STILL'S DISEASE

HELP TAKE THE FIRE OUT OF AUTOINFLAMMATORY DISEASE

THE ONLY FDA-APPROVED TREATMENT FOR STILL'S 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)

*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

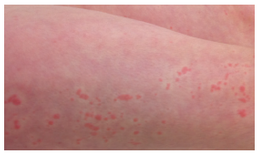
ILARIS has been associated with an increased risk of serious infections. Physicians should exercise caution when administering ILARIS to patients with infections, a history of recurring infections or underlying conditions, which may predispose them to infections.

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

ILARIS® (canakinumab)
150 mg subcutaneous injection

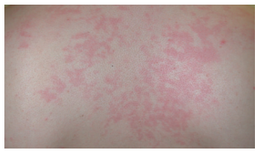
SJIA and AOSD, which often present similarly, are the juvenile and adult forms of Still's disease[1-4]

In patients **younger than 16 years**, Still's disease is called SJIA (typical age of onset is 1 to 5 years old)[2,3]

SJIA[3]	
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
Rash	 • Transient, salmon colored, macular or maculopapular • Typically found on the trunk, neck, and proximal extremities
Arthritis/ Arthralgia	• Can range from oligoarticular to polyarticular patterns • Primarily affects wrists, knees, and ankles

The most common signs and symptoms of Still's disease are a triad of fever, rash, and arthritis/arthralgia[3,4]

In patients **16 years of age and older**, Still's disease is called AOSD (typical age of onset is 16 to 35 years old)[2,4]

AOSD[4]	
Fever	• Occurs daily or twice daily, lasting <4 hours • Temperature can spike to ≥39 °C (≥102.2 °F)
Rash	 • Evanescent, salmon-pink colored, maculopapular • Typically found on the trunk and proximal extremities
Arthritis/ Arthralgia	• Arthritis may be symmetrical with most developing polyarthritis with fever spikes • Primarily affects wrists, knees, and ankles

Overlapping features and symptoms with other conditions, such as autoimmune diseases, may lead to a **delay in diagnosis or a misdiagnosis**.[3,4]

IMPORTANT SAFETY INFORMATION

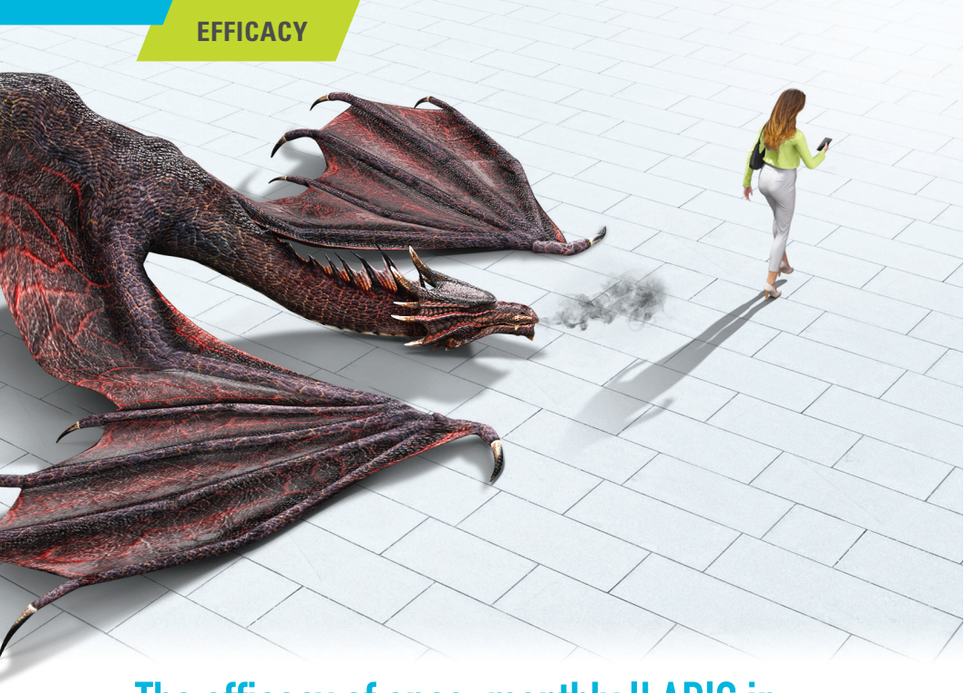
WARNINGS AND PRECAUTIONS (cont)

Serious Infections (cont)

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.

Rash images credits: Courtesy of Pr Isabelle Koné-Paut (SJIA), DermNetNZ.org (AOSD).

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



The efficacy of once-monthly ILARIS in adults with AOSD is based on the established efficacy of ILARIS in patients with SJIA.[5*]

THE ONLY FDA-APPROVED TREATMENT FOR STILL'S DISEASE[†]

*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.[5]

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

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont)

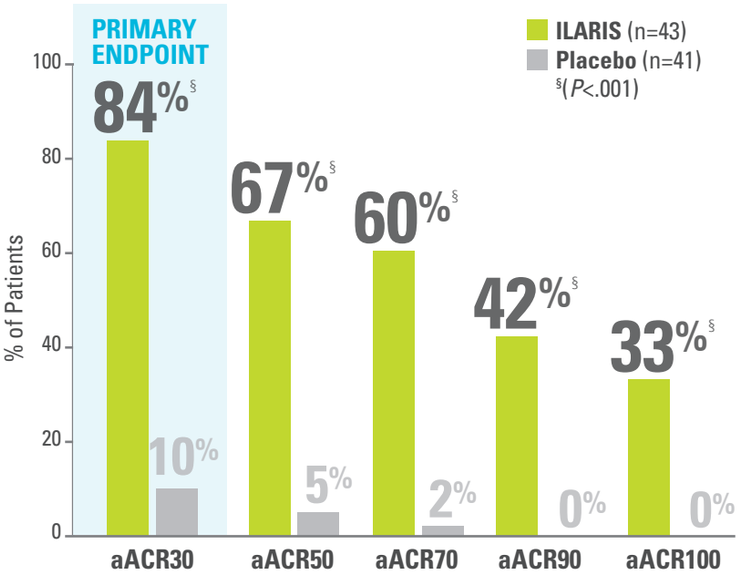
Serious Infections (cont)

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.

In patients with SJIA,

Significant improvements in aACR responses were seen with once-monthly ILARIS at Day 15[5-7]

aACR Responses[‡] After the First Dose of ILARIS vs Placebo at Day 15[5-7]



SJIA Study 1 Design[5,7]

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.**

‡**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).[6,7]

aACR=adapted JIA American College of Rheumatology; CHAQ-DI=Child Health Assessment Questionnaire-Disability Index; CRP=C-reactive protein.

IMPORTANT SAFETY INFORMATION

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.

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

ILARIS® (canakinumab) 150 mg subcutaneous injection

In patients with SJIA,

ILARIS decreased use of steroids within 5 months of treatment[5,7]

Of the 92 patients who attempted to taper their corticosteroids,

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

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

In patients with SJIA,

ILARIS significantly reduced the risk of flare[5,7]

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)[5,7,8]

SJIA Study 2 Design (Part 1)[5-7]

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)[5-7]

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**

*__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.[6]

†__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.[5]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont)

Serious Infections (cont)

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.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (cont)

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.

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.

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Safety profile of ILARIS from core SJIA clinical trials[5]

Pivotal Studies	SJIA Study 1	
	ILARIS (n=43)	Placebo (n=41)
All Infections, %*	30	12
Exposure-adjusted incidence rate per 100 patient-days	1.26	1.37
Abdominal pain (upper), %	7	2
Exposure-adjusted incidence rate per 100 patient-days	0.25	0.23
Mild injection site reaction, %	0	7
Moderate injection site reaction, %	0	0

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

- 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[5]
- 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[5]
- 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[5]

Additional safety for ILARIS throughout SJIA clinical trials[5]

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.**[5]

ILARIS did not appear to increase the incidence of MAS[5]

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.

DOSING

ILARIS is dosed once monthly in patients with Still's disease (SJIA and AOSD)[5]

- For patients ≥7.5 kg, the recommended dose of ILARIS is 4 mg/kg (with a maximum of 300 mg) every 4 weeks
- ILARIS is given subcutaneously by a health care professional and can be administered in office, patients' homes, or at another location outside of the physician's office

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

*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.

†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.

MAS=macrophage activation syndrome.

Please see additional Important Safety Information throughout and click here for the 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

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 information 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

Increased access can help elevate patient care[9-11]

MAXIMIZING PATIENT ACCESS

≈90% OF COMMERCIAL PATIENTS ARE COVERED ON ILARIS[9‡]

HIGH PA APPROVAL RATE

≈80% OF PRIOR AUTHORIZATION (PA) REQUESTS ARE APPROVED[10]

TREATMENT IN 30 DAYS OR LESS

≈70% OF PATIENTS RECEIVE A COMMERCIAL DISPENSE OF ILARIS WITHIN 1 MONTH[11]

866-972-8315

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

*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.

‡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).

IMPORTANT SAFETY INFORMATION

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.

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ILARIS® (canakinumab) 150 mg subcutaneous injection

THE ONLY FDA-APPROVED TREATMENT FOR STILL'S DISEASE*

HELP TAKE THE FIRE OUT OF AUTOINFLAMMATORY DISEASE

Learn more about ILARIS and the wide range of services and support available through ILARIS Companion. Visit **www.ILARISHCP.com**

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

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.

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.

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

References: 1. Jamilloux Y, Gerfaud-Valentin M, Martinon F, Belot A, Henry T, Sève P. Pathogenesis of adult-onset Still's disease: new insights from the juvenile counterpart. *Immunol Res.* 2015;61(1-2):53-62. doi:10.1007/s12026-014-8561-9 **2.** Rossi-Semerano L, Koné-Paut I. Is Still's disease an autoinflammatory syndrome? *Int J Inflam.* 2012;2012:480373. doi:10.1155/2012/480373 **3.** Lee JJY, Schneider R. Systemic juvenile idiopathic arthritis. *Pediatr Clin North Am.* 2018;65(4):691-709. doi:10.1016/ j.pcl.2018.04.005 **4.** Efthimiou P, Paik PK, Bielory L. Diagnosis and management of adult onset Still's disease. *Ann Rheum Dis.* 2006;65(5):564-572. doi:10.1136/ard.2005.042143 **5.** ILARIS [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2020. **6.** Data on file. CACZ885G2305 SJIA Study 1 Clinical Study Report. Novartis Pharmaceuticals Corporation; 2011. **7.** Ruperto N, Brunner HI, Quartier P, et al; PRINTO; PRCSG. Two randomized trials of canakinumab in systemic juvenile idiopathic arthritis. *N Engl J Med.* 2012;367(25):2396-2406. doi:10.1056/NEJMoa1205099 **8.** Data on file. CACZ885G2301 SJIA Study 2 Clinical Study Report. Novartis Pharmaceuticals Corporation; 2012. **9.** Data on file. ILARIS Commercial Access Coverage 6/2020. Novartis Pharmaceuticals Corporation; 2020. **10.** Data on file. ILARIS CRM Executive Summary Report 12/1/2018-12/31/2019. Novartis Pharmaceuticals Corporation; 2019. **11.** Data on file. ILARIS Dispense Analysis (Time to Dispense) 1/2019-12/2019. Novartis Pharmaceuticals Corporation; 2020.

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ILARIS® (canakinumab) 150 mg subcutaneous injection

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