PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

TREVICTA®

Prolonged-release suspension for intramuscular injection

Composition: The active ingredient and its quantity/concentration:

Paliperidone (as palmitate) 200 mg/ml
Trevicta 175 mg contains: 175 mg paliperidone (as palmitate) in 0.88 ml
Trevicta 263 mg contains: 263 mg paliperidone (as palmitate) in 1.32 ml
Trevicta 350 mg contains: 350 mg paliperidone (as palmitate) in 1.75 ml
Trevicta 525 mg contains: 525 mg paliperidone (as palmitate) in 2.63 ml

Inactive and allergenic ingredients in the preparation – see section 6 – " Further Information".

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed to treat your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.
The medicine is intended for treatment of adults over the age of 18.

1. WHAT IS THE MEDICINE INTENDED FOR?

- Trevicta is given as an injection once in 3 months to treat schizophrenia in adults whose clinical condition is stable on a once-monthly paliperidone (as palmitate) injection.

Therapeutic group: antipsychotic preparations

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient paliperidone or to any of the additional ingredients contained in the medicine (see section 6 – "Further Information").
- You are sensitive (allergic) to another antipsychotic medicine that contains risperidone.

Special warnings regarding use of the medicine

This preparation has not been tested in elderly patients with dementia, however, an increased risk of stroke or death has been observed in elderly patients with dementia taking medicines similar to Trevicta (see section 4 – "Side Effects").
Use of Trevicta may lead to an exacerbation of certain medical conditions and it is therefore important that you discuss with your doctor any of the following

conditions, which may worsen during treatment with Trevicta.

Before treatment with Trevicta, tell the doctor if:

- You have Parkinson's disease.
- You have been diagnosed in the past with Neuroleptic Malignant Syndrome, characterized by symptoms that include high body temperature and muscle stiffness.
- You have ever had involuntary movements of the face, tongue, or other parts of your body (Tardive Dyskinesia).
- You have had a low levels of white blood cells in the past (resulting from use of other medicines or other reasons).
- You have diabetes or are prone to diabetes.
- You have had breast cancer or a tumor in the pituitary gland.
- You have a heart disease or heart disease treatment you take makes you more prone to low blood pressure.
- You have low blood pressure upon transitioning suddenly to a standing or sitting position.
- You have had seizures in the past.
- You have kidney problems.
- You have liver problems.
- You have a prolonged and/or painful erection.
- You have a problem regulating body temperature or with overheating of the body.
- You have an abnormally high level of the hormone prolactin in your blood or if you have a possible prolactin-dependent tumor.
- You or someone else in your family has a history of blood clots, since an association has been found between taking antipsychotics and the formation of blood clots.

If you have any of these conditions, consult the doctor, since he/she may decide to change the dosage of the medicine for you or to closely monitor your condition when using Trevicta.

In addition, talk to your doctor in the following situations:

- A low and dangerous count of certain white blood cells necessary to fight infection in the blood has been observed very rarely in patients taking this medicine. The attending doctor may check your white blood cell counts.
- Even if you have not previously had an allergic reaction to oral treatment with risperidone or paliperidone, rarely, allergic reactions can occur after receiving a Trevicta injection. Refer to a doctor or emergency room immediately if you experience a rash, swelling of the throat, itching or problems breathing, as these symptoms may be a sign of a serious allergic reaction.
- This preparation may cause weight gain. Significant weight gain may be harmful to your health. The attending doctor must monitor your weight.
- Since onset of diabetes mellitus or worsening of pre-existing diabetes mellitus has been observed in patients taking this preparation, the attending doctor will

monitor for signs of high blood sugar levels. In patients who have pre-existing diabetes mellitus before starting Trevicta treatment, blood sugar levels should be monitored frequently.
- Since this preparation may reduce the urge to vomit, the normal response to ingestion of a toxic substance or to another medical condition may be masked.
- During an operation to correct cloudiness of the lens (cataract), the pupil (the black circle in the middle of the eye) may not dilate as needed. Also, the iris (the colored part of the eye) may become floppy during surgery, which may lead to eye damage. If you are planning to undergo an eye operation, tell the eye doctor that you are taking Trevicta.

Children and adolescents
Trevicta is not intended for the treatment of children and adolescents under 18 years of age. There are no data regarding the safety and efficacy of using this preparation in children and adolescents.

Drug interactions
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Especially if you are taking:
- Carbamazepine (to treat epilepsy or as a mood stabilizer); may require a change to your dose of Trevicta.
- Psychiatric preparations, opioids, antihistamines and sleep medications; since these preparations primarily act on the brain, taking these medicines with Trevicta, which also primarily acts on the brain, can lead to exacerbation of side effects, such as sleepiness or other effects on the brain.
- Since Trevicta can lower blood pressure, exercise caution when combining it with other medicines that are known to lower blood pressure.
- Trevicta may lower the efficacy of preparations to treat Parkinson's disease and restless legs syndrome, e.g., levodopa.
- Trevicta may cause an abnormal electrical tracing of the heart (ECG), indicating a condition in which the electric signal takes a long time to pass through a certain part of the heart, also known as "QT prolongation". Other medicines with this effect include certain medicines to treat heart rhythm disorders, to treat infections and other psychiatric medicines.
- If you have a history of seizures, Trevicta may cause an increased risk of seizures. Additional medicines that may have a similar effect include medicines to treat depression, medicines to treat infections and other antipsychotics.
- Trevicta should be used with caution with medicines that increase the activity of the central nervous system (psychostimulants such as methylphenidate).

Use of the medicine and alcohol consumption
Avoid consuming alcohol when using Trevicta.

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you may be pregnant or are planning to

become pregnant during the course of treatment, refer to a doctor or pharmacist for consultation before commencing treatment with the medicine. Do not use Trevicta during pregnancy, unless the doctor approves. The following symptoms may occur in newborns whose mothers used paliperidone in the last trimester (the last three months of pregnancy): shaking, muscle stiffness and/or weakness, sleepiness, agitation, breathing problems, and difficulty in feeding. If your baby develops any of these symptoms, take your baby to the doctor for medical treatment.
Trevicta can pass from the mother to the baby via the breast milk and harm your baby. Therefore, do not breastfeed during treatment with Trevicta.

Driving and operating machinery
Dizziness, extreme tiredness and vision problems may occur when using the medicine (see section 4 – "Side Effects"). This should be considered in cases where full alertness is necessary, such as driving a car or operating machinery.

Important information about some of the ingredients in this medicine
The preparation contains less than 1 mmol sodium (23 mg) per dose, that is to say, it is essentially 'sodium-free'.

3. HOW SHOULD THE MEDICINE BE USED?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.
The dosage and treatment regimen will be determined by the doctor only.
Trevicta is administered by the doctor or another medical staff member. The doctor will tell you when you need your next injection. It is important not to miss your next scheduled injection. If you cannot get to your scheduled appointment, call right away to schedule another appointment as soon as possible.
Trevicta will be given to you by injection in the upper arm or buttocks, once in 3 months.
Depending on your symptoms, the doctor will increase or decrease the Trevicta dosage that will be given to you at the time of your next injection.

Patients with kidney problems
If you have a mild kidney problem, the doctor will determine the Trevicta dosage appropriate for you, based on the dosage of the paliperidone (as palmitate) injection you received once a month. If you have a moderate to severe kidney problem, do not use the preparation.

Elderly
If your kidney function is abnormal, the doctor will determine the Trevicta dosage appropriate for you.

Do not exceed the recommended dose.

If you accidentally received a higher dosage of Trevicta
Trevicta will be given to you under medical supervision; therefore, the chance of

you receiving too high a dosage is small.
Patients who have received too high a paliperidone dosage may experience the following symptoms: drowsiness or sedation, fast heart rate, low blood pressure, an abnormal ECG (electrical tracing of the heart), slow and abnormal movements of the face, body, arms or legs.

If you stop taking this medicine
If you stop receiving injections, the schizophrenia symptoms may get worse. Do not stop taking the preparation unless explicitly instructed to do so by the doctor.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.
If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Trevicta may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Refer to a doctor immediately if:
- You are suffering from 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 and cause chest pain and difficulty breathing. If you notice any of these symptoms, seek medical treatment immediately.
- You are suffering from dementia and experience a sudden change in your mental state, sudden weakness, numbness of the face, arms or legs, especially if it occurs on one side, slurred speech, even for a short period of time. These may be signs of a stroke.
- You are suffering from fever, muscle stiffness, sweating or a lowered level of consciousness, an effect called neuroleptic malignant syndrome. You may need immediate medical treatment.
- You are a man and are suffering from a prolonged or painful erection. This effect is called priapism. You may need immediate medical treatment.
- You are suffering from involuntary and rhythmic movements of the face, tongue and mouth. You may have to stop taking the preparation.
- You are suffering from a severe allergic reaction characterized by fever, swollen mouth, face, lips or tongue, shortness of breath, itching, skin rash and sometimes drop in blood pressure (amounting to an anaphylactic reaction). Even if you have not previously suffered from an allergic reaction to oral treatment with risperidone or paliperidone, rarely, allergic reactions occur after receiving a paliperidone injection.
- You are planning to undergo an eye operation. Tell your eye doctor that you are taking this medicine. During an operation to correct cloudiness of the lens (cataract), the iris (the colored part of the eye) may become floppy during

surgery, a condition called “floppy iris syndrome”, which may lead to eye damage.
- You have a dangerously low count of certain white blood cells that are essential for fighting infection in the blood.

Very common side effects – may occur in more than 1 user in 10:
- Difficulty falling or staying asleep.

Common side effects – may occur in up to 1 user in 10:
- Symptoms of the common cold, urinary tract infection, feeling like you have the flu.
- Trevicta can lead to an increase in the level of a hormone called “prolactin” found in a blood test, which may or may not cause symptoms. When symptoms of high levels of prolactin occur, they may include: in men – breast swelling, difficulty in achieving or maintaining an erection over time, or other sexual dysfunction; in women – breast discomfort, leakage of milk from the breasts, irregular menstrual periods or other menstrual problems.
- High blood sugar levels, weight gain, weight loss, decreased appetite.
- Irritability, depression, anxiety.
- A feeling of restlessness.
- Parkinsonism: This condition may include slow or impaired movement, a sensation of muscle stiffness (causing jerky movements), and sometimes even a sensation of movement “freezing up” and then restarting. Other signs of parkinsonism include a slow shuffling walk, tremor while at rest, increased production of saliva and/or drooling, and a loss of facial expression.
- Restlessness, a feeling of sleepiness or decreased alertness.
- Dystonia: This is a condition that involves slow or sustained involuntary contraction of the muscles. While this condition can occur in 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 – a condition involving involuntary muscle movements, and can include repetitive, spastic or writhing movements.
- Tremor.
- Headache.
- Rapid heart rate.
- High blood pressure.
- Cough, stuffy nose.
- Abdominal pain, vomiting, nausea, constipation, diarrhea, indigestion, toothache.
- Increased liver transaminase levels in the blood.
- Muscle or bone ache, back pain, joint pain.
- Loss of menstrual periods.
- Fever, weakness, fatigue.

- A reaction at the injection site, including itching, pain and swelling.

Uncommon side effects – may occur in up to 1 user in 100:

- Pneumonia, bronchitis, infection of the breathing passages, sinus infection, bladder infection, ear infection, tonsillitis, fungal infection of the nails, infection of the skin, abscess under the skin.
- Decrease in white blood cell count, decrease in the type of white blood cells that help protect the body against infection, anaemia.
- Allergic reaction.
- Diabetes or worsening of pre-existing diabetes, increased insulin (a hormone that controls blood sugar levels) levels in the blood.
- Increased appetite, loss of appetite, resulting in malnutrition and low body weight.
- High blood triglyceride (a fatty compound) levels, increased blood cholesterol levels.
- Sleep disorders, elated mood (mania), decreased sexual drive, nervousness, nightmares.
- You are suffering from involuntary movements, jerking and twitching of the face, tongue or other parts of the body (tardive dyskinesia). Tell the doctor immediately if you experience involuntary movements, rhythmic movements of the tongue, mouth and face. Treatment with the medicine may have to be discontinued.
- Fainting, an uncontrollable urge to move parts of the body, dizziness upon standing up, concentration disturbance, problems with speech, loss or abnormal sense of taste, reduced sensation of the skin to touch and pain, a sensation of tingling, pricking or numbness of the skin.
- Blurry vision, eye infection or conjunctivitis (pink eye), dry eye.
- Sensation of spinning (vertigo), ringing in the ears, ear pain.
- A disturbance in the electrical conduction between the upper and lower part of the heart, abnormal electrical conduction of the heart, prolongation of the QT interval, rapid heartbeat upon standing up, slow heart rate, abnormal electrical tracing of the heart (ECG), a fluttering or pounding feeling in the chest (palpitations).
- Low blood pressure, low blood pressure upon standing up (consequently, some patients taking Trevicta will feel faint, dizzy, or may pass out when they suddenly transition to a standing or sitting position).
- Shortness of breath, sore throat, nosebleeds.
- Abdominal discomfort, stomach or intestinal infection, difficulty swallowing, dry mouth, increased bloating and wind.
- Increased GGT (a liver enzyme called gamma-glutamyl transferase) levels in the blood, increased liver enzyme levels in the blood.
- Hives (or “nettle rash”), itching, rash, hair loss, eczema, dry skin, skin redness, acne.
- Increased CPK (creatine phosphokinase) levels in the blood, an enzyme which

is sometimes released with muscle breakdown.
- Muscle spasms, joint stiffness, muscle weakness.
- Urinary incontinence, frequent passing of urine, pain upon passing urine.
- Difficulty in achieving or maintaining an erection over time (erectile problems), ejaculation problems, irregular menstrual periods or other problems with the menstrual cycle (women), development of breasts in men, sexual dysfunction, breast pain, leakage of milk from the breasts.
- Swelling of the face, mouth, eyes, lips, swelling of the body, arms, legs.
- Increased body temperature.
- A change in the way you walk.
- Chest pain, chest discomfort, general unwell feeling.
- Hardening of the skin.
- Falls.

Rare side effects – may occur in up to 1 user in 1,000:
- Eye infection.
- Skin inflammation caused by mites, flaky, itchy scalp or skin.
- Increase in eosinophil (a type of white blood cells) levels in the blood.
- Decrease in platelets (blood cells that help you stop bleeding).
- Inappropriate secretion of a hormone that regulates urine volume.
- Sugar in the urine.
- Life-threatening complications arising from uncontrolled diabetes.
- Low blood sugar levels.
- Excessive drinking of water.
- Confusion.
- Shaking of the head.
- Not moving or responding while awake (catatonia).
- Sleepwalking (somnambulism).
- Lack of emotion.
- Inability to reach orgasm.
- Neuroleptic malignant syndrome (confusion, reduced or loss of consciousness, high body temperature 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, convulsions (fits), balance disorder.
- Abnormal coordination.
- Glaucoma (increased intraocular pressure).
- Problem with eye movement, eye rolling.
- Hypersensitivity of the eyes to light, increased tearing, redness of the eyes.
- Atrial fibrillation (abnormal heart rhythm), irregular heart rate.
- 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, refer to a doctor immediately.
- Blood clot in the lungs causing chest pain and difficulty in breathing. If you

notice any of these symptoms, refer to a doctor immediately.
- Flushing.
- Breathing problems during sleep (sleep apnea).
- Lung congestion, congestion of breathing passages, wheezing.
- Crackly lung sounds.
- Inflammation of the pancreas, swollen tongue, stool incontinence, very hard stool.
- A blockage in the bowels.
- Chapped lips.
- Skin rash related to drug treatment, thickening of the skin, dandruff.
- Joint swelling.
- Inability to pass urine.
- Breast discomfort, enlargement of the glands in the breasts, breast enlargement.
- Vaginal discharge.
- Priapism – a prolonged penile erection that may require surgical treatment.
- Very low body temperature, chills, feeling thirsty.
- Withdrawal symptoms.
- Accumulation of pus caused by infection at the injection site, deep skin infection, a cyst at the injection site, bruising at injection site.

Side effects of unknown frequency (cannot be estimated based on the existing data):
- A low and dangerous count of certain white blood cells necessary to fight infection in the blood.
- Severe allergic reaction characterized by fever, swelling of the mouth, face, lip or tongue, shortness of breath, itching, skin rash and sometimes drop in blood pressure.
- Drinking excessive and dangerous quantities of water.
- Sleep-related eating disorders.
- Coma due to uncontrolled diabetes.
- Fast and shallow breathing, pneumonia caused by inhaling food, voice disorders.
- Decreased oxygen in certain parts of the body (following decreased blood flow).
- Lack of bowel movement that causes bowel obstruction.
- Yellowing of the skin and the eyes (jaundice).
- 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).
- Serious allergic reaction that includes swelling, which may involve the throat and lead to difficulty breathing.
- Skin discoloration.
- Abnormal posture.
- Newborn babies born to mothers who have taken Trevicta during pregnancy may

experience side effects of Trevicta and/or withdrawal symptoms, such as irritability, slow or sustained muscle contraction, shaking, sleepiness, breathing or feeding problems.
- A decrease in body temperature.
- Dead skin cells at the injection site and an ulcer at the injection site.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Store at a temperature below 30° C.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains –

Polysorbate 20, Polyethylene glycol 4000, Citric acid monohydrate, Sodium dihydrogen phosphate monohydrate, Sodium hydroxide, Water for injection.

- What the medicine looks like and the contents of the package:
  Trevicta is a prolonged-release, white to off-white suspension provided in a pre-filled syringe, which the doctor or nurse will shake vigorously to resuspend before administration of the injection.
- Each package contains one pre-filled syringe and two needles.
- **Manufacturer:** Janssen Pharmaceutica NV, Turnhoutseweg 30, B-2340 Beerse, Belgium.
- **Registration Holder:** J-C Health Care Ltd., Kibbutz Shefayim 6099000, Israel.

Revised in August 2023 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 157-43-34606-00

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