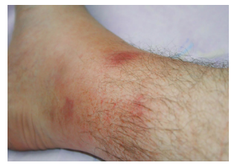
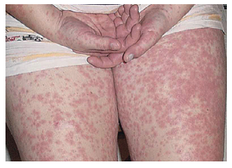
- Elevated ESR and CRP
- Leukocytosis
- Thrombocytosis
- Elevated ferritin levels, 5x upper limit of normal
  — Glycosylated ferritin is an important marker—in patients with AOSD, glycosylation of ferritin is often <20%

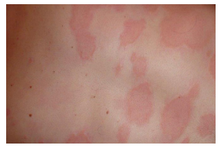
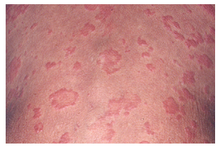
AOSD=adult-onset Still's disease; CRP=C-reactive protein; ESR=erythrocyte sedimentation rate; IgM=immunoglobulin M; ILAR=International League of Associations for Rheumatology; SJIA=systemic juvenile idiopathic arthritis.

Please see Important Safety Information on pages 26 and 27 and click here for the full Prescribing Information, including Medication Guide, for ILARIS.

Periodic fever syndromes are characterized by[24,25]:

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

	FMF[1,24-29]	HIDS/MKD[1,24-26,30,31]
Predominant ethnic distribution	Turkish, Armenian, Arab, Jewish, Italian	Dutch or Northern European
Worldwide prevalence or number of cases	1 to 5 in 10,000	>180
Typical age at onset	<20 years	<1 year
Duration of attacks	12 hours to 3 days	3 to 7 days
Frequency of attacks	Irregular; once per week to once every 5 to 10 years	Irregular; 2- to 8-week intervals
Gene mutation	MEFV	MVK
Inheritance	Autosomal recessive	Autosomal recessive
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	 • 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 • Chest pain • Arthritis/monoarthritis	• Abdominal pain • Lymphadenopathy • Aphthous ulcers
High serology	Increase in CRP, ESR, and SAA	Increase in CRP, ESR, IgD, and SAA

	TRAPS[1,24-26,32-36]	CAPS: FCAS	CAPS: MWS[1,24-27,37,38]
Predominant ethnic distribution	All ethnicities	Mostly European	
Worldwide prevalence or number of cases	>1000	<1 in 1,000,000*	
Typical age at onset	Varies; <3 years to <20 years	<1 year	<20 years
Duration of attacks	7 to 28 days; nearly continuous in one-third of patients	12 to 24 hours	2 to 3 days
Frequency of attacks	Irregular; 5 weeks to months or years	Variable; triggered by generalized cold exposure	Variable; triggered by cold, fatigue, and stress
Gene mutation	TNFRSF1A	NLRP3	
Inheritance	Autosomal dominant	Autosomal dominant	
Cutaneous findings	 • Erythematous, migratory rash • Often overlies an area of myalgia and migrates together in a centrifugal pattern • Often found on the torso or extremity	 • 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	• Abdominal pain • Musculoskeletal pain • Eye manifestations, such as periorbital edema	• Headache • Arthralgia • Fatigue • Myalgia • Conjunctivitis	• Headache • Arthralgia • Fatigue • Conjunctivitis
High serology	Increase in CRP, ESR, and SAA	Increase in CRP, ESR, and SAA	

Rash images credits: Reproduced with permission from Emedmd.com (FMF). Petty RE et al. *Textbook of Pediatric Rheumatology.* 7th ed. Philadelphia, PA: Elsevier; 2016 (HIDS/MKD). Rareconnect.org (TRAPS). Petty RE et al. *Textbook of Pediatric Rheumatology.* 7th ed. Philadelphia, PA: Elsevier; 2016 (CAPS).

CAPS=cryopyrin-associated periodic syndromes; CRP=C-reactive protein; ESR=erythrocyte sedimentation rate; FCAS=familial cold autoinflammatory syndrome; FMF=familial Mediterranean fever; HIDS=hyperimmunoglobulin D syndrome; IgD=immunoglobulin D; MKD=mevalonate kinase deficiency; MWS=Muckle-Wells syndrome; NOMID=neonatal onset multisystem inflammatory disease; PFS=periodic fever syndromes; SAA=serum amyloid A; TRAPS=tumor necrosis factor receptor–associated periodic syndrome.

*Prevalence includes patients with FCAS, MWS, and NOMID.

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NOW FDA APPROVED FOR ADULT-ONSET STILL'S DISEASE*

The efficacy of ILARIS in adults with AOSD is based on the established efficacy of ILARIS in patients with SJIA.[16†]

ILARIS®
(canakinumab)
150 mg subcutaneous injection

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Serious Infections (continued)

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, patients should be evaluated 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. Patients testing positive in TB screening should be treated by standard medical practice prior to therapy with ILARIS. All patients should be instructed 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.

*ILARIS is approved for the treatment of active Still's disease including AOSD and SJIA in patients ≥2 years old.

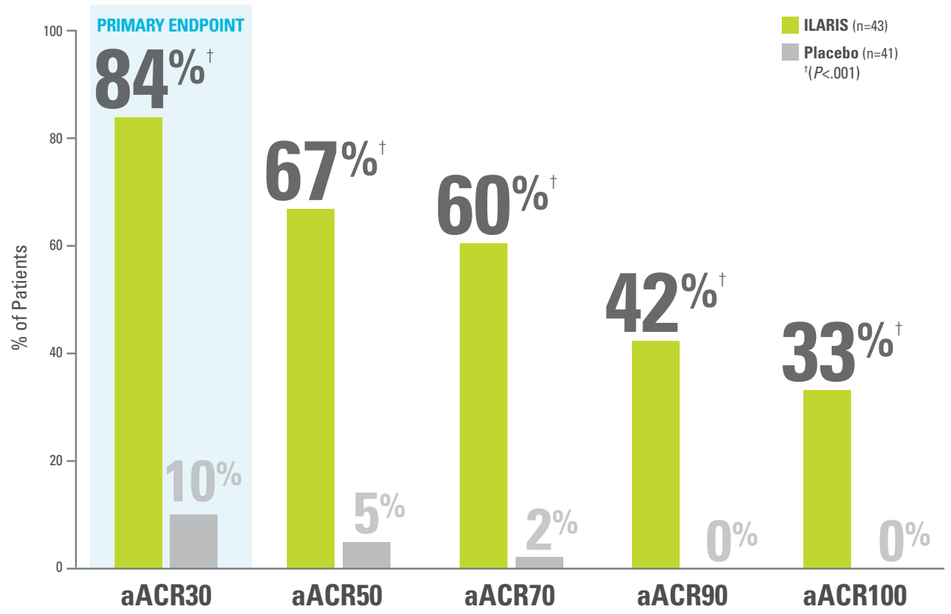
†The efficacy of ILARIS in adults with AOSD is based on the pharmacokinetic exposure and extrapolation of the established efficacy of ILARIS in SJIA patients. Efficacy of ILARIS was also assessed in a randomized, double-blind, placebo-controlled study that enrolled 36 patients (22 to 70 years old) diagnosed with AOSD. The efficacy data were generally consistent with the results of a pooled efficacy analysis of SJIA patients.[18]

AOSD=adult-onset Still's disease; SJIA=systemic juvenile idiopathic arthritis.

Please see Important Safety Information on pages 26 and 27 and click here for the full Prescribing Information, including Medication Guide, for ILARIS.

Significant improvements in aACR responses were seen with ILARIS at Day 15[16,39,40]

aACR Responses* After the First Dose of ILARIS vs Placebo at Day 15[16,39,40]



- At day 29, 81% (n/N=35/43) of patients receiving ILARIS compared with 10% (n/N=4/41) of patients receiving placebo achieved aACR30[41]

POST HOC

At Day 15, one-third (33%) of patients achieved inactive disease‡ (vs 0% of patients receiving placebo).[39,40]

- Analysis is exploratory and has not been adjusted for multiple comparisons; no conclusions can be drawn

SJIA Study 1 Design[16,40]

A randomized, double-blind, placebo-controlled study in 84 patients with SJIA assessed the efficacy of a single subcutaneous dose of ILARIS (4 mg/kg) vs placebo over 29 days. **The primary endpoint was aACR30 at Day 15.**

IMPORTANT SAFETY INFORMATION

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.

ILARIS decreased steroid use and significantly reduced risk of flare[16,40‖]

Decreased use of steroids within 5 months of treatment

Of the 92 patients who attempted to taper their corticosteroids,

62% SUCCESSFULLY TAPERED§ THEIR STEROID DOSE (n/N =57/92)

ALMOST HALF (46%) WERE STEROID FREE (n/N =42/92)

Significant reductions in the risk of flare

64% REDUCTION IN RELATIVE FLARE RISK

74% PROBABILITY OF REMAINING FLARE‖ FREE VS 25% WITH PLACEBO

- The study was ended after 37 flare events occurred. Median duration with ILARIS was 221.5 days vs 163.5 days with placebo. Hazard ratio was 0.36 (95% CI, 0.17-0.75)[16,40,41]

SJIA Study 2 Design (Part 1)[16,39,40]

An open-label steroid-tapering phase in which 177 patients were treated with a 4-mg/kg subcutaneous dose of ILARIS every 4 weeks for 12 to 32 weeks. Patients receiving concomitant corticosteroids at the beginning of the study were allowed to taper corticosteroid use from Week 9 through Week 28 if they achieved minimum aACR50.

- **The primary endpoint was corticosteroid tapering in at least 25% of patients being treated with corticosteroids (45% [57/128] were able to taper their dose of corticosteroids by the end of the steroid-tapering period in Study 2 [Part 1])**

SJIA Study 2 Design (Part 2)[16,39,40]

A double-blind withdrawal trial in which patients from Study 2, Part 1 who achieved and sustained aACR30 or above in Part 1 and were not taking corticosteroids or who had undergone successful corticosteroid tapering were subsequently randomized to ILARIS 4 mg/kg (n=50) or placebo (n=50) every 4 weeks.

- **The primary endpoint was time to flare event with ILARIS vs placebo. This study continued until 37 flares had occurred**

*aACR response: Percentage improvement (at least 30%, 50%, 70%, 90%, 100%) from baseline in at least 3 of the 6 pediatric ACR core outcome components along with the absence of fever (≤38 °C in the preceding 7 days) and worsening of >30% in no more than 1 of the remaining components. The disease activity components include CRP level, number of joints with active arthritis, number of joints with limited range of motion, physician's global assessment of disease activity, parent's or patient's global assessment of patient's overall well-being, and functional ability (CHAQ-DI).[39,40]

†**Inactive disease:** Absence of active arthritis, fever, rheumatoid rash, serositis, splenomegaly, hepatomegaly, or generalized lymphadenopathy attributable to SJIA; normal ESR or CRP; physician's global assessment of disease activity indicating no disease activity. *P* values were not determined for comparison regarding inactive disease.[39,40]

§**Successful corticosteroid tapering:** Oral prednisone (or equivalent) dose reduction from >0.8 to ≤0.5 mg/kg/day, or from ≥0.5 and ≤0.8 mg/kg/day by at least 0.3 mg/kg/day, or from any initial dose to ≤0.2 mg/kg/day, while maintaining a minimum aACR30 response.[39]

‖**Flare:** Worsening of ≥30% in at least 3 of the 6 core aACR response variables combined with improvement of ≥30% in no more than 1 of the 6 variables, or reappearance of fever not due to infections for at least 2 consecutive days.[16]

aACR=adapted JIA American College of Rheumatology; CHAQ-DI=Child Health Assessment Questionnaire-Disability Index; CRP=C-reactive protein; ESR=erythrocyte sedimentation rate; SJIA=systemic juvenile idiopathic arthritis.

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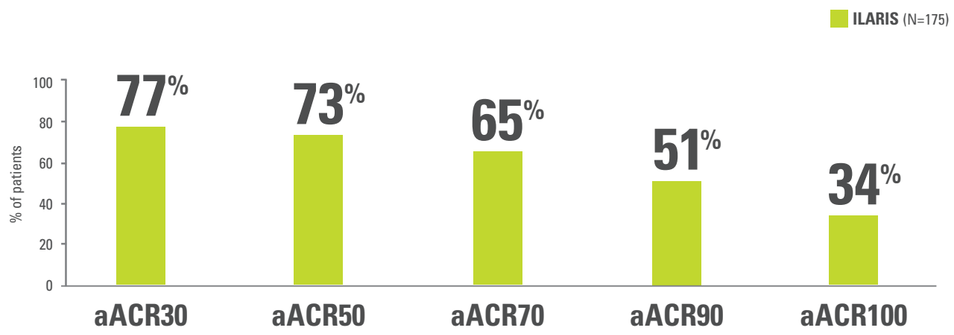
ILARIS® (canakinumab) 150 mg subcutaneous injection

Many ILARIS-treated patients achieved aACR responses at the end of the study (≤8 months) and were fever free at day 3[39-41]

aACR Responses at the End of Study 2 (Part 1)[40,41]



Study 2 (Part 1) lasted up to 8 months[40,41]

- End of Study 2 (Part 1) results shown are based on patients' last available assessments

After the initial dose, nearly all patients in the ILARIS group were fever-free at Day 3 of each pivotal trial[39,41]

Only 3 Days After Their First Dose of ILARIS:

STUDY 1

100%

OF PATIENTS WERE FEVER FREE

(n/N=43/43) vs 87% with placebo (n/N=33/38)

STUDY 2 (Part 1)

99%

OF PATIENTS WERE FEVER FREE

(n/N=139/141)

IMPORTANT SAFETY INFORMATION

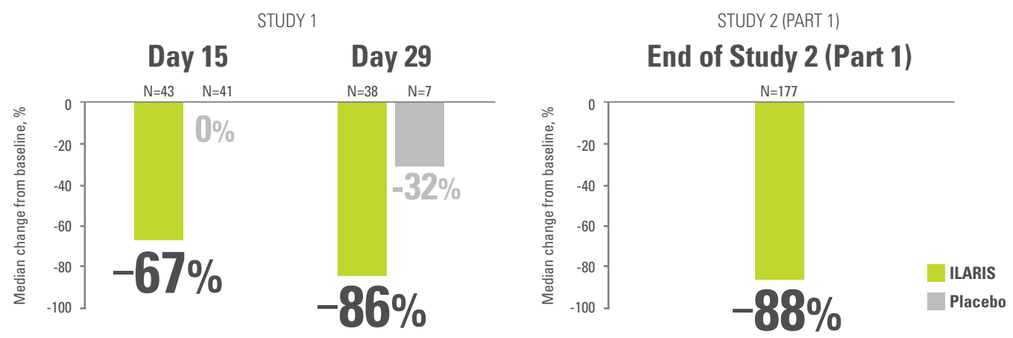
WARNINGS AND PRECAUTIONS

Hypersensitivity

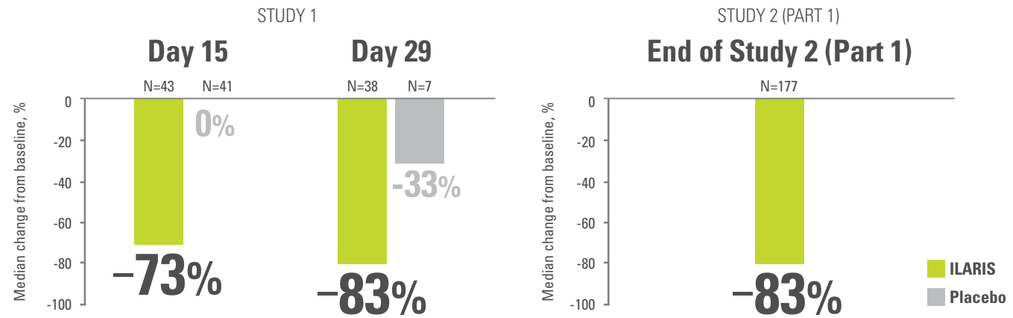
Hypersensitivity reactions have been reported with ILARIS therapy. During clinical trials, no anaphylactic reactions attributable to treatment with canakinumab have been reported. It should be recognized that symptoms of the underlying disease being treated may be similar to symptoms of hypersensitivity. If a severe hypersensitivity reaction occurs, administration of ILARIS should be discontinued and appropriate therapy initiated.

Once-monthly ILARIS provided systemic and arthritic improvements consistent with overall aACR response[39,41]

Median Reduction in Number of Active Arthritic Joints in Study 1 and Study 2 (Part 1)



Median Reduction in Number of Joints With Limited Range of Motion in Study 1 and Study 2 (Part 1)



ILARIS-treated patients achieved a median reduction in CRP levels of approximately 90% in both pivotal trials

- In Study 1, patients receiving ILARIS (n=43) achieved a **91% median reduction from baseline in CRP level at Day 15** vs a 5% median increase in patients receiving placebo (n=25)[39]
- In Study 2 (Part 1), patients receiving ILARIS (n=177) achieved an **87% median reduction from baseline in CRP level at the end of Study 2 (Part 1)**[41]

The analysis of the aACR components have not been adjusted for multiple comparisons. No conclusions of statistical or clinical significance can be drawn.

aACR=adapted JIA American College of Rheumatology; CRP=C-reactive protein; SJIA=systemic juvenile idiopathic arthritis.

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ILARIS® (canakinumab) 150 mg subcutaneous injection

Safety profile of ILARIS from core SJIA clinical trials[16]

Pivotal Studies	SJIA Study 1		SJIA Study 2		
			Corticosteroid-tapering phase	ILARIS-withdrawal phase	
	ILARIS (n=43)	Placebo (n=41)	ILARIS (n=177)	ILARIS (n=50)	Placebo (n=50)
All Infections, %*	30	12	55	54	38
Exposure-adjusted incidence rate per 100 patient-days	1.26	1.37	0.91	0.59	0.63
Abdominal pain (upper), %	7	2	14	16	12
Exposure-adjusted incidence rate per 100 patient-days	0.25	0.23	0.16	0.15	0.08
Mild injection site reaction, %	0	7	11	12	4
Moderate injection site reaction, %	0	0	1	2	0

*The most commonly reported infections were nasopharyngitis and (viral) upper respiratory tract infection. Other infections included pneumonia, rhinitis, pharyngitis, tonsillitis, sinusitis, urinary tract infection, gastroenteritis, and viral infections.

- ILARIS has been associated with an increased risk of serious infections. Infections, predominantly of the upper respiratory tract, in some instances serious, have been reported with ILARIS[16]
- Generally, the observed infections in ILARIS clinical trials 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[16]
- Serious infections (eg, pneumonia, varicella, gastroenteritis, measles, sepsis, otitis media, sinusitis, adenovirus, lymph node abscess, pharyngitis) were observed in approximately 4% to 5% (0.02 to 0.17 per 100 patient-days) of patients receiving ILARIS in pivotal studies[16]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Immunizations

Live vaccines should not be given concurrently with ILARIS. Prior to initiation of therapy with ILARIS, patients should receive all recommended vaccinations. In addition, because ILARIS may interfere with normal immune response to new antigens, vaccinations may not be effective in patients receiving ILARIS.

Additional safety for ILARIS throughout SJIA clinical trials[16]

- **No injection site reactions led to study discontinuation**
- **No anaphylactic reactions attributable to treatment with canakinumab were reported**
- **No neutralizing antibodies were detected**†

AOSD

The safety profile of ILARIS in patients with AOSD in a randomized, double-blind, placebo-controlled study in 36 adults, 22 to 70 years old, **was similar to what was observed in patients with SJIA**.[16]

ILARIS did not appear to increase the incidence of MAS[16]

Eleven cases of MAS were observed in 201 patients with SJIA treated with ILARIS 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 conclusions can be made.

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.

†Antibodies against ILARIS were observed in approximately 3.1% of the patients treated with ILARIS for SJIA. No apparent correlation of antibody development to clinical response or adverse events was observed.

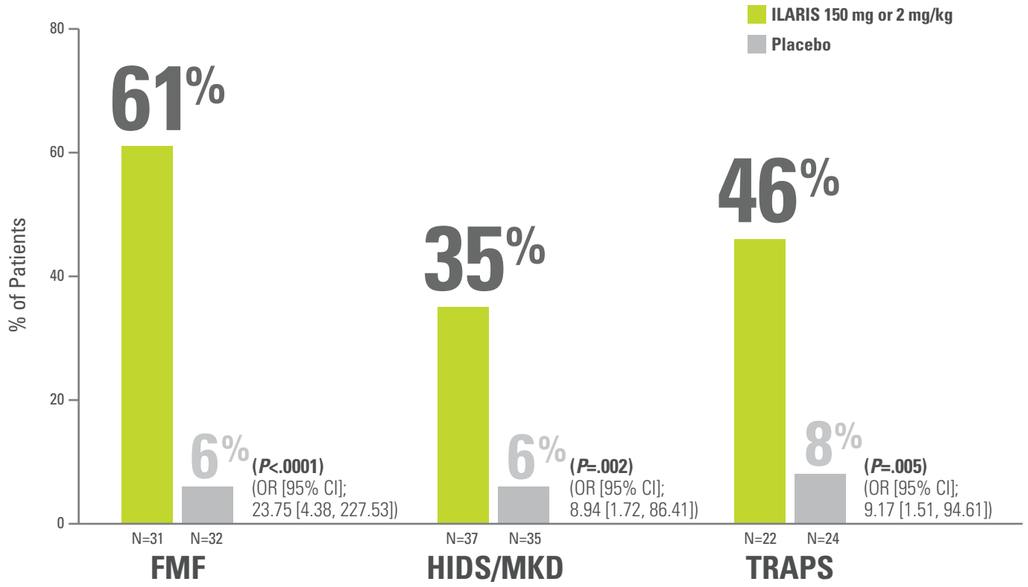
AOSD=adult-onset Still's disease; IL=interleukin; MAS=macrophage activation syndrome; SJIA=systemic juvenile idiopathic arthritis.

Please see Important Safety Information on pages 26 and 27 and click here for the 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[16]

Percent of Patients Achieving Complete Response* vs Placebo at Week 16[16]



- 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 rapid 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)

FMF, TRAPS, and HIDS/MKD Study Design[16]

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.

The primary endpoint of the 16-week treatment period was the proportion of patients achieving a complete response without any dose adjustments.

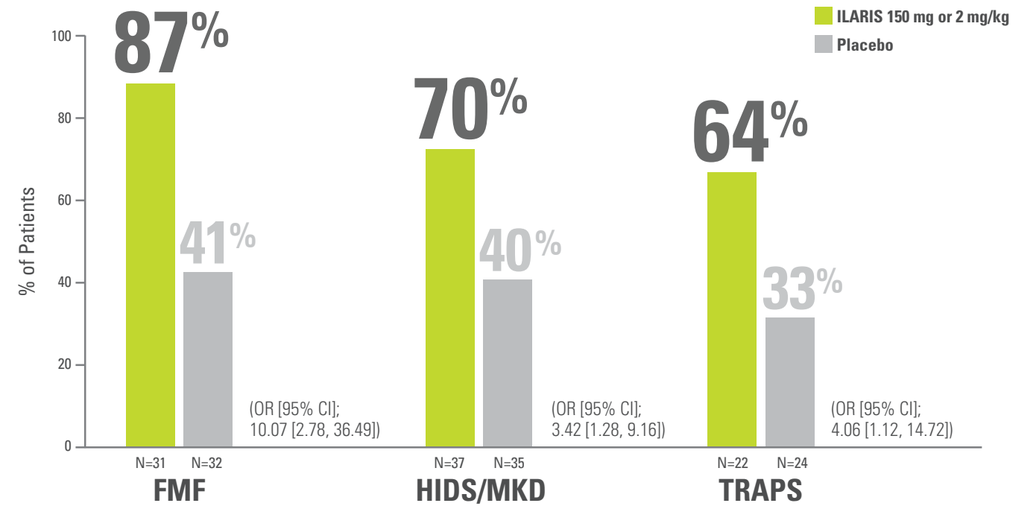
***Complete response defined as resolution of index flare (PGA < 2 and CRP ≤10mg/L or a ≥70% reduction from baseline) at Day 15 and no new flare (PGA ≥2 and CRP ≥30 mg/L) throughout the 16-week treatment period.**

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.

In the same study,

After the initial dose at Day 15, ILARIS improved disease activity as measured by PGA, as well as CRP levels[16,42]

Percent of Patients Showing No or Minimal Signs of Disease Activity (PGA score <2) vs Placebo at Day 15[16]



PGA scores at baseline[42]:

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

At Day 15, CRP ≤10 mg/L Achieved By[16]:

FMF	HIDS/MKD	TRAPS
90%	**68%**	**59%**
of patients receiving ILARIS (n/N=28/31) vs **28% receiving placebo** (n/N=9/32)	of patients receiving ILARIS (n/N=25/37) vs **26% receiving placebo** (n/N=9/35)	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]).

CRP=C-reactive protein; FMF=familial Mediterranean fever; HIDS=hyperimmunoglobulin D syndrome; MKD=mevalonate kinase deficiency; PFS=periodic fever syndromes; PGA=Physician's Global Assessment; TRAPS=tumor necrosis factor receptor–associated periodic syndrome.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Immunizations (continued)

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.

Please see Important Safety Information on pages 26 and 27 and click here for the 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[16,43]

Percent of Patients Achieving Complete Clinical Response With ILARIS:

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[16,43]:

- 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[16,43]

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 disease flare or relapse in Part 2.

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

†Ten patients in the placebo group met the criteria for clinical relapse, and 3 patients discontinued Part 2 due to unsatisfactory therapeutic effect.[44]

‡**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.[16]

§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.[16,44]

CAPS=cryopyrin-associated periodic syndromes; CRP=C-reactive protein; FCAS=familial cold autoinflammatory syndrome; MWS=Muckle-Wells syndrome; PFS=periodic fever syndromes; SAA=serum amyloid A.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

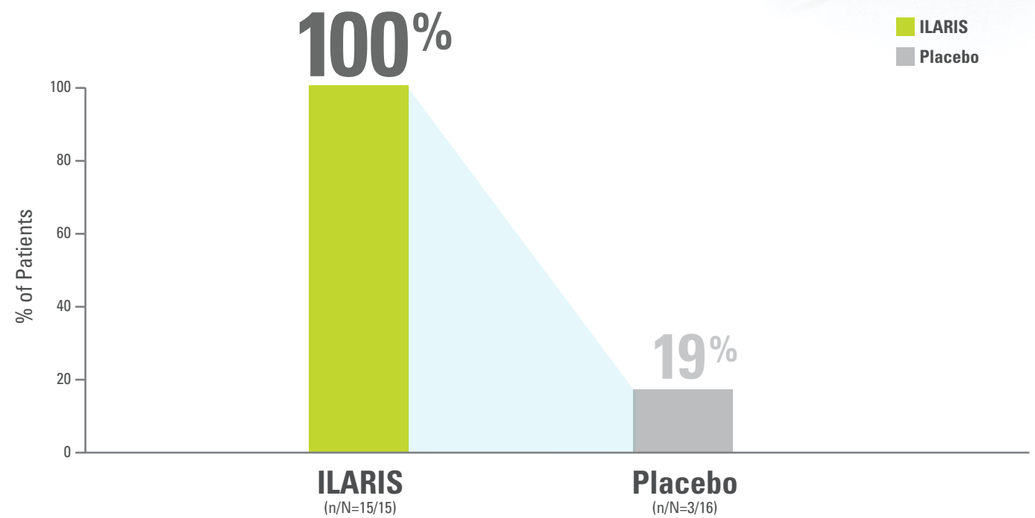
Macrophage Activation Syndrome

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.

In Part 2,

After 3 doses* of ILARIS, 100% of patients remained flare free through 24 weeks[16,43†]

Percent of Patients Who Were Flare Free vs Placebo at Week 32



None of the patients treated with ILARIS had a disease relapse‡ over 24 weeks[43]

- 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[44§]

Physician's Global Assessment of Disease Activity and Assessment of Skin Disease:

At the end of 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 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

Please see Important Safety Information on pages 26 and 27 and click here for the 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[16]

- In Part 2, 90 patients were initially randomized to ILARIS 150 mg and 91 patients were randomized to placebo every 4 weeks
  - —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

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

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
- Serious infections (eg, conjunctivitis, pneumonia, pharyngitis, pharyngotonsillitis) were observed in approximately 2.4% (0.03 per 100 patient-days) of patients receiving ILARIS

No new or unexpected safety findings of ILARIS emerged in the PFS clinical trial[42]

Among all 3 patient cohorts in the ILARIS group:

No deaths were reported

No anti-ILARIS 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

Safety profile of ILARIS from CAPS clinical trials[16]

AEs by Preferred Term Occurring in >10% of Patients Throughout Entire Study

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
  - —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
  - —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.[16]

AE=adverse event; CAPS=cryopyrin-associated periodic syndromes; FMF=familial Mediterranean fever; HIDS=hyperimmunoglobulin D syndrome; MKD=mevalonate kinase deficiency; PFS=periodic fever syndromes; TRAPS=tumor necrosis factor receptor–associated periodic syndrome.

Please see Important Safety Information on pages 26 and 27 and click here for the full Prescribing Information, including Medication Guide, for ILARIS.

ILARIS® (canakinumab) 150 mg subcutaneous injection

ILARIS is dosed once monthly or once every 2 months[16]

Once monthly in Still's disease, FMF, HIDS/MKD, and TRAPS and once every 2 months in CAPS (including FCAS and MWS)

ILARIS Is Given Subcutaneously by a Health Care Professional and Is Dosed According to Body Weight

Body Weight	Recommended Dose	Recommended Titration
STILL'S DISEASE: SJIA and AOSD		
≥7.5 kg	4 mg/kg (with a maximum of 300 mg) every 4 weeks	–
PFS: FMF, HIDS/MKD, and TRAPS		
≤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*
PFS: CAPS		
≥15 kg to ≤40 kg	2 mg/kg every 8 weeks	Dose can be increased to 3 mg/kg*
>40 kg	150 mg every 8 weeks	–

*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)

IMPORTANT SAFETY INFORMATION

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.

Dedicated and dependable support with ILARIS Companion

ILARIS companion
Dedicated and dependable support

A Wide Range of Services and Support

Home Health Nurse Service
Allows patients to have injections administered in their homes or at another location outside of the physician's office

Co-pay Savings Offer†
Helps make ILARIS more affordable for eligible patients, who pay no more than $30 per month (subject to annual cap)

Coverage Review and Support
Identifies financial support programs for uninsured and underinsured patients

Specialty Pharmacy Outreach
Works with a patient's specialty pharmacy on patient follow up

First Dose Program†
Ships the initial dose of ILARIS to eligible patients free of charge, if a payer approval is not received within 2 weeks

Prior Authorization Support
Assists in determining specific prior authorization criteria, if required

Benefits Investigation‡
Verifies health plan benefits and provides reimbursement policies for ILARIS

Clinical Appeals
Provides support with insurance appeals

Product Delivery Support
Works with a health plan's preferred specialty pharmacy to support coordination and delivery of ILARIS to the patient's home or physician's office

†Limitations apply. See Program Terms and Conditions on the Service Request Form (SRF) available at www.ilaris-support.com. **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.

‡Allows patients to learn the coverage and cost of ILARIS.

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; PFS=periodic fever syndromes; SJIA=systemic juvenile idiopathic arthritis; TRAPS=tumor necrosis factor receptor–associated periodic syndrome.

Please see Important Safety Information on pages 26 and 27 and click here for the full Prescribing Information, including Medication Guide, for ILARIS.

ILARIS® (canakinumab)
150 mg subcutaneous injection

How to get patients started with ILARIS Companion

To Prescribe ILARIS and Enroll Your Patients in ILARIS Companion

Submit a Service Request Form (SRF)

1 **Download and fill out the SRF,** available at **www.ilaris-support.com** or from your Account Manager.

2 **Print and fax the completed SRF,** signed by you and your patient, to **866-972-8316**.

Please note, a missing patient signature will delay the start of program services.
If patients are unavailable to sign the SRF, they can provide consent at www.hipaaconsent.com.

ILARIS is available through a specialty distributor and a select system of specialty pharmacies

SPECIALTY PHARMACIES
- Accredo
- CVS Specialty
- Walgreens

Provides access to ILARIS without a physician having to directly purchase or bill for a product.

SPECIALTY DISTRIBUTOR
- CuraScript SD

Provides priority health care distribution of ILARIS for office or clinic administration (buy and bill).

IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

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.

Increased access can help elevate patient care[45-47]

MAXIMIZING PATIENT ACCESS

≈90% OF COMMERCIAL PATIENTS ARE COVERED ON ILARIS[45*]

HIGH PA APPROVAL RATE

≈80% OF PRIOR AUTHORIZATION (PA) REQUESTS ARE APPROVED[46]

TREATMENT IN 30 DAYS OR LESS

≈70% OF PATIENTS RECEIVE A COMMERCIAL DISPENSE OF ILARIS WITHIN 1 MONTH[47]

ILARIS companion
Dedicated and dependable support

866-972-8315

If you have questions about services, contact a program representative Monday to Friday, 9 AM to 6 PM ET.

*For SJIA only. Based on combined lives across Pharmacy and Medical plans. Only includes plans where data are available through Managed Markets Insights & Technology (MMIT).

Please see Important Safety Information on pages 26 and 27 and click here for the full Prescribing Information, including Medication Guide, for ILARIS.

ILARIS® (canakinumab) 150 mg subcutaneous injection

IMPORTANT SAFETY INFORMATION

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

ILARIS® (canakinumab) 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 aged 2 years and older.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

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

WARNINGS AND PRECAUTIONS

Serious Infections

ILARIS has been associated with an increased risk of serious infections. Physicians should 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 administered to patients during an active infection requiring medical intervention. Administration of ILARIS should be discontinued 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, patients should be evaluated 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. Patients testing positive in TB screening should be treated by standard medical practice prior to therapy with ILARIS. All patients should be instructed 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.

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

Hypersensitivity reactions have been reported with ILARIS therapy. 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. If a severe hypersensitivity reaction occurs, administration of ILARIS should be discontinued and appropriate therapy initiated.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Immunizations

Live vaccines should not be given concurrently with ILARIS. Prior to initiation of therapy with ILARIS, patients should receive all recommended vaccinations. 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.

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*ILARIS is approved for the treatment of active Still's disease including AOSD and SJIA in patients ≥2 years old.

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

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Serious Infections

ILARIS has been associated with an increased risk of serious infections. Physicians should 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 administered to patients during an active infection requiring medical intervention. Administration of ILARIS should be discontinued 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.

Please see Important Safety Information on pages 26 and 27 and click here for the full Prescribing Information, including Medication Guide, for ILARIS.

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