1.3.2.1 Patient Information Leaflet

SCHEDULING STATUS

S4

SIGNIFOR® LA 20 mg, powder for suspension for injection

SIGNIFOR® LA 40 mg, powder suspension for injection

SIGNIFOR® LA 60 mg, powder for suspension for injection

Pasireotide

Contains sugar: Mannitol 90.0 mg in 2 ml solution

SIGNIFOR LA solvent for suspension for injection

Read all of this leaflet carefully before you are given SIGNIFOR LA

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.

What is in this leaflet

1. What SIGNIFOR LA is and what it is used for.

2. What you need to know before you are given SIGNIFOR LA.

3. How SIGNIFOR LA will be given.

4. Possible side effects.

5. How to store SIGNIFOR LA.

6. Contents of the pack and other information.

1. What SIGNIFOR LA is and what it is used for

- SIGNIFOR LA is used to treat acromegaly in adults.
- Acromegaly is caused by a type of tumour called a pituitary adenoma which develops in the pituitary gland at the base of the brain. The adenoma leads the body to over produce hormones that control growth of tissues, organs and bones, resulting in an increase in the size of bones and tissues, especially in the hands and feet.
- SIGNIFOR LA reduces the production of these hormones and possibly also the size of the adenoma. As a result, it reduces the symptoms of acromegaly, which include headache, increased sweating, numbness of the hands and feet, tiredness and joint pain.

If you have any questions about how SIGNIFOR LA works or why this medicine has been prescribed for you, ask your doctor.

2. What you need to know before you are administered SIGNIFOR LA

SIGNIFOR LA should not be administered to you:

- if you are hypersensitive (allergic) to pasireotide or any of the other ingredients of SIGNIFOR LA (listed in section 6);
- if you suffer from severe liver disorder.

If this applies to you, do not use SIGNIFOR LA and tell your doctor.

Warnings and precautions

Tell your doctor or healthcare provider before being given the injection if:

- you currently have or ever had problems with your blood sugar levels, either too high (hyperglycaemia/diabetes) or too low (hypoglycaemia);

- you have heart disorders or a heart rhythm disorder, such as an irregular heartbeat or an abnormal electrical signal called “prolongation of the QT interval”, or “QT prolongation”;
- you recently had a heart attack, have congestive heart failure (a type of heart disease where the heart cannot pump enough blood around the body) or sudden and oppressive chest pain (usually felt as pressure, heaviness, tightening, squeezing or aching across the chest);
- you have low levels of potassium or magnesium in your blood;
- you have gallstones;
- or if you are taking anticoagulants (medicines used to reduce the clotting ability of the blood), your doctor will monitor your coagulation parameters and may adjust your anticoagulant dose.

Tell your doctor or pharmacist immediately if you get any of the following symptoms during treatment with SIGNIFOR LA:

- SIGNIFOR LA controls over-production of cortisol. If you experience any signs or symptoms ~~like~~ such as extreme weakness, weight loss, nausea, vomiting, low blood pressure (potential signs of a low level of cortisol), tell your doctor straight away.

Monitoring during your treatment with SIGNIFOR LA:

- SIGNIFOR LA may cause your blood sugar to increase. Your doctor will monitor your blood sugar levels and may need to start you on or adjust your antidiabetic medication.
- SIGNIFOR LA may lower your heart rate. Your doctor may monitor your heartbeat by using a machine that measures electrical activity of the heart (a test called an "ECG”

or an electrocardiogram). If you take a heart medicine, your doctor may also need to adjust its dosage.

- Your doctor may wish to check your gallbladder, as gallstones occur frequently, liver enzymes and pituitary hormones periodically.

Children/ and adolescents

Do not give SIGNIFOR LA to children and adolescents below 18 years old because no data are available in this age group.

Other medicines and SIGNIFOR LA

Always tell your healthcare provider if you are taking any other medicine (this includes complementary or traditional medicines).

Tell your doctor if you are taking any of the following medicines:

- medicines used in organ transplantation to reduce the activity of the immune system such as ciclosporin;
- medicines to treat blood sugar levels that are too high (as in diabetes) or too low (hypoglycaemia), such as:
    - o insulin;
    - o metformin, liraglutide, vildagliptin, nateglinide (antidiabetic medicines).
- medicines used to treat irregular heartbeat such as amiodarone, disopyramide, procainamide, quinidine, sotalol; dofetilide, ibutilide, or dronedarone
- medicines to treat bacterial infections (by mouth: clarithromycin, moxifloxacin; via injection: erythromycin, pentamidine);
- medicines to treat fungal infections (ketoconazole, except in shampoo);

- medicines to treat certain psychiatric disorders (chlorpromazine, thioridazine, fluphenazine, pimozide, haloperidol, tiapride, amisulpride, sertindole, methadone);
- medicines to treat hay fever and other allergies (terfenadine, astemizole, mizolastine);
- medicines used in the prevention or treatment of malaria (chloroquine, halofantrine, lumefantrine);
- medicines to control blood pressure such as:
    - beta blockers (metoprolol, carteolol, propranolol, sotalol)
    - calcium channel blockers (bepridil, verapamil, diltiazem)
    - cholinesterase inhibitors (rivastigmine, physostigmine);
- medicines to control electrolytes (potassium, magnesium) balance in your body;

Pregnancy and breastfeeding and fertility

- The safety of SIGNIFOR LA during pregnancy has not been established.
- If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before being administered SIGNIFOR LA.
- If you are a sexually active woman, you should use an effective method of contraception during treatment.
- You should not breastfeed your child while using SIGNIFOR LA. It is not known if SIGNIFOR LA passes into breast milk.
- It is unknown whether SIGNIFOR LA has an effect on human fertility.

Driving and using machinery

It is not always possible to predict to what extent SIGNIFOR LA may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which SIGNIFOR LA affects them.

However, some of the side effects you may experience while using SIGNIFOR LA, such as headache, dizziness and tiredness, may reduce your ability to drive and use machinery safely.

SIGNIFOR LA contains mannitol and sodium

SIGNIFOR LA contains mannitol and may have a laxative effect.

This medicine contains less than 1 mmol (23 mg) sodium per dose, i.e. it is essentially 'sodium-free'.

3. How to use SIGNIFOR LA

Do not share medicines prescribed for you with any other person.

Always use SIGNIFOR LA exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

How much SIGNIFOR LA to use

The usual dose is:

- The recommended initial dose of SIGNIFOR LA is 40 mg administered by deep intramuscular injection every 4 weeks.
- If you have or had liver problems in the past your doctor may want to start your treatment with a lower initial dose of 20 mg of SIGNIFOR LA.

- Depending on how you respond to the treatment with SIGNIFOR LA your doctor may prescribe you a higher or lower dose. This may involve measuring the levels of growth hormone or other hormones in your blood.
- Depending on the results and how you are feeling, the dose of SIGNIFOR LA given in each injection may need to be reduced or increased. The dose should not exceed 60 mg.
- Your doctor will tell you how long your treatment with SIGNIFOR LA will last.
- If you have the impression that the effect of SIGNIFOR LA is too strong or too weak, tell your doctor or pharmacist.

How to receive SIGNIFOR LA

- You will not be expected to give yourself SIGNIFOR LA.
- Your doctor or nurse will inject SIGNIFOR LA.
- SIGNIFOR LA is intended for intramuscular use. This means that it is injected through a needle into the muscles of your buttocks.

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

How long to use SIGNIFOR LA

- Continue taking SIGNIFOR LA every 4 weeks for as long as your doctor tells you.
- This is a long-term treatment, possibly lasting for years.
- Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.
- If you have questions about how long to take SIGNIFOR LA, talk to your doctor or your pharmacist.

If you stop using SIGNIFOR LA

- If you interrupt your treatment with SIGNIFOR LA your symptoms may come back. Therefore, do not stop using SIGNIFOR LA unless your doctor tells you to.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

If you received more SIGNIFOR LA than you should

Since a healthcare professional will administer SIGNIFOR LA, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you missed a dose of SIGNIFOR LA

Since a healthcare provider will administer SIGNIFOR LA, it is unlikely that the dose will be missed.

4. Possible side effects

SIGNIFOR LA can have side effects.

Not all side effects reported for SIGNIFOR LA are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking SIGNIFOR LA, please consult your healthcare provider for advice.

Some side effects may be serious. Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- high level of sugar in the blood (you may experience excessive thirst, high urine output, increased appetite with weight loss, tiredness, nausea, vomiting, abdominal pain),

- gallstones (you may experience sudden back pain or pain on the right side of your abdomen, fever, chills, yellowing of skin/eyes),
- slow heartbeat,
- an abnormal electrical signal in your heart that can be seen in tests (prolonged QT interval),
- low cortisol levels (you may experience extreme weakness, weight loss, nausea, vomiting, low blood pressure, tiredness),
- problems with bile flow (cholestasis). You may experience yellowing of the skin, dark urine, pale stools and itching,
- inflammation of the gallbladder (cholecystitis).

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

The following side effects have been reported frequently:

- diarrhoea
- nausea
- abdominal pain
- fatigue
- tiredness, fatigue, pale skin (signs of low level of red blood cells)
- loss of appetite
- headache
- bloating
- vomiting
- dizziness

- pain, discomfort, pruritis and swelling at the injection site
- change in liver function test results
- abnormal blood test results (sign of high level of creatine phosphokinase, glycosylated haemoglobin, lipase in the blood)
- hair loss

The following side effects have been reported less frequently:

- change in pancreatic function blood test results (amylase)
- abnormal blood coagulation properties

The following side effects have been reported but the frequency is unknown:

- increased levels of ketone bodies (a group of substances produced in the liver) in your urine or blood (diabetic ketoacidosis) as a complication of an increased level of sugar in your blood. You may experience fruity scented breath, trouble breathing and confusion,
- oily or fatty stools,
- discoloured stools.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist or nurse. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (whoumc.org) found on SAHPRA's website. By reporting side effects, you can help provide more information on the safety of SIGNIFOR LA.

5. How to store SIGNIFOR LA

- Store all medicines out of reach of children.
- Store at or between 2 °C – 8 °C (in a refrigerator).
- Do not freeze.
- Do not store in a bathroom.
- Do not use after the expiry date stated on the label/carton.
- Return all unused medicine to your pharmacist.
- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).
- From a microbiological point of view, the product should be used immediately.
- If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 1 hour at controlled room temperature, unless reconstitution has taken place in controlled and validated aseptic conditions.
- Do not use SIGNIFOR LA if you notice the powder in the vial has changed its colour, or if you notice that the solution is not clear or contains particles.
- The solution should be free of visible particles, clear and colourless.

6. Contents of the pack and other information

The active substance is:

Each vial contains:

SIGNIFOR LA 20 mg - 20 mg pasireotide

SIGNIFOR LA 40 mg - 40 mg pasireotide

SIGNIFOR LA 60 mg - 60 mg pasireotide

Each pre-filled syringe contains:

SIGNIFOR LA solvent for suspension for injection

The other 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 SIGNIFOR LA looks like and contents of the pack:

What SIGNIFOR LA looks like:

SIGNIFOR LA is a powder and solvent for injection.

Powder:

Slightly yellowish-to-yellowish powder in vial

Solvent for suspension for injection:

Clear, colourless to slightly yellow to slightly brown solution in pre-filled syringe.

Contents of the pack:

SIGNIFOR LA is supplied in a vial containing 20 mg, 40 mg or 60 mg pasireotide powder, with pre-filled syringe containing the diluent solution for reconstitution, with vial adapter and with safety injection needle.

Holder of Certificate of Registration and Manufacturer

Key Oncologics (Pty) Ltd

39 Eleventh Avenue

Houghton Estate, 2198

South Africa

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SIGNIFOR LA 20 mg - 49/32/0272

SIGNIFOR LA 40 mg – 49/32/0273

SIGNIFOR LA 60 mg – 49/32/0274

Access to the corresponding Professional Information

Can be obtained on the SAHPRA website.