See pages 2 and 10 for recommended dosing

Preparation and Injection

ILARIS® 150 mg Powder for Solution for Injection

A guide for patients and health care professionals for reconstituting and administering ILARIS® for the treatment of Systemic Juvenile Idiopathic Arthritis (SJIA)

ILARIS®
(canakinumab)
150 mg subcutaneous injection

Before You Begin

What is ILARIS®

ILARIS® is used to treat active Systemic Juvenile Idiopathic Arthritis in patients aged 2 years and older *if other treatments have not worked well enough. ILARIS® can be used alone or in combination with methotrexate (text in italic: in the EU SmPC).*

It is suitable for adults and children aged 2 years and older with body weight of 7.5 kg or above.

ILARIS® is conveniently injected under the skin as a single dose of 4 mg/kg (up to a maximum of 300 mg) once every 4 weeks. The simple step-by-step instructions provided will make preparing and injecting ILARIS® easier. Preparing the injection takes about 30 minutes.

Your doctor will tell you the right dose of ILARIS® to use. Your dose: _____

Important Reminder

You and your doctor should decide together whether or not you will inject ILARIS® yourself. If you will be injecting ILARIS® yourself, then your doctor will show you the proper way to do it. Do not try to inject yourself if you have not been properly trained, or if you are not sure how.

Read these instructions all the way through. If you have any questions about any of the steps, talk with your doctor before getting started. This guide is intended to remind you how to inject ILARIS®. See the full instructions for use in the package leaflet. Then:

- Find a clean place to prepare and inject ILARIS®
- Wash your hands with soap and water
- Check the expiry dates on the vials and syringes. Do not use after expiry date
- Always use new, unopened needles and syringes. Do not touch the needles and the tops of the vials

Prescribing Considerations

- Each vial should be used for one dose only
- Use the medicine immediately after you reconstitute the solution
-
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- The vials contain more medicine than you will need. Be sure to withdraw only the amount needed for your dose
- The smallest volume that can reliably be withdrawn using a 1.0 mL syringe is 0.2 mL

Getting Started...

Gather together the items you will need

Included in the pack

- One vial ILARIS® powder

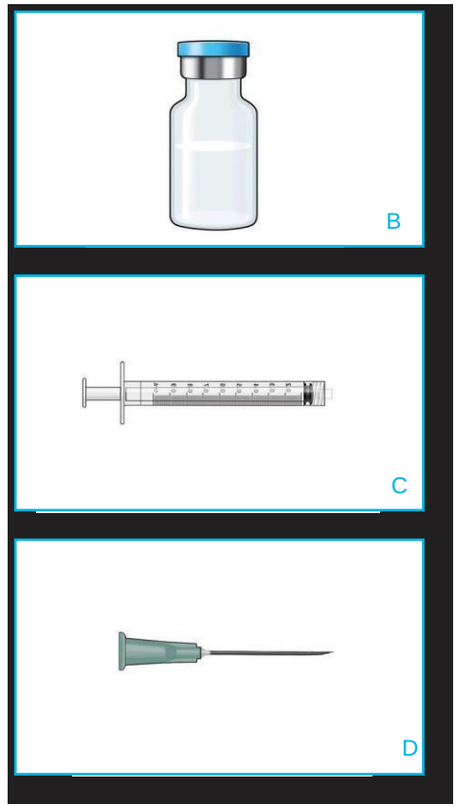
Important storage instructions
Always follow these storage instructions for ILARIS®:

- Store in a refrigerator (2°C-8°C)
- Do not freeze
- Store in the original package in order to protect from light

If ILARIS® is not used immediately as directed upon reconstitution:

- Refrigerate (2°C-8°C) and use within 24 hours

Not included in the pack



-
  (do not refrigerate)
- One 1.0 mL syringe
- One 18 G x 2" (50 mm) needle for reconstituting the powder ("transfer needle")

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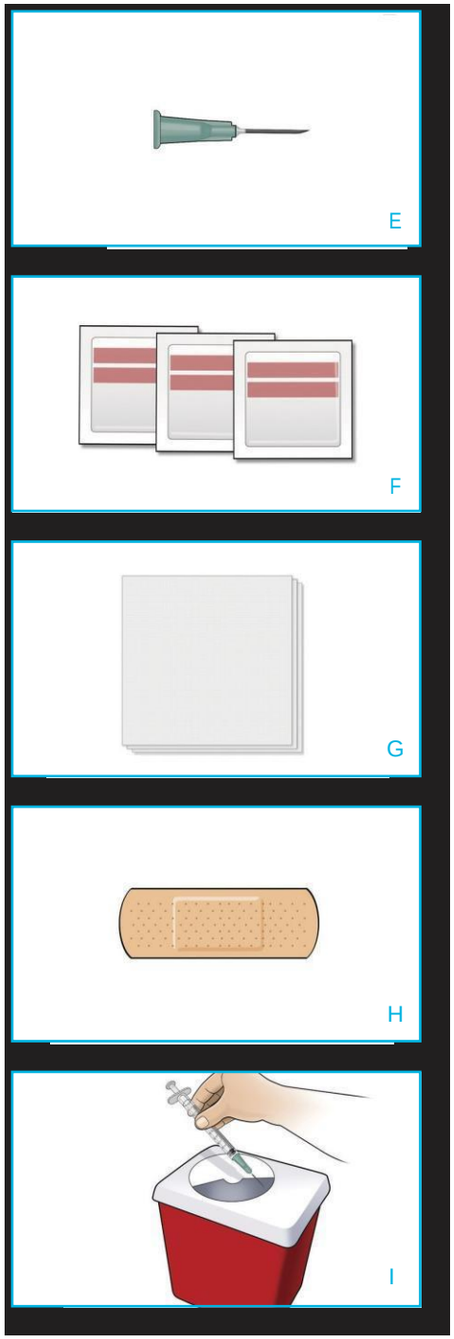
Getting Started (cont'd)

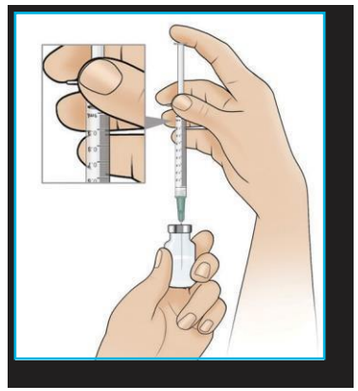


- One 27 G x 0.5" (13 mm) needle for injecting ("injection needle")
- Alcohol swabs
- Clean, dry cotton swabs
- An adhesive bandage
- A proper container for disposing of used needles, syringe, and vials (sharps container)

How to Mix ILARIS®

Dissolve the powder

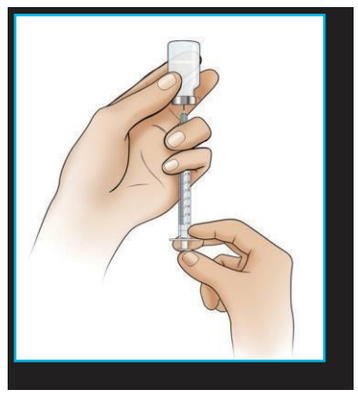
First...



1. Remove the protective caps from the "ILARIS®" (A) and "water" (B) vials. Do not touch the vial stoppers. Clean the stoppers with the alcohol swab (F).
2. Open the wrappers containing the "syringe" (C) and the "transfer needle" (D) and attach the needle to the syringe.
3. Carefully remove the cap from the transfer needle and set the cap aside. Pull the plunger all the way down to the 1.0 mL mark, filling the syringe with air. Push the needle into the

   rubber stopper.
4. Gently push the plunger all the way down until air is injected into the vial.

Next...



5. Turn the vial and syringe upside down together and bring to eye level.
6. Make sure the tip of the transfer needle is covered by the water and slowly pull the syringe plunger down to slightly past the 1.0 mL mark. If you see bubbles in the syringe, remove them as instructed by your doctor or pharmacist.
7. Make sure 1.0 mL of water is in the syringe, then withdraw the needle from

   in the vial.)

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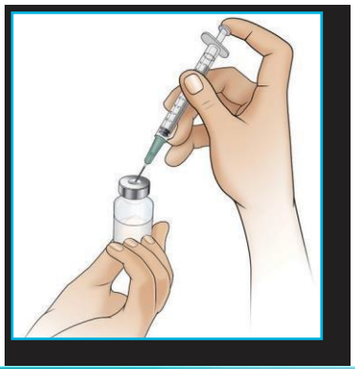
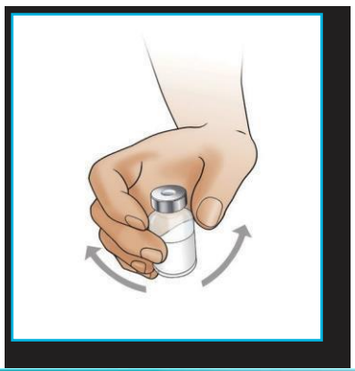
How to Mix ILARIS® (cont'd)

You're getting there...



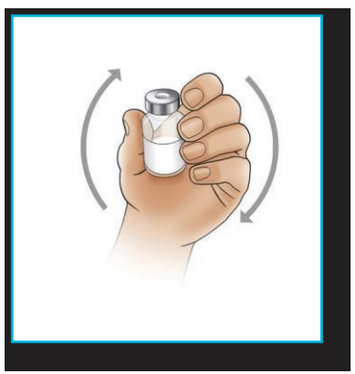
8. Push the transfer needle through the centre of the stopper of the vial of ILARIS® powder, without touching the needle or the stopper. Slowly inject 1.0 mL of sterile water into the vial.
9. Carefully remove the syringe with the transfer needle from the vial. Then, recap the needle as instructed by your doctor or pharmacist.

Almost done...



10. Without touching the rubber stopper, swirl (do not shake) the vial slowly at an angle of about 45 degrees for about 1 minute. Allow to stand for 5 minutes.

Just a few more steps...

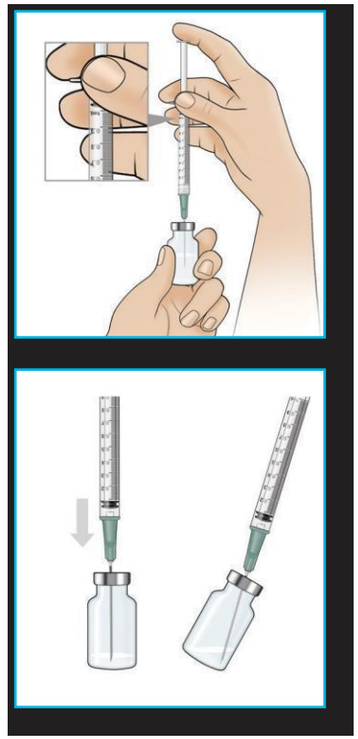


11. Now, gently turn the vial upside down and back again 10 times, without touching the rubber stopper.
12. Allow the vial to stand for about 15 minutes at room temperature until the liquid becomes clear or nearly clear. Do not shake. Do not use if the solution looks murky.
13. Make sure all of the solution is in the bottom of the vial. If drops remain on the stopper, tap the side of the vial to remove them. The solution should be a clear to nearly clear liquid.

If you are not going to use the solution right away, it should be stored in the refrigerator (2°C-8°C) and used within 24 hours.

Preparing the injection

You are now ready to prepare the ILARIS® injection.



14. Clean the rubber stopper on the vial holding the ILARIS® solution with a new alcohol swab.
15. Uncap the transfer needle again. Pull the plunger of the syringe all the way down to the 1.0 mL mark, filling the syringe with air. Stick the syringe needle into the vial of ILARIS® solution through the centre of the rubber stopper. Then, gently push the plunger all the way down until air is injected into the vial. Do not inject air into the medicine.
16. Do not turn the vial and syringe upside down. Push the needle all the way into the vial until it reaches the bottom edge.
17. Tip the vial so that the needed amount of solution can be pulled into the syringe. The amount depends on the dose to be injected (0.2 mL to 1.0 mL). Your doctor will instruct you on the right amount for you.
18. Slowly pull the syringe plunger up to the correct mark (0.2 mL to 1.0 mL), filling the syringe with ILARIS® solution. If there are air bubbles in the syringe, remove them as instructed by your doctor. Be sure that the correct amount of solution is in the syringe.
19. Remove the syringe and needle from the vial. (There may be solution remaining in the vial.) Recap the transfer needle as instructed by your doctor or pharmacist. Remove the transfer needle from the syringe. Place the transfer needle in the sharps container (I).
20. Open the wrapper containing the "injection needle" (E) and attach it to the syringe. Set the syringe aside.

If you have any questions about how to prepare the ILARIS® injection, contact your doctor or nurse.

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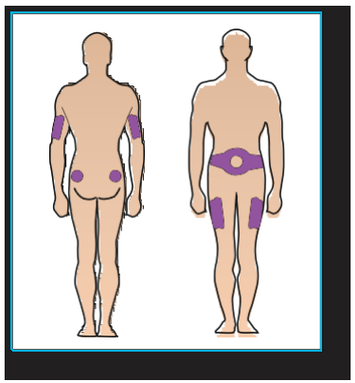
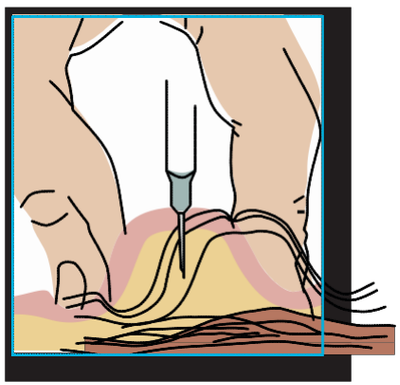
Giving the Injection

You can do it...





21. Choose an injection site on the upper arm, upper thigh, abdomen, or buttocks. Do not use an area that has a rash or broken skin, or is bruised or lumpy. Do not inject into scar tissue, as this may keep ILARIS® from working as well as it should. Avoid injecting into a vein.

22. Clean the injection site with a new alcohol swab. Allow the area to dry. Uncap the injection needle.

23. Gently pinch the skin up at the injection site. Hold the syringe at a 90-degree angle and in a single, smooth motion, push the needle straight down completely into the skin.

24. Keep the needle all the way in the skin while slowly pushing the syringe plunger down until the barrel is empty. Release the pinched skin and pull the needle straight out. Dispose of the needle and syringe in the sharps container, without recapping or removing the needle.

After the Injection

You're just about done...

25. Do not rub the injection area. If there is any bleeding, place a clean, dry cotton swab over the area and press gently for 1 to 2 minutes, or until the bleeding stops. Then put on an adhesive bandage (H).

26. Be sure to place the needles and syringe in the sharps container or as your doctor or pharmacist instructs you. Never use any of the syringes or needles more than once.

27. Properly dispose of the vials containing the remaining water and ILARIS® solution (if any is left) as your doctor or pharmacist instructs you. Dispose of any unused product or waste material as your community requires.

Keep the sharps container out of reach of children. Dispose of it as directed by your doctor or pharmacist.

If you have any questions about how to inject ILARIS®, contact your doctor or nurse.

ILARIS®
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150 mg subcutaneous injection

The recommended dose of ILARIS® for SJIA patients, aged 2 years and older

- 4 mg/kg (up to a maximum of 300 mg) for patients with body weight ≥7.5 kg
- This is administered every 4 weeks as an injection under the skin
- These calculations are based on using ILARIS® 150 mg reconstituted in 1.0 mL of sterile water

Weight range (kg)*	4 mg/kg dose	
	Volume (mL)	Dose (mg)
7.5-8.5	0.2	30
>8.5-10	0.25	37.5
>10-12	0.3	45
>12-14	0.35	52.5
>14-<16	0.4	60
16-<18	0.45	67.5
18-<20	0.5	75
20-<22	0.55	82.5
22-23	0.6	90
>23-25	0.65	97.5
>25-27	0.7	105
>27-29	0.75	112.5
>29-<31	0.8	120
31-<33	0.85	127.5
33-<35	0.9	135
35-<37	0.95	142.5
37-<39	1	150
39-<41#	1.05	157.5
41-42#	1.1	165
>42-44#	1.15	172.5
>44-46#	1.2	180
>46-48#	1.25	187.5
>48-50#	1.3	195
>50-52#	1.35	202.5
>52-<54#	1.4	210
54-55#	1.45	217.5
>55-57#	1.5	225
>57-59#	1.55	232.5
>59-61#	1.6	240
>61-63#	1.65	247.5
>63-65#	1.7	255
>65-67#	1.75	262.5
>67-<68#	1.8	270
68-<71#	1.85	277.5
71-<73#	1.9	285
73-74#	1.95	292.5
>74->75#	2	300

* Dosing accuracy has been established for patients 7.5 kg or more with a dose of 4 mg/kg. Prior to dosing, please ensure that the most current body weight is considered.

For these body weights, two vials of ILARIS® are needed.

NOVARTIS PHARMACEUTICALS

ILARIS®
(canakinumab)
150 mg subcutaneous injection

Important note: Before prescribing, consult full prescribing information, including instructions for use. **Presentation:** canakinumab. Powder for solution for subcutaneous injection or powder and solvent for solution for injection (convenience kit). Each vial contains 150 mg of canakinumab. **Indications:** •Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflammatory Syndrome (FCAS) / Familial Cold Urticaria (FCU), Muckle-Wells Syndrome (MWS•Systemic Juvenile Idiopathic Arthritis (SJIA) in patients aged 2 years and older. •. **Dosage and administration:** •For **CAPS** patients (adults and children): 150 mg or 2 mg/kg for patients ≥4 years with body weight of more than 40 kg or between 15 kg and 40 kg, respectively.. With starting dose of 150 mg or 2 mg/kg, if rash and generalized inflammation symptoms do not resolve seven days after treatment start, a second dose of 150 mg or 2 mg/kg can be considered. If a satisfactory clinical response has not been achieved 7 days after this increased dose, a third dose at 300 mg or 4 mg/kg can be considered. With a starting dose of 4 mg/kg, if a satisfactory clinical response has not been achieved after 7 days, a second dose of 4 mg/kg can be considered. Administered every 8 weeks as a single dose via subcutaneous injection. •For **SJIA:** the recommended dose of ILARIS® for SJIA patients with a body weight of 7.5 kg and above is 4 mg/kg (up to a maximum of 300 mg). •Administered every 4 weeks via subcutaneous injection. For maximum effect. Patients who do not respond to an initial treatment should not be retreated with ILARIS®. In patients who respond and require re-treatment, there should be an interval of at least 12 weeks before a new dose of ILARIS® may be administered. Management of hyperuricemia with appropriate urate lowering therapy (ULT) should be instituted or optimised. •ILARIS® should be administered by a healthcare professional. **Contraindications:** Confirmed hypersensitivity to the active substance or to any of the excipients.
Warnings/Precautions: •**Infections:** associated with serious infections, exercise caution when administering to patients with chronic infections, history of recurring infections, underlying conditions which may predispose them to infections. Treatment of gouty arthritis: should not be administered during an active infection. Treatment of CAPS: should not be initiated or continued in patients with an active infection requiring medial intervention. Concomitant use with tumor necrosis factor (TNF) inhibitors not recommended as may increase risk of serious infections. •**Tuberculosis and opportunistic infections:** may increase the riskof reactivation of tuberculosis or other opportunistic infections; before, during and after treatment patients should be monitored for active and latent tuberculosis infection. Due to potential false positive PPD skin test results, alternative means of screening for a tuberculosis infection should be considered for patients presenting with a positive PPD test while treated. •**Malignancy events:** The risk of malignancies with anti-interleukin-1 therapy is unknown. •**Hypersensitivity:** as with other injectable proteins, hypersensitivity reactions can occur, no anaphylactoid or anaphylactic reactions reported. •**Vaccinations:** should not be given concurrently with live vaccines. •**Neutropenia:** should not be initiated in patients with neutropenia. Assess neutrophil count prior to use.
•**Macrophage activation syndrome (SJIA):** Macrophage activation syndrome (MAS) is a known, life-threatening disorder that may develop in patients with rheumatic conditions, in particular SJIA, and should be aggressively treated. Physicians should be attentive to symptoms of infection or worsening of SJIA, as these are known triggers for MAS. Based on the clinical trial experience, ILARIS® does not appear to increase the incidence of MAS in SJIA patients, but no definitive conclusion can be made. •**Women of child-bearing potential, pregnancy:** should not be used in pregnant women unless clearly necessary and not recommended during breast-feeding. **Adverse reactions: Very common (≥10%):** infections (e.g. nasopharyngitis, sinusitis, (viral) upper respiratory tract infection, pneumonia, rhinitis, pharyngitis, tonsillitis, sinusitis, bronchitis, ear infection, cellulitis, urinary tract infection, influenza, gastroenteritis, viral infection), abdominal pain (upper), injection site reaction. **Common (1 to 10%):** back pain, fatigue/asthenia, dizziness/vertigo, laboratory abnormalities. **Uncommon (0.1 to 1%):** gastroesophageal reflux disease. **Adverse reaction from spontaneous report:** opportunistic infections. **Interactions:** CYP450 substrates with a narrow therapeutic index: Upon initiation therapeutic monitoring of the effects or active substance should be performed with individual dose adjustment when needed. **Packs and prices:** Country specific. **Legal classification:** Country specific.

References: 1. Kuemmerle-Deschner JB, Ramos E, Blank N, et al. Canakinumab (ACZ885, a fully human IgG1 anti-IL-1b mAb) induces sustained remission in pediatric patients with cryopyrin-associated periodic syndrome (CAPS). *Arthritis Res Ther*. 2011;13(1):R34. **2.** Yu JR, Leslie KS. Cryopyrin-associated periodic syndrome: an update on diagnosis and treatment response. *Curr Allergy Asthma Rep*. 2011;11(1):12-20. **3.** Lachmann HJ, Kone-Paut I, Kuemmerle-Deschner JB, et al. Use of canakinumab in the cryopyrin-associated periodic syndrome. *N Engl J Med*. 2009;360(23):2416-2425. **4.** Toker O, Haskes PJ. Critical appraisal of canakinumab in the treatment of adults and children with cryopyrin-associated periodic syndrome (CAPS). *Biologics*. 2010;4:131-138. **5.** Krause K, Gratten CE, Bindslev-Jensen C, et al. How not to miss autoinflammatory disease masquerading as urticaria. *Allergy*. 2012;67(12):1465-1474. **6.** Miyamae T. Cryopyrin- associated periodic syndromes. Diagnosis and management. *Pediatr Drugs*. 2012;14(2):109-117. **7.** Haas N, Küster W, Zuberbier T, Henz BM. Muckle-Wells syndrome: clinical and historical skin findings compatible with cold air urticaria in a large kindred. *Br J Dermatol*. 2004;151(1):99-104. **8.** Gandi C, Healy C, Wanderer AA, Hoffman HM. Familial atypical cold urticaria: description of a new hereditary disease. *J Allergy Clin Immunol*. 2009;124:1245-50. **9.** Siebenhaar F, Weller K, Mlynek A, et al. Acquired cold urticarial: clinical picture and update on diagnosis and treatment. *Clin Exp Dermatol*. 2007;32(3):241-245. **10.** Krause K, Zuberbier T, Maurer M. Modern approaches to the diagnosis and treatment of cold contact urticaria. *Curr Allergy Asthma Rep*. 2010;10(4):243-249. **11.** Zuberbier T. Chronic urticaria. *Curr Allergy Asthma Rep*. 2012;12(4):267-272. **12.** Schaefer P. Urticaria: evaluation and treatment. *Am Fam Physician*. 2011;83(9):1078-1084. **13.** de Jesus AA, Goldbach-Mansky R. Monogenic autoinflammatory diseases: concept and clinical manifestations. *Clin Immunol*. 2013;147:155-174. **14.** ILARIS® (canakinumab) Summary of Product Characteristics. Novartis, 2013.

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

† Images courtesy of PD Dr Norbert Blank, Uniklinik Heidelberg, Germany, and Dr Gordon Sussman, University of Toronto, Canada.

‡ Complete response (clinical and biomarker) and disease relapse/flare defined as composite of: physician's global assessment of autoinflammatory disease activity and assessment of skin disease ≤minimal and CRP or SAA values <10 mg/L. Physician's global assessment of disease activity was based upon a composite of the following symptoms: urticarial skin rash, fatigue/malaise, conjunctivitis, headache/migraine, myalgia, and arthralgia.3

You can report any problem or adverse events through:

Novartis Consulting AG.
Saudi Arabia: P.O. Box 16032, Riyadh 11464, Tel: +966114658882
DS&E
Phone: +996112658100
Fax: +966112658107
Email: adverse.events@novartis.com

National Pharmacovigilance and drug safety Center
Toll free phone: 8002490000
Fax: +966112057662
E-mail: npc.drug@sfda.gov.sa
Or by online: https://ade.sfda.gov.sa

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