

## PART III: CONSUMER INFORMATION

### **P<sup>r</sup>SIGNIFOR<sup>®</sup> LAR<sup>®</sup>** Pasireotide for injectable suspension

This leaflet is part III of a three-part "Product Monograph" published when SIGNIFOR LAR was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about SIGNIFOR LAR. Contact your doctor or pharmacist if you have any questions about the drug.

#### ABOUT THIS MEDICATION

##### What the medication is used for:

SIGNIFOR LAR is used to treat Acromegaly and Cushing's disease. It is used in adults who cannot have surgery or for whom surgery has not worked well enough. It is not known if SIGNIFOR LAR is safe and effective for use in children or adolescents under 18 years old.

Acromegaly is caused by an enlargement in the pituitary gland called a pituitary adenoma. This adenoma causes the body to make too much growth hormone. This hormone normally controls how tissues, organs, and bones grow. Thus, too much growth hormone can cause bones and tissues (especially those in the hands and feet) to increase in size.

Cushing's disease is caused when a pituitary adenoma makes too much of a hormone called adrenocorticotrophic hormone (ACTH). This then causes the body to make too much of another hormone called cortisol. Too much cortisol can cause weight gain especially around the body, moon-shaped face, excess sweating, thinning of skin with easy bruising and dryness as well as muscle and bone weakness, menstrual abnormalities, excessive body and facial hair, muscle wasting with generalized weakness and tiredness, depression, and decreased libido.

SIGNIFOR LAR should only be prescribed by a qualified doctor. It can be given by qualified health care providers. They work under the supervision of that doctor.

##### What it does:

In Acromegaly, SIGNIFOR LAR lowers the production of growth hormone and insulin-like growth factor-1 to reduce the symptoms of acromegaly.

In Cushing's disease, SIGNIFOR LAR lowers the production of ACTH to lower the production of cortisol and reduce symptoms.

##### When it should not be used:

- If you are allergic to pasireotide or to any other ingredient in the medication or its container
- If you have moderate or severe liver problems

- If you have uncontrolled diabetes
- If you are pregnant
- If you are a woman of childbearing potential and not using contraception (birth control)
- If you are breastfeeding
- If you have heart problems

##### What the medicinal ingredient is:

Pasireotide pamoate

##### What the important nonmedicinal ingredients are:

**Vial:** Poly (D,L-lactide-co-glycolide) (50-60:40-50), Poly(D,L-lactide-co-glycolide) (50:50).

**Pre-filled syringe:** Carmellose sodium, mannitol, poloxamer 188, water for injections.

##### What dosage forms it comes in:

SIGNIFOR LAR is a powder and solvent for injection.

Powder: Slightly yellowish to yellowish powder in vial.

Solvent for suspension for injection: clear, colorless to slightly yellow to slightly brown solution in pre-filled syringe.

SIGNIFOR LAR is available as powder in vials and is supplied in a kit which includes:

- One vial containing SIGNIFOR LAR powder 10 mg, 20 mg, 30 mg, 40 mg, or 60 mg pasireotide for injectable suspension.
- One pre-filled syringe containing 2 mL of the diluent solution for reconstitution. There is a peel-off label on this syringe.
- One vial adapter to be used for delivering the diluent from the pre-filled syringe to the vial, without a needle.
- One safety injection needle (20G x 1.5").
- An instruction booklet
- The package insert

#### WARNINGS AND PRECAUTIONS

##### Serious Warnings and Precautions

Serious side effects include:

- Liver problems
- Heart problems (i.e. slow or irregular heart beat)
- Changes in blood glucose levels

##### **BEFORE you use SIGNIFOR LAR talk to your doctor or pharmacist if:**

- You have problems with your blood sugar levels, either too high (hyperglycemia) or too low (hypoglycemia).
- You have diabetes.
- You have problems with your liver.

- You have severe kidney problems.
- You have or have had heart problems including an abnormal heart rate or rhythm, or problems with the electrical system of your heart called QT prolongation.
- You take medicines to control your heart beat (anti-arrhythmics) or medicines that may affect the way the electrical system of your heart works.
- You have low levels of potassium or magnesium in your blood.
- You have conditions such as severe vomiting, diarrhea, dehydration.
- You have a history of fainting or near fainting spells.
- You have gallstones (cholelithiasis).
- You have low levels of pituitary hormones.
- You are pregnant, may be pregnant, or thinking of becoming pregnant. It is not known if SIGNIFOR LAR will harm your unborn baby.
- You are breastfeeding. It is not known if SIGNIFOR LAR passes into breast milk.
- You take medicines to control your blood pressure (such as beta-blockers or calcium channel blockers).
- You take medicines that affect how your blood clots.
- You take medicines to control electrolytes (potassium, magnesium) levels in your body.
- Your doctor may wish to check your blood sugar levels. You may need to start taking medicines to control your blood sugar levels or your doctor may adjust the medicines you are now taking to control your blood sugar levels.

**Before you receive SIGNIFOR LAR for the first time,** your doctor should do certain tests including:

- Blood test to check your fasting blood sugar and hemoglobin A1c levels
- Liver function tests
- Electrolytes level tests
- Electrocardiogram, to measure the electrical activity of the heart
- Gallbladder ultrasound

**These tests should be repeated during treatment.**

You will need to check your blood sugar levels during treatment with SIGNIFOR LAR, especially after you start treatment with SIGNIFOR LAR and after your dose is increased. Your doctor will tell you how often you should check your blood sugar levels.

Your doctor may wish to check your gallbladder, liver enzymes, and pituitary hormones on a regular basis.

**During your treatment with SIGNIFOR LAR**

Tell your doctor straight away if:

- You are feeling very weak
- You lose weight

- You have nausea or vomiting
- You have low blood pressure

If you get hyperglycemia (high blood sugar levels) while receiving SIGNIFOR LAR, your doctor may give you another medicine to lower your blood sugar. Your doctor may also change your dose of SIGNIFOR LAR or advise you to stop receiving it.

**Children and adolescents (under 18 years old)**

SIGNIFOR LAR is not to be used in children or adolescents.

To prevent pregnancy, female patients of childbearing potential should use adequate birth control. The ability to get pregnant can change because you are taking SIGNIFOR LAR. If you want to get pregnant, you must wait two months after stopping SIGNIFOR LAR. Discuss this with your doctor.

**Driving and Using Machines:** Before you perform tasks which may require special attention, wait until you know how you respond to SIGNIFOR LAR as fatigue, headache, or dizziness can occur.

## INTERACTIONS WITH THIS MEDICATION

**Tell your doctor or pharmacist if you are taking or recently took any other medicines,** including prescription medicines, medicines you got without a prescription, vitamins, and herbal supplements.

SIGNIFOR LAR and other medicines may affect each other, causing side effects. SIGNIFOR LAR may affect the way other medicines work, and other medicines may affect how SIGNIFOR LAR works. Your doctor may need to change your dose of SIGNIFOR LAR or your other medicines. You must tell your doctor if you are taking any of the following medicines.

The following list includes some, but not all, of the drugs that may increase the risk of heart rhythm problems while receiving SIGNIFOR LAR. You should check with your doctor or pharmacist before taking any other medication with SIGNIFOR LAR.

**Drugs that may interact with SIGNIFOR LAR include:**

- Anti-arrhythmics used to treat irregular heart beat such as amiodarone, disopyramide, procainamide, quinidine, sotalol, ibutilide, dronedarone, flecainide, propafenone
- Medicines that may have an unwanted effect on the function of the heart (QT prolongation) such as:
  - Antipsychotics (e.g., haloperidol, pimozide, droperidol, ziprasidone, chlorpromazine)
  - Antidepressants (e.g., imipramine, citalopram, amitriptyline, maprotiline, venlafaxine)
  - Methadone
  - Antibiotics (e.g., clarithromycin, moxifloxacin, erythromycin, azithromycin, tacrolimus, levofloxacin, ciprofloxacin)
  - Antimalarials (e.g., chloroquine, quinine)

- Antifungals (e.g., ketoconazole, fluconazole, voriconazole)
- Dopamine receptor antagonists (e.g. domperidone)
- Antiemetics (e.g., intravenous ondansetron)
- Cancer drugs (e.g., sunitinib, nilotinib, vandetanib, lapatinib, vorinostat)
- Asthma drugs (e.g., formoterol, salmeterol)
- Diuretics (water pills)
- Laxatives and enemas
- Amphotericin B
- High dose corticosteroids
- Medicines that decrease heart rate and prolong the PR interval
  - Antihypertensives (e.g., atenolol, diltiazem, verapamil, clonidine)
  - Drugs to treat heart failure (e.g., digoxin)
  - Drugs to treat multiple sclerosis (e.g., fingolimod)
  - Drugs to treat HIV infection (e.g., atazanavir)
- Certain other medicines, such as cyclosporine, bromocriptine
- Medicines that work to prevent blood clots (anticoagulants)
- Antidiabetic drugs, including insulin and oral medicines

This list includes some, but not all, of the drugs that may increase the risk of side effects while receiving SIGNIFOR LAR. Tell your doctor or pharmacist if you are taking these or any other medicines even those not prescribed (including any over the counter drugs, vitamins, or herbal medicines).

### PROPER USE OF THIS MEDICATION

SIGNIFOR LAR is a powder and solvent for injection.

Powder: Slightly yellowish to yellowish powder in vial.

Solvent for suspension for injection: clear, colorless to slightly yellow to slightly brown solution in pre-filled syringe.

Do not use SIGNIFOR LAR if you notice the powder in the vial has changed its color, if you notice that the solvent is not clear or contains particles.

Your health care provider will mix and examine SIGNIFOR LAR before the injection.

**Only** use SIGNIFOR LAR if the suspension is milky, slightly yellowish to yellowish and homogeneous with no visible particles.

#### Usual dose:

#### **Recommended Initial Dose:**

- Acromegaly: 40 mg every 4 weeks.
- Cushing's disease: 10 mg every 4 weeks.

Depending on test results or on how you feel, your doctor may prescribe a higher or a lower dose.

SIGNIFOR LAR is injected:

- By your doctor or nurse (only by a trained healthcare provider)
- Deep into the muscle of the buttocks
- Every 4 weeks
- Alternately into the left and right buttocks

Your doctor will tell you how much SIGNIFOR LAR you will receive and when you will receive it. Your doctor may change the dose of SIGNIFOR LAR or the length of time between your injections.

If you have any questions, contact your doctor, nurse or pharmacist.

#### **How long to take SIGNIFOR LAR**

Your doctor will regularly check your condition to see if the treatment is working. Your doctor will tell you how long you need to receive SIGNIFOR LAR and when you may need to stop taking it temporarily or permanently.

#### **Overdose:**

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

#### **Missed Dose:**

If you miss your injection, please contact your doctor as soon as possible.

### SIDE EFFECTS AND WHAT TO DO ABOUT THEM

The common side effects of SIGNIFOR LAR include:

- Diarrhea, nausea, abdominal pain, abdominal discomfort, bloating, vomiting, loss of appetite, constipation, gas, indigestion, frequent bowel movements
- Hair loss
- Headache, dizziness
- fainting
- Altered sense of taste
- Insomnia
- Pain, discomfort, itch and swelling at the injection site
- Back pain
- Fatigue
- Fatigue, weakness, inactivity
- Dry, peeling or flaking skin
- Itching
- Eye irritation, blurred vision
- Chest pain
- Muscle pain, muscle spasm, joint pain

- High blood pressure
- Limb swelling
- Increase in the level of some enzymes or substances in your blood (e.g., creatinine phosphokinase, alkaline phosphatase, lactate dehydrogenase, uric acid, urea, creatinine, triglycerides, lipids)

If any of these affects you severely, **tell your doctor.**

SIGNIFOR LAR can cause abnormal blood test results. Your doctor will decide when to perform blood tests and will interpret the results.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM			
Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if severe	In all cases	
<b>Very Common</b>			
<b>High level of sugar in the blood (hyperglycemia) or diabetes:</b> Excessive thirst, high urine output, increased appetite with weight loss, tiredness, nausea, vomiting, abdominal pain			√
<b>Gallstones (cholelithiasis) or complications:</b> Sudden back pain or pain on the right side of your abdomen, sudden pain in your right shoulder or between your shoulder blades, yellowing of your skin and whites of your eyes, fever with chills, nausea			√
<b>Common</b>			
<b>Low cortisol Levels (hypocortisolism):</b> Extreme weakness, weight loss, nausea, vomiting, low blood pressure			√
<b>Low level of red blood cells (anemia):</b> Tiredness, fatigue, pale skin			√
<b>Slow heart Beat (bradycardia):</b> Weakness, tiredness, shortness of breath, light-headedness, fainting or near fainting			√
<b>Changes in the electrical system of your heart (Prolonged QT interval):</b> Dizziness, palpitations, fainting or near fainting, seizures			√

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM			
Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if severe	In all cases	
<b>Liver Disorder (higher than normal liver function tests):</b> Itching, yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite			√
<b>Inflammation of the Pancreas (pancreatitis):</b> Abdominal pain that lasts, radiates to your back, or gets worse when you lie down, indigestion, nausea, vomiting, diarrhea, swollen and tender abdomen, and bloating			√
<b>Change in blood coagulation parameters:</b> Severe bruising or unusual bleeding from the skin or other areas			√
<b>Inflammation of the gallbladder (cholecystitis):</b> Severe pain in your upper right abdomen, pain that radiates to your shoulder or back, nausea, vomiting, fever			√
<b>Reported from Post-Marketing with Unknown Frequency</b>			
<b>Increased ketones in your urine or blood:</b> fruity scented breath, trouble breathing, confusion			√

*This is not a complete list of side effects. For any unexpected effects while taking SIGNIFOR LAR, contact your doctor or pharmacist.*

### HOW TO STORE IT

- Keep out of the reach and sight of children.
- Do not use SIGNIFOR LAR after the expiry date, which is stated on the carton box.
- Store at 2 to 8°C.
- Do not freeze.

Medicines should not be thrown away in household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

### **Reporting Side Effects**

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

*NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

### **MORE INFORMATION**

This document plus the full product monograph, prepared for health professionals, can be found at [www.novartis.ca](http://www.novartis.ca) or by contacting the sponsor, Novartis Pharmaceuticals Canada Inc., at 1-800-363-8883.

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This leaflet was prepared by:  
Novartis Pharmaceuticals Canada Inc.  
385 Bouchard Blvd.  
Dorval, Quebec  
H9S 1A9

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