PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

Schedule 5

TREVICTA 175 mg (prolonged release suspension for injection)

TREVICTA 263 mg (prolonged release suspension for injection)

TREVICTA 350 mg (prolonged release suspension for injection)

TREVICTA 525 mg (prolonged release suspension for injection)

Paliperidone

Sugar free

Read all of this leaflet carefully before you are given TREVICTA

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

What is in this leaflet

1. What TREVICTA is and what it is used for
2. What you need to know before you use TREVICTA
3. How to use TREVICTA
4. Possible side effects
5. How to store TREVICTA
6. Contents of the pack and other information

1. What TREVICTA is and what it is used for

TREVICTA contains the active substance paliperidone which is an antipsychotic medicine and is used in adults as maintenance treatment for the symptoms of schizophrenia.

If your schizophrenia symptoms have responded well to treatment with paliperidone palmitate injection given once a month, your doctor may start treatment with TREVICTA which is a once every 3 months injection.

2. What you need to know before you use TREVICTA

TREVICTA should <u>not</u> be administered to you

- if you are hypersensitive (allergic) to paliperidone or any of the other ingredients of TREVICTA (listed in section 6).
- if you are allergic to another antipsychotic medicine including the substance risperidone.
- If you have moderate to severe loss of kidney function.
- If you have Parkinson's disease or Dementia with Lewy Bodies.

Warnings and precautions

Talk to your doctor or healthcare provider **before** being given the injection:

- If you are an elderly patient with dementia, you may have an increased risk of stroke or death (see section 4).

TREVICTA can worsen the symptoms of other medical conditions. For that reason, it is important to discuss with your doctor any of the following conditions which can potentially worsen during treatment with TREVICTA

- if you have Parkinson's disease
- if you have ever been diagnosed with a condition whose symptoms include high temperature and muscle stiffness (also known as Neuroleptic Malignant Syndrome)
- if you have ever experienced twitching or jerking movements that you cannot control in your face, tongue, or other parts of your body (Tardive Dyskinesia)
- if you know that you have had low levels of white blood cells in the past (which may or may not have been caused by other medicines)
- if you are diabetic or prone to diabetes
- if you have had breast cancer or a tumour in the pituitary gland in your brain
- if you have a heart disease or heart disease treatment that makes you prone to low blood pressure
- if you have low blood pressure when you stand up or sit up suddenly
- if you have a history of seizures
- if you have kidney problems
- if you have liver problems
- if you have prolonged and/or painful erection
- if you have problems with controlling body temperature or overheating
- if you have an abnormally high level of the hormone prolactin in your blood or if you have a possible prolactin-dependent tumour
- if you or someone else in your family has a history of blood clots, as antipsychotics have been associated with formation of blood clots.

If you have any of these conditions, please talk to your doctor as he/she may want to adjust your dose or monitor you for a while.

As very low numbers of a certain type of white blood cell needed to fight infection in your blood has been seen in patients taking TREVICTA, your doctor may check your white blood cell counts.

Even if you have previously tolerated oral paliperidone or risperidone, allergic reactions may occur after receiving injections of TREVICTA. Seek medical attention right away if you experience a rash, swelling of your throat, itching, or problems breathing as these may be signs of a serious allergic reaction.

TREVICTA may cause you to gain weight. Significant weight gain may be bad for your health. Your doctor should regularly measure your body weight.

As diabetes mellitus or worsening of pre-existing diabetes mellitus have been seen with patients taking TREVICTA, your doctor should check for signs of high blood sugar. In patients with pre-existing diabetes mellitus blood glucose should be monitored regularly.

Since TREVICTA may reduce your urge to vomit, there is a chance that it may mask the body's normal response to ingestion of toxic substances or other medical conditions.

During an operation on the eye for cloudiness of the lens (cataract), the pupil (the black circle in the middle of your eye) may not increase in size as needed. Also, the iris (the coloured part of the eye) may become floppy during surgery and that may lead to eye damage. If you are planning to have an operation on your eye, make sure you tell your eye doctor that you are taking TREVICTA.

Children and adolescents

Do not use TREVICTA in children and adolescents under 18 years of age. It is not known if it is safe and effective in these patients.

Other medicines and TREVICTA

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

Taking TREVICTA with carbamazepine (an anti-epileptic and mood stabiliser) may require a change to your dose of TREVICTA.

Since TREVICTA works primarily in the brain, using other medicines that work in the brain can cause an exaggeration of side effects such as sleepiness or other effects on the brain such as other psychiatric medications, opioids, antihistamines and sleep medication.

Since TREVICTA can lower blood pressure, care should be taken when TREVICTA used with other medicines that lower blood pressure.

TREVICTA can reduce the effect of medicines against Parkinson's disease and restless legs syndrome (e.g., levodopa).

TREVICTA may cause an electrocardiogram (ECG) abnormality demonstrating a long time for an electrical impulse to travel through a certain part of the heart (known as "QT prolongation"). Other medicines that have this effect include some medicines used to treat the rhythm of the heart or to treat infection, and other antipsychotics.

If you have a history of seizures, TREVICTA may increase your chance of experiencing them. Other medicines that have this effect include some medicines used to treat depression or to treat infection, and other antipsychotics.

TREVICTA should be used with caution with medicines that increase the activity of the central nervous system (psychostimulants such as methylphenidate).

TREVICTA with alcohol

Alcohol should be avoided.

Pregnancy and breastfeeding

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 health care provider for advice before taking TREVICTA.

You should not use this medicine during pregnancy unless this has been discussed with your doctor. TREVICTA should not be used during pregnancy unless clearly necessary. The following symptoms may occur in newborn babies of mothers that have used paliperidone as contained in TREVICTA in the last trimester (last three months of their pregnancy): shaking, muscle stiffness and/or weakness, sleepiness, agitation, breathing problems, and difficulty in feeding. If your baby develops any of these symptoms seek medical attention for your baby.

TREVICTA can pass from mother to baby through breast milk and may harm the baby. Therefore, you should not breastfeed your baby when using TREVICTA.

Driving and using machines

TREVICTA may interfere with your ability to drive and use machines.
Dizziness, extreme tiredness and vision problems may occur during treatment with TREVICTA. (see section 4). You should not drive and use machines until you know how treatment with TREVICTA affects you.

TREVICTA contains

Less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

3. How TREVICTA is used

TREVICTA is administered by your doctor or other health care professional. Your doctor will tell you when you need your next injection. It is important not to miss your scheduled dose. If you cannot keep your appointment with the doctor, make sure you call him right away so another appointment can be made as soon as possible.

Your doctor will tell you how long your treatment with TREVICTA will last. Do not stop treatment early because if you stop receiving your injections, your symptoms of schizophrenia may get worse. You should not stop using TREVICTA unless told to do so by your doctor. If you have the impression that the effect of TREVICTA is too strong or too weak, tell your doctor or pharmacist.

You will receive an injection of TREVICTA in the upper arm or buttocks once every 3 months.

Depending on your symptoms, your doctor may increase or decrease the amount of medicine you receive at the time of your next scheduled injection.

Patients with kidney problems

If you have mild kidney problems your doctor will determine the appropriate dose of TREVICTA based on the dose of 1-monthly paliperidone palmitate injectable that you have been receiving. If you have moderate or severe kidney problems TREVICTA should not be used.

Elderly

Your doctor will determine your dose of TREVICTA if your kidney function is reduced.

If you are given more TREVICTA than needed

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

Patients who have been given too much paliperidone such as TREVICTA may experience the following symptoms:
drowsiness or sedation, fast heart rate, low blood pressure, an abnormal electrocardiogram (electrical tracing of the heart), or slow or abnormal movements of the face, body, arms or legs.

If you forget to use TREVICTA

Since a healthcare professional will administer TREVICTA, it is unlikely that the dose will be missed. It is very important to keep all your appointments and get your injections on time. If you think you are going to miss an appointment, call your healthcare professional and arrange treatment as soon as you can.

If you stop using TREVICTA

If you stop receiving your injections, your symptoms of schizophrenia may get worse. You should not stop using TREVICTA unless told to do so by your doctor.

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

4. Possible side effects

TREVICTA can have side effects.

Not all side effects reported for TREVICTA are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking TREVICTA, please consult your doctor, pharmacist or other healthcare professional for advice.

Tell your doctor immediately if you:

- experience blood clots in the veins, especially in the legs (symptoms include swelling, pain, and redness in the leg), which may travel through blood vessels to the lungs causing chest pain and difficulty breathing. If you notice any of these symptoms seek medical advice immediately.
- have dementia and experience a sudden change in your mental state or sudden weakness or numbness of your face, arms or legs, especially on one side, or slurred speech, even for a short period of time. These may be signs of a stroke.
- experience fever, muscle stiffness, sweating or a lowered level of consciousness (a disorder called “Neuroleptic Malignant Syndrome”). Immediate medical treatment may be needed.
- are a man and experience prolonged or painful erection. This is called priapism. Immediate medical treatment may be needed.
- experience involuntary rhythmic movements of the tongue, mouth and face. Withdrawal of paliperidone may be needed.
- experience a severe allergic reaction characterised by fever, swollen mouth, face, lip or tongue, shortness of breath, itching, skin rash and sometimes drop in blood pressure (amounting to an ‘anaphylactic reaction’). Seek medical attention right away if any of these symptoms occur.

- are planning to have an operation on your eye, make sure you tell your eye doctor that you are taking TREVICTA. During an operation on the eye for cloudiness of the lens (cataract), the iris (the coloured part of the eye) may become floppy during surgery (known as “floppy iris syndrome”) that may lead to eye damage.
- are aware of having very low numbers of a certain type of white blood cell needed to fight infection in your blood.

Frequent Side effects:

- difficulty falling or staying asleep.
- common cold symptoms, urinary tract infection, feeling like you have the flu.
- TREVICTA can raise your levels of a hormone called "prolactin" found on a blood test (which may or may not cause symptoms). When symptoms of high prolactin occur, they may include: (in men) breast swelling, difficulty in getting or maintaining erections, or other sexual dysfunction; (in women) breast discomfort, leakage of milk from the breasts, missed menstrual periods, or other problems with your cycle.
- high blood sugar, weight gain, weight loss, decreased appetite.
- irritability, depression, anxiety.
- feeling restless.
- parkinsonism: This condition may include slow or impaired movement, sensation of stiffness or tightness of the muscles (making your movements jerky), and sometimes even a sensation of movement "freezing up" and then restarting. Other signs of parkinsonism include a slow shuffling walk, a tremor while at rest, increased saliva and/or drooling, and a loss of expression on the face.
- restlessness, feeling sleepy, or less alert.
- dystonia: This is a condition involving slow or sustained involuntary contraction of muscles. While it can involve any part of the body (and may result in abnormal

posture), dystonia often involves muscles of the face, including abnormal movements of the eyes, mouth, tongue or jaw.

- dizziness.
- dyskinesia: This is a condition involving involuntary muscle movements, and can include repetitive, spastic or writhing movements, or twitching.
- tremor (shaking).
- headache.
- rapid heart rate.
- high blood pressure.
- cough, stuffy nose.
- abdominal pain, vomiting, nausea, constipation, diarrhoea, indigestion, toothache.
- increased liver transaminases in your blood.
- bone or muscle ache, back pain, joint pain.
- loss of menstrual periods, leakage of milk from the breasts.
- fever, weakness, fatigue (tiredness).
- a reaction at the injection site, including itching, redness, pain or swelling.

Less frequent side effects:

- pneumonia (infection and inflammation of the lung tissue), infection of the airways in the lung (bronchitis), infection of the breathing passages, sinus infection, bladder infection, ear infection, tonsillitis, fungal infection of the nails, infection of the skin.
- white blood cell count decreased, decrease in the type of white blood cells that help to protect you against infection, decrease in platelets (blood cells that help you stop bleeding), anaemia.
- allergic reaction.

- diabetes or worsening of diabetes, decreased insulin (a hormone that controls blood sugar levels) in your blood.
- increased appetite.
- loss of appetite resulting in malnutrition and low body weight.
- high blood triglycerides (a fat), increased cholesterol in your blood.
- sleep disorder, elated mood (mania), decreased sexual drive, nervousness, nightmares.
- tardive dyskinesia (twitching or jerking movements that you cannot control in your face, tongue, or other parts of your body). Tell your doctor immediately if you experience involuntary rhythmic movements of the tongue, mouth and face. Withdrawal of this medicine may be needed.
- fainting, a restless urge to move parts of your body, dizziness upon standing, disturbance in attention, problems with speech, loss or abnormal sense of taste, reduced sensation of skin to pain and touch, a sensation of tingling, pricking, or numbness of skin.
- blurry vision, eye infection or "pink eye", dry eye.
- sensation of spinning (vertigo), ringing in the ears, ear pain.
- an interruption in conduction between the upper and lower parts of the heart, abnormal electrical conduction of the heart, prolongation of the QT interval from your heart, rapid heartbeat upon standing, slow heart rate, abnormal electrical tracing of the heart (electrocardiogram or ECG), a fluttering or pounding feeling in your chest (palpitations).
- low blood pressure, low blood pressure upon standing (consequently, some people taking TREVICTA may feel faint, dizzy, or may pass out when they stand up or sit up suddenly).
- shortness of breath, congestion of breathing passages, wheezing, sore throat, nosebleeds.

- abdominal discomfort, stomach or intestinal infection, difficulty swallowing, dry mouth, excessive passing of gas or wind.
- increased GGT (a liver enzyme called gamma-glutamyltransferase) in your blood, increased liver enzymes in your blood.
- hives (or "nettle rash"), itching, rash, hair loss, eczema, dry skin, skin redness, acne.
- an increase of CPK (creatine phosphokinase) in your blood, an enzyme which is sometimes released with muscle breakdown.
- muscle spasms, joint stiffness, muscle weakness, neck pain.
- incontinence (lack of control) of urine, frequent passing of urine, pain when passing urine.
- erectile dysfunction, ejaculation disorder, missed menstrual periods or other problems with your cycle (females), development of breasts in men, sexual dysfunction, breast pain.
- swelling of the face, mouth, eyes, or lips, swelling of the body, arms, or legs.
- an increase in body temperature.
- a change in the way you walk.
- chest pain, chest discomfort, feeling unwell.
- hardening of the skin.
- fall.
- eye infection.
- skin inflammation caused by mites, abscess under the skin.
- increase in eosinophils (a type of white blood cell) in your blood.
- inappropriate secretion of a hormone that controls urine volume.
- sugar in the urine.
- life threatening complications of uncontrolled diabetes.
- low blood sugar.

- excessive drinking of water.
- confusion.
- not moving or responding while awake (catatonia).
- sleep walking.
- lack of emotion.
- inability to reach orgasm.
- neuroleptic malignant syndrome (confusion, reduced or loss of consciousness, high fever, and severe muscle stiffness), blood vessel problems in the brain, including sudden loss of blood supply to brain (stroke or "mini" stroke), unresponsive to stimuli, loss of consciousness, low level of consciousness, convulsion (fits), balance disorder.
- abnormal coordination.
- glaucoma (increased pressure within the eyeball).
- problems with movement of your eyes, eye rolling, oversensitivity of the eyes to light, increased tears, redness of the eyes.
- atrial fibrillation (an abnormal heart rhythm), irregular heartbeat.
- blood clots in the veins especially in the legs (symptoms include swelling, pain and redness in the leg). If you notice any of these symptoms seek medical advice immediately.
- flushing.
- trouble breathing during sleep (sleep apnoea).
- lung congestion.
- crackly lung sounds.
- inflammation of the pancreas, swollen tongue, stool incontinence, very hard stool.
- chapped lips.
- rash on skin related to medicine, thickening of skin, dandruff.
- joint swelling.

- inability to pass urine.
- breast discomfort, enlargement of the glands in your breasts, breast enlargement.
- vaginal discharge.
- very low body temperature, chills, feeling thirsty.
- symptoms of medicine withdrawal.
- accumulation of pus caused by infection at injection site, deep skin infection, a cyst at the injection site, bruising at injection site.
- dangerously low numbers of a certain type of white blood cell needed to fight infection in your blood.
- severe allergic reaction characterised by fever, swollen mouth, face, lip or tongue, shortness of breath, itching, skin rash and sometimes drop in blood pressure.
- dangerously excessive intake of water.
- sleep-related eating disorder.
- coma due to uncontrolled diabetes.
- shaking of the head.
- blood clot in the lungs causing chest pain and difficulty in breathing. If you notice any of these symptoms seek medical advice immediately.
- fast, shallow breathing, pneumonia caused by inhaling food, voice disorder.
- decreased oxygen in parts of your body (because of decreased blood flow).
- a blockage in the bowels, lack of bowel movement that causes blockage
- yellowing of the skin and the eyes (jaundice).
- serious allergic reaction with swelling that may involve the throat and lead to difficulty breathing.
- Severe or life-threatening rash with blisters and peeling skin that may start in and around the mouth, nose, eyes, and

genitals and spread to other areas of the body (Stevens-Johnson syndrome or toxic epidermal necrolysis)

- skin discolouration, flaky, itchy scalp or skin.
- abnormal posture.
- newborn babies born to mothers who have taken TREVICTA during pregnancy may experience side effects of the medicine and/or withdrawal symptoms, such as irritability, slow, or sustained muscle contractions, shaking, sleepiness, breathing, or feeding problems.
- priapism (a prolonged penile erection that may require surgical treatment)
- a decrease in body temperature.
- dead skin cells at injection site, an ulcer at injection site.

Reporting of side effects

If you get side effects, talk to your doctor. 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 TREVICTA.

5. How to store TREVICTA

- Store all medicines out of reach of children
- Store at or below 30°C
- Protect from light
- Store in the original package/container
- Keep the container in the outer carton
- This medicinal product does not require any special storage conditions

- Do not use TREVICTA after the expiry date which is stated on the carton. The expiry date refers to the last day of that month
- TREVICTA is for single use only. Any unused portion should be discarded.
- Return all unused medicine to your pharmacist
- Do not dispose of unused medicine in drains or sewerage system (e.g. toilets).

6. Contents of the pack and other information

What TREVICTA contains

The active substance is paliperidone.

Each TREVICTA 175 mg pre-filled syringe contains 273 mg paliperidone palmitate.

Each TREVICTA 263 mg pre-filled syringe contains 410 mg paliperidone palmitate.

Each TREVICTA 350 mg pre-filled syringe contains 546 mg paliperidone palmitate.

Each TREVICTA 525 mg pre-filled syringe contains 819 mg paliperidone palmitate.

The other ingredients are:

Citric acid monohydrate

Polyethylene glycol 4000

Polysorbate 20

Sodium dihydrogen phosphate monohydrate

Sodium hydroxide (for pH adjustment)

Water for injection

What TREVICTA looks like and contents of the pack

TREVICTA is a white to off-white prolonged release suspension for injection in a pre-filled syringe that your doctor or nurse will shake vigorously to resuspend the suspension before it is given as an injection.

Each pack contains 1 pre-filled syringe and 2 needles.

Not all pack sizes may be marketed.

HOLDER OF CERTIFICATE OF REGISTRATION

JANSSEN PHARMACEUTICA (PTY) LTD

(Reg. No. 1980/011122/07)

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Registration/Application numbers

TREVICTA 175 mg - 50/2.6.5/0699

TREVICTA 263 mg - 50/2.6.5/0700

TREVICTA 350 mg - 50/2.6.5/0701

TREVICTA 525 mg - 50/2.6.5/0702

Access to the corresponding Professional Information

Included in the carton, accompanying this patient information leaflet.