PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S4

PRINOLID 3,75 3,75 mg Lyophilised microspheres for injection

Leuprolide acetate

Contains sugar (mannitol): 6,60 mg per vial lyophilised powder.

Contains sugar (mannitol): 75 mg per vial sterile solvent.

Read all of this leaflet carefully before you are given PRINOLID 3,75

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

What is in this leaflet

1. What PRINOLID 3,75 is and what it is used for

PRINOLID 3,75 is a synthetic hormone which can be used to reduce the levels of testosterone and estrogen circulating in the body.

PRINOLID 3,75 is used to treat prostate cancer in men and to treat breast cancer in women.

PRINOLID 3,75 can also be used in women to manage endometriosis (often a painful disorder in which tissue similar to the tissue that normally lines the inside of your uterus grows outside your uterus), including pain relief, for up to six months.

Use in children:

PRINOLID 3,75 is a synthetic hormone which can be used to reduce the levels of testosterone and estrogen circulating in the body. PRINOLID 3,75 is used to treat premature puberty caused by a release of certain hormones from the pituitary gland, namely central precocious puberty.

2. What you need to know before you PRINOLID 3,75

PRINOLID 3,75 should not be administered to you:

- If you or your child is hypersensitive (allergic) to leuprolide acetate, a similar medicine, the other ingredients of PRINOLID 3,75 (listed in section 6), or to synthetic gonadotropin releasing hormones or derivates.
- If you are pregnant, planning to become pregnant or are breastfeeding.
- If you have abnormal vaginal bleeding which you have not discussed with your doctor.
- If you are a pre- or perimenopausal women, for the treatment of breast cancer:
  - your estrogen levels must have been adequately suppressed with PRINOLID 3,75 before you start treatment with an aromatase inhibitors such as exemestane and should be checked every three months during combination treatment with PRINOLID 3,75 and an aromatase inhibitor (see ‘Warnings and precautions’ in the section below for more information).
- In girls with central precocious puberty who are pregnant or breastfeeding, or has undiagnosed vaginal bleeding.

Warnings and precautions

Tell your doctor or healthcare professional before being given the injection:

Take special care with PRINOLID 3,75:

Both men and women

- If you are diabetic, PRINOLID 3,75 can aggravate existing diabetes therefore, you may need more frequent monitoring of your blood glucose levels.
- If you have diabetes or suffer from heart problems.
- If you are at an increased risk of thinning of the bones (osteoporosis).

  Risk factors include:

  - If you or any of your close family have thinning of the bones.
  - If you drink excessive amounts of alcohol, and/or smoke heavily.
  - If you take medicines for epilepsy or have taken steroids such as hydrocortisone or prednisolone for a long time.
- If you experience jaundice (yellowing of the skin) of experience symptoms of low blood pressure (such as dizziness or tiredness).
- If you are taking PRINOLID 3,75 and develop a depressed mood, as there have been reports of depression in patients taking PRINOLID 3,75 which may be severe.
- If you are experiencing seizures, have a history of seizures (convulsions), seizure disorders or have a high risk of developing seizures.

Men only

- In the event of an abscess occurring at the injection site your doctor may measure your testosterone levels as there could be reduced absorption of leuprolide from the injection site.
- If you suffer from urinary obstruction or spinal cord compression, including metastatic vertebral lesions. Your doctor will supervise you closely for the first few

weeks of treatment.

- If you are a man with prostate cancer, and have had injections of a synthetic hormone in the past that has not worked, or you have had an operation to remove your testicles.
- If you have any heart or blood vessel conditions, including heart rhythm problems (dysrhythmia), or are being treated with medicines for these conditions. The risk of heart rhythm problems may be increased when using PRINOLID 3,75.
- If you have high blood glucose levels or are diabetic PRINOLID 3,75 can increase your blood glucose levels or aggravate existing diabetes therefore you may need more frequent monitoring of the blood glucose levels.

Women only

- If you continue to have periods (menstruate) after starting treatment with PRINOLID 3,75.
- If you are a woman of child-bearing age, you should use non-hormonal contraception whilst receiving PRINOLID 3,75. Although PRINOLID 3,75 causes periods to stop, it is not itself a contraceptive. If you are unsure about this talk to your

  doctor.
- If you are being given PRINOLID 3,75 for the treatment of breast cancer:
  - Your doctor may assess your bone density and ovarian function before you start treatment with PRINOLID 3,75 and monitor your bone density and ovarian function throughout treatment.
  - PRINOLID 3,75 must be started at least 6-8 weeks before you start treatment with an aromatase inhibitor and should continue throughout treatment with the aromatase inhibitor.
  - If you have had chemotherapy, PRINOLID 3,75 treatment should only commence once you have completed chemotherapy and premenopausal

status has been confirmed.

- If you are being given PRINOLID 3,75 in combination with an aromatase inhibitor, your doctor may monitor your blood pressure, heart function and blood glucose levels during treatment.
- If you have depression or a history of depression, please inform you doctor so that they can additionally monitor your symptoms of depression during treatment with PRINOLID 3,75.
- If you are unsure about this, speak to your doctor.

In children

- In the event of a sterile abscess at the injection site (mostly reported after injection into the muscle) your doctor will monitor your hormone levels as there could be reduced absorption of PRINOLID 3,75 from the injection site. Your doctor will then change the injection method to administer PRINOLID 3,75 under the skin of e.g. abdomen, bottom or thigh.
- If the child has a progressive brain tumour your doctor will decide if treatment with PRINOLID 3,75 is appropriate.

In girls with central precocious puberty

- After the first injection, vaginal bleeding (spotting) and discharge may occur as a sign of hormone withdrawal. Vaginal bleeding beyond the first/second month of treatment needs to be investigated.
- Bone density may decrease during treatment of central precocious puberty with PRINOLID 3,75. However, after treatment is stopped, subsequent bone mass growth is preserved and peak bone mass in late adolescence does not seem to be affected by treatment.

- Discontinuation of PRINOLID 3,75 treatment may lead to a slipping of the growth plate of the thigh bone.

Other medicines and PRINOLID 3,75

Always tell your health care provider if you are taking any other medicine.
(This includes all complementary or traditional medicines.)

PRINOLID 3,75 might interfere with some medicines used to treat heart rhythm problems (e.g. quinidine, procainamide, amiodarone and sotalol) or might increase the risk of heart rhythm problems when used with some other medicines e.g. methadone (used for pain relief and part of drug addiction detoxification), moxifloxacin (an antibiotic), and antipsychotics used for serious mental illnesses.

PRINOLID 3,75 with food and drink

PRINOLID 3,75 can be taken with or without food.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advise before using PRINOLID 3,75.

PRINOLID 3,75 must not be administered in pregnant or breastfeeding women or girls.
Do not breastfeed your infant while receiving PRINOLID 3,75 treatment.

If you are a woman of child-bearing age, you should use non-hormonal contraception whilst receiving PRINOLID 3,75. Although PRINOLID 3,75 causes periods to stop, it is not itself a contraceptive. If you are unsure about this talk to your doctor.

Driving and using machines

Do not drive or operate machinery if you experience drowsiness, dizziness or visual disturbances whilst being treated with PRINOLID 3,75.

It is not always possible to predict to what extent PRINOLID 3,75 may interfere with your daily activities. You should ensure that you do not engage in activities requiring mental alertness, judgment and/or sound coordination and vision e.g. driving, riding, flying, sailing or operating machines/equipment until you are aware of the measure to which PRINOLID 3,75 affects you.

3. How to use PRINOLID 3,75

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

Route of administration: subcutaneous or intramuscular injection.

You will not be expected to give yourself PRINOLID 3,75. It will be given to you by a person who is qualified to do so.

The injection will normally be given in your arm, thigh or abdomen. The injection site should be varied at regular intervals.

You will normally be given an injection once a month.

<u>Prostate cancer</u>

If you have prostate cancer, you will be given PRINOLID 3,75 once a month.

Endometriosis

If you have endometriosis, you will be given PRINOLID 3,75 for a period of six months only.

Breast cancer

If you have breast cancer, you will be given PRINOLID 3,75 once a month.
PRINOLID 3,75 can be given in combination with tamoxifen or an aromatase inhibitor. A minimum of one injection of PRINOLID 3,75 should be given before you start treatment with an aromatase inhibitor or tamoxifen.

Use in children

Your child's doctor will determine the starting dose based on your child's weight. Depending on the central precocious puberty activity, your doctor may increase the dosage in the presence of inadequate suppression (e.g. vaginal bleeding). Your doctor will determine the minimal effective dose with the help of a blood test.

The duration of treatment depends on the clinical signs at the start of treatment or during the course of treatment and is decided by your doctor together with the legal guardian and, if appropriate, the treated child. Your doctor will determine the bone age of the child in regular intervals.

In girls with bone maturation of older than 12 years and boys with bone maturation of older than 13 years your doctor will consider discontinuing the treatment, depending on the clinical effects in your child.

In girls, pregnancy should be excluded before the start of treatment. The occurrence of pregnancy during treatment cannot be generally excluded. In such cases, please talk to your doctor.

The therapy is a long-term treatment, adjusted individually. Please arrange with your doctor that PRINOLID 3,75 is administered as precisely as possible at regular monthly intervals.

If you take use more PRINOLID 3,75 than you should

Since a healthcare professional will administer PRINOLID 3,75, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you missed a dose of PRINOLID 3,75

Since a healthcare professional will administer PRINOLID 3,75, it is unlikely that the dose will be missed.

Women only

If PRINOLID 3,75 injection is missed, breakthrough bleeding or ovulation may occur with the potential for conception. If you think you may be pregnant you should stop using PRINOLID 3,75 and contact your doctor immediately.

If you stop taking PRINOLID 3,75

If you are being given PRINOLID 3,75 for the treatment of breast cancer in combination with an aromatase inhibitor, you must not stop your treatment with PRINOLID 3,75 whilst you are taking such an aromatase inhibitor. If you are going to discontinue treatment with

PRINOLID 3,75, your aromatase inhibitor treatment must also be discontinued within 1 month of your last PRINOLID 3,75 injection.

4. Possible side effects

PRINOLID 3,75 can have side effects.

Not all side effects reported for PRINOLID 3,75 are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking PRINOLID 3,75, please consult your health care provider for advice.

If any of the following happens, tell your doctor immediately or go to the casualty department at your nearest hospital:

- sever rash,
- itching,
- shortness of breath or difficulty in breathing.

These are all very serious side effects. If you have them, you may have had a serious reaction to PRINOLID 3,75. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- If you get a severe headache which does not get better when you take painkillers.
- If you suffer from any unexplained bruising or bleeding or feel generally unwell whilst taking PRINOLID 3,75. These could be symptoms of changes in the number of red or white blood cells.

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

Tell your doctor if you notice any of the following:

Men

- When men with prostate cancer first start treatment with PRINOLID 3,75, levels of testosterone can increase and in some people this may cause a temporary increase in local pain. In some cases, to prevent this from happening, your doctor may give you another type of medicine (anti-androgen medicine) before and just after your first PRINOLID 3,75 injection. If you do get worsening pain, weakness or loss of feeling in your legs or difficulty passing urine, contact your doctor immediately.
- There may be an increased risk of loss of blood to the pituitary area (if you have an existing pituitary lesion), which may cause permanent damage. This occurs rarely.
- Blood sugar levels may be altered during treatment with PRINOLID 3,75, which may affect control in diabetic patients and require more frequent monitoring.
- If you have a blood test your doctor may notice a change in blood lipid (cholesterol) levels or in values for tests on how the liver is working. These changes do not usually cause any symptoms.

<u>Frequent side effects:</u>

- weight changes,
- hot flushes, hypotension and postural hypotension,
- sweating,
- muscle weakness,
- bone pain,
- loss of interest in sexual intercourse,
- inability to have an erection,
- a reduction in size and function of the testes,
- swelling of the penis, pain of the tested and prostate,
- pain, tiredness,
- skin reactions at the injection site (these include skin hardening, redness, pain,

abscesses, swelling, nodules, ulcers,

skin damage),

- loss of appetite,
- difficulty sleeping,
- depression and headache,
- mood changes (with long-term use),
- nausea (feeling sick), vomiting, diarrhoea,
- abnormalities in blood tests, liver function or liver blood tests,
- skin rash, dry skin, itchy skin, hives, skin pigmentation, abonormal hair growth and excessive body hair,
- joint pain,
- swelling, tenderness, pain and enlargment of the breast tissue,
- swelling in your ankles.

<u>Less frequent side effects:</u>

- mood changes (with short-term use) and sleep disorders,
- dizziness,
- sleepiness and weakness,
- tingling in the hands or feet,
- muscle ache,
- weakness and pain in the legs,
- amblyopia (also called lazy eye), ear pain, tinnitus, and rhinitis,
- skin infection, hair loss, red bumpy rash,
- abnormal heart rhythm or beats, angina, hypertension, circulatory problems or diseases of the blood vessels, chest pain,
- nose bleeds, coughing up blood,
- painful or discomfort during urination, blood in urine, frequent urination, passing large volume of urine and urine retention.

Side effects with an unknown frequency:

- blood tests may show anaemia (low red cell counts), low counts in white cells or platelets,
- allergic reactions (may include symptoms of rash, itching, wheals or a serious allergic reaction which causes difficulty breathing or dizziness),
- changes in blood lipids (cholesterol) or blood sugar,
- paralysis,
- seizure,
- altered vision,
- heart failure, heart attack, pounding heartbeats,
- changes in ECG (QT prolongation),
- blood clots in lungs,
- high or low blood pressure,
- jaundice, abnormal liver function or liver injury,
- fracture of the spine,
- thinning of bone,
- difficulty passing urine,
- fever,
- inflammation of lungs or lung disease.

Women

- Many of the side effects of PRINOLID 3,75 are related to the decrease in estrogen level. Estrogen level returns to normal after treatment is stopped. Common side effects include hot flushes, mood swings, depression and vaginal dryness.
- As can happen naturally when women reach the menopause, PRINOLID 3,75 can

cause a small amount of bone thinning.

- Vaginal bleeding may occur during treatment.
- If you have an existing pituitary lesion, there may be an increased risk of loss of blood to the area, which may cause permanent damage. This occurs rarely.
- Blood sugar levels may be altered during treatment with PRINOLID 3,75, which may affect control in diabetic patients and require more frequent monitoring.
- If you have a blood test your doctor may notice a change in blood lipid (cholesterol) levels or in values for tests on how the liver is working. These changes do not usually cause any symptoms.

Frequent side effects:

- difficulty sleeping, nervousness, anxiety,
- headaches,
- hot flushes and low blood pressure,
- weight changes,
- mood changes and changes in libido (sex drive),
- depression,
- tingling in hands or feet,
- dizziness,
- joint pain,
- muscle weakness,
- breast tenderness,
- changes in breast size,
- vaginal dryness or discharge, vaginal bleeding,
- menopausal symptoms, painful sexual intercourse ,
- acne, eczema, hair growth or loss, excessive sweating, dry skin, and hives,
- altered or blurred vision,
- nausea, vomiting, diarrhoea, abdominal pain, constipation

- swelling in ankles or skin reactions at the injection site (these include skin hardening, redness, pain, abscesses, swelling, nodules, ulcers and skin damage),
- changes in blood lipids (cholesterol).

Less frequent side effects:

- loss of appetite,
- pounding heartbeats,
- abnormalities in liver blood tests,
- muscle aches,
- fever,
- tiredness.

Side effects with an unknown frequency:

- blood tests may show anaemia (low red cell counts), low counts in white cells or platelets,
- allergic reactions (may include symptoms of rash, itching, wheals or a serious allergic reaction which causes difficulty breathing or dizziness),
- changes in blood sugar,
- paralysis,
- seizure,
- heart failure, heart attack, abnormal heart rhythm,
- blood clots in lungs,
- high or low blood pressure,
- jaundice, abnormal liver function or liver injury,
- fracture of the spine,
- thinning of bone,
- difficulty passing urine,
- inflammation of lungs or lung disease.

Children

In the initial phase of treatment, a short-term rise in the sex hormone levels occurs, followed by a fall to values within the prepuberty range. Due to this effect, side effects may occur particularly at the start of treatment.

Frequent side effects:

- mood swings,
- headache,
- abdominal pain / abdominal cramps,
- feeling sick / nausea and vomiting,
- acne, skin rash including red bumpby rash, skin odour,
- vaginal bleeding,
- spotting,
- discharge, local vaginal infection,
- breast enlargement in males,
- reduced growth, weight gain,
- pain, injection site reactions including abcess.

Less frequent side effects:

- general allergic reactions (fever, rash, itching),
- serious allergic reaction which causes difficulty in breathing or dizziness,
- if you have an existing pituitary lesion, there may be an increased risk of loss of blood to the area, which may cause permanent damage,
- infection, sore throat, sinusitis, flu, runny nose / rhinitis,
- cervical growth,
- thyroid enlargement,

- increased appetite,
- nervousness, depression,
- drowsiness, fainting, twitching,
- high blood pressure, slow heart beat,
- asthma, nose bleeds,
- constipation, indigestion, difficulty in swallowing, inflammation and redness of the gums,
- hair loss, excessive bodily hair growth, nail disorders, white patches / purple coloured spots on the skin, thickening of the skin,
- muscle and joint pain, muscle and joint disorders,
- loss of bladder control,
- menstrual cramps, disoders of the cervix or menses, breast enlargement and pain, feminisation,
- swelling of ankles, fever, aggravation of condition,
- changes in certain blood tests / results of blood tests.

<u>Side effects with an unknown frequency:</u>

- seizure,
- inflammation of lungs, lung disease,
- hot flushes,
- abdominal pain,
- flushing, increased sweating,
- decreased size of testes / disorder of the testes, prostate pain,
- uterine bleeding,
- chest pain.

In general, if vaginal bleeding (spotting) occurs with continued treatment (after possible withdrawal bleeding in the first month of treatment), this may be a sign of potential underdosage. Please tell your doctor if vaginal bleeding occurs.

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 nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the **6.04 Adverse Drug Reaction Reporting Form**, found online under SAHPRA"s publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of PRINOLID 3,75.

5. How to store PRINOLID 3,75

Store all medicines out of reach of children.

- Store at or below 30 °C.
- Protect from light.

Reconstituted suspension: Since PRINOLID 3,75 microspheres and its solvent contains no preservative, the reconstituted suspension should be used immediately after preparation and any unused portion should be discarded.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

Discard the needle in an appropriate manner (i.e. medical sharps waste bin).

6. Contents of the pack and other information

What PRINOLID 3,75 contains

The active substance is leuprolide acetate.

The other ingredients are carmellose sodium 30 cps, gelatin, mannitol, poly(lacticglycolic) acid 75:25, polysorbate 80 and water for injection.

What PRINOLID 3,75 looks like and contents of the pack

PRINOLID 3,75 is a powder and solvent for suspension for injection.

Powder

White powder without discoloration or superficial foreign particles.

Single dose administration kit containing one 6 mL clear type I glass vial, with a 20 mm dark grey rubber stopper and aluminium crimp cap with blue plastic flip cap; 1 glass ampoule containing; 1 disposable syringe and two 22 G 1½ needles.

Solvent

Limpid, colourless liquid, without suspended particles.

2 mL colourless glass ampoule, with yellow identification ring and white cutting ring.

Holder of Certificate of Registration

Eurolab (Pty) Ltd.

Woodmead Office Park,

3 Stirrup Lane

Van Reenens Avenue

Woodmead

2144

This leaflet was last revised in

January 2023

Registration/Application number

53/21.10/0733