PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986
The medicine is dispensed with a doctor's prescription only

Fludecate

Solution for intramuscular injection

Composition:
Each 1 ml ampoule contains:
Fluphenazine decanoate 25 mg

Inactive and allergenic ingredients in the preparation – see section 2 "Important information about some of the ingredients of the medicine" and section 6 "Further information".

Read the 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 you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Fludecate is a long-term antipsychotic given by injection, intended for use in patients in need of a long-term antipsychotic (e.g., to treat chronic schizophrenia).
Therapeutic group: phenothiazine derivative, antipsychotic.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:
- You are sensitive (allergic) to fluphenazine decanoate, sesame oil or any of the additional ingredients contained in the medicine (for the list of inactive ingredients, please see section 6 – "Further information").
- You suffer from hypersensitivity to antipsychotics, especially phenothiazine derivatives, which manifests by jaundice as a result of cholestasis, allergic skin disease and other allergic reactions.
- You suffer from severe poisoning as a result of use of depressants of the central nervous system (e.g., certain painkillers [opiates], hypnotics, other medicines for the treatment of mental disorders [antidepressants, antipsychotics, tranquillizers]) or alcohol.
- You suffer from prolactin-dependent tumors (e.g., breast cancer, a tumor in the pituitary gland).
- You suffer from an excessive reduction in the number of white cells (leukopenia) or other disorders of the blood system related to the formation of blood cells.
- You suffer from severe disturbances in blood cells or bone marrow.
- You suffer from Parkinson's disease.
- You have a history of neuroleptic malignant syndrome.
- You suffer from a severe liver disease.
- You suffer from severe depression.
- The patient is in a coma.
- The patient is a child under 12 years of age.

Special warnings regarding use of the medicine
Speak to your doctor or pharmacist before treatment with **Fludecate**.
Special caution should be exercised when using **Fludecate** in the following situations:
- You suffer from liver or kidney dysfunctions.
- You suffer from an adrenal gland tumor called "pheochromocytoma".
- If you suffered in the past from damage to the heart muscle, you were born with long QT syndrome or you have a family history of long QT syndrome (specific changes in the electrocardiogram [ECG]), coronary heart disease, conduction system disorder, arrhythmias.
- You suffer from significant changes in blood pressure (decreased blood pressure, increased blood pressure, orthostatic pressure changes [reduced blood pressure when getting up from a sitting or lying position]).
- You suffer from a slow heart rate (bradycardia), and from a low blood potassium level (hypokalemia).
- You are taking medicines that cause a prolongation of the QT interval in the ECG or lead to a reduction in the potassium level or changes in the blood electrolyte balance (see "Drug interactions" section).
- You have a history of organic brain syndrome and epileptic seizures.
- You suffer from brain damage or there is suspicion that you will suffer from brain damage.
- You suffer from depression.
- You suffer from chronic breathing problems or asthma.
- You suffer from a loss of consciousness.
- You suffer from glaucoma, narrowing of the pylorus (the opening from the stomach into the duodenum), enlargement of the prostate gland, or from difficulties passing urine (urinary retention).
- You expect to be exposed to a high temperature.
- You were recently exposed to organophosphate insecticides.
- Avoid taking antipsychotics concomitantly with **Fludecate** (see "Drug interactions" section).

Also use with special caution in the following situations:
- You have an increased risk of stroke or you are suffering from a reduction in the amount of blood reaching the brain.
- You or a relative has a history of venous thrombosis (blood clots); these types of medicines are associated with the occurrence of blood clots.
- You have risk factors for stroke (e.g., smoking, high blood pressure).
- Patients suffering from epilepsy.
- Patients suffering from depression.
- Patients due to undergo surgery must inform the healthcare staff that they are being treated with **Fludecate**. This is because **Fludecate** in combination with anesthetics may lead to a sharp drop in blood pressure.

In the above-mentioned cases, your doctor will assess the risk versus benefit of using the medicine before prescribing **Fludecate**.

Elderly patients with dementia
Elderly patients with dementia who are treated with antipsychotics may be at higher risk of death compared to untreated patients.
In addition, elderly patients are at risk of suffering from the anticholinergic effect of **Fludecate**. In particular, elderly women may develop extrapyramidal side effects (e.g., gait and movement disturbances, tremor, skeletal muscle stiffness, and in certain cases, irreversible brain damage may occur), even with low dosages. The sedative effect and drop in blood pressure are more pronounced in elderly patients.

Tests and follow-up
- Before starting treatment with **Fludecate**, the doctor will refer you for a complete blood count (including platelet and white blood cell count).
  Continue performing blood counts regularly during the course of treatment with **Fludecate**.
  At the beginning of treatment with **Fludecate**, a blood test should be done once a week during the first 4 months of treatment; thereafter, if the results are normal, a test should be done once a month.
  If the white cell count falls sharply or if there are other changes in the blood tests, the doctor will tell you to stop treatment with **Fludecate**.
- Body weight, blood glucose level, blood lipid level, and dental status should be monitored during the course of treatment with **Fludecate**.
- If you suffer from a high fever, gum inflammation or inflammation of the oral mucosa, throat ache, pustular tonsillitis or flu-like symptoms, do not take medicines at your own discretion, especially if the symptoms occur during the first three months of treatment. Consult your doctor immediately to receive appropriate treatment.
- During the course of treatment with **Fludecate**, it is recommended to monitor liver and kidney functions, especially in elderly patients sensitive to antipsychotics.
- Heart rhythm disturbances may occur during the course of treatment with **Fludecate**, especially in elderly patients or patients with an existing heart disturbance. Therefore, tests that assist in diagnosing heart diseases (including ECG) should be routinely performed.

Children and adolescents
There is no adequate information regarding the safety and effectiveness of fluphenazine decanoate in children and adolescents. **Fludecate** can be given to children from the age of 12 and to adolescents only after evaluation of the risk versus benefit of use of the preparation.

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:
The following medicines may increase the risk of side effects, if taken together with **Fludecate**:
- Other antipsychotics.
- Hypnotics.
- Analgesics.
- Anesthetics.
- Medicines to treat allergy or cold (antihistamines).
- Tricyclic antidepressants.
- Medicines that prolong the QT interval (Class IA or Class III antiarrhythmics, macrolide antibiotics, antihistamines, antimalarials, antidepressants and other antipsychotics).
- Diuretics.
- Medicines that inhibit the breakdown of fluphenazine decanoate in the liver (paroxetine, fluoxetine).
- Lithium salts.
- Dopamine antagonists (metoclopramide and alizapride).
- Anticholinergics (antidepressants, atropine, biperiden).
- Sympathomimetics (epinephrine).
- Antihypertensives (guanethidine, clonidine, methyldopa).
- Monoamine oxidase (MAOI) enzyme inhibitors.
- Anthelmintics.
- Medicines to treat seizures (pentetrazol).
- Medicines that cause low blood pressure (e.g., metrizamide).
- Antibiotics, such as colistin, polymyxin B.
- Medicines to treat schizophrenia (clozapine).
- Non-selective beta blockers (propranolol).
- Phenylalanine and neuroleptics.
- Preparations containing primrose oil taken by schizophrenia patients.
- SSRI antidepressants.
- Medicines to treat Parkinson's disease (levodopa, bromocriptine, amantadine, cabergoline).
- Appetite suppressants and amphetamines.
- Preparations containing reserpine.
- Blood thinners.
- Antiepileptics (barbiturates, carbamazepine or phenytoin).
- Hormonal therapy (gonadorelin, dehydroepiandrosterone [DHEA]).
- Medicines to treat diabetes (insulin).

A pregnancy test may show an erroneous result (false positive) when performed during the course of treatment with **Fludecate**.

Use of the medicine and alcohol consumption
Avoid drinking alcohol during the course of treatment with **Fludecate** since alcohol may cause an unpredictable increase in fluphenazine levels.

Pregnancy, breastfeeding and fertility
If you are pregnant or breastfeeding, think you are pregnant or are planning to become pregnant, refer to a doctor or pharmacist before using the medicine.

Pregnancy
Since the safety of use of **Fludecate** during pregnancy has not been demonstrated, only use the preparation if the doctor decides that the medicine is essential for treating your ailment and after the benefit to the mother has been weighed against the risk the fetus may experience.
Fludecate can cross the placenta and may be related to motor or behavioral changes in infants born to mothers who received **Fludecate** during the last trimester of pregnancy.
In addition, if you are treated with **Fludecate** during the last trimester of pregnancy up to delivery, you must be aware of the fact that the following effects may occur in the newborn: tremor, muscle stiffness, muscle flaccidity, drowsiness, restlessness, difficulty breathing and difficulties feeding. Refer to a doctor immediately if your baby shows any of these symptoms.

Breastfeeding
Fluphenazine passes into breast milk; therefore, do not breastfeed during the course of treatment with the preparation.

Driving and operating machinery
Use of **Fludecate** may impair your responsiveness; therefore, your ability to drive or operate machinery is impaired. This effect increases in conjunction with alcohol. Therefore, avoid driving, operating machinery, or performing dangerous activities, at least at the beginning of treatment with **Fludecate**. The attending doctor will decide what should be done in all of the above situations. The decision will be made in accordance with the patient's response and dosage he takes.

Important information about some of the ingredients of the medicine
1 ml of **Fludecate** contains 15 mg benzyl alcohol.
Benzyl alcohol may cause allergic reactions. Consult the doctor or pharmacist if you have a liver or kidney disease or if you are pregnant or breastfeeding. This is because large amounts of benzyl alcohol may accumulate in your body and cause a side effect called 'metabolic acidosis'.
In addition, this medicine contains sesame oil, which may, in rare cases, cause a severe allergic reaction.

3. HOW SHOULD YOU USE THE MEDICINE?

The medicine will be given by the healthcare staff.

If you were accidentally treated with a high dosage
The following symptoms may occur with increased severity, depending on the dosage administered:
- Deep sleep up to loss of consciousness or coma.
- Agitation and confusion with hallucinations.
- Extrapyramidal disorders: involuntary muscle movements (dyskinesia) and involuntary muscle spasms (dystonia), spasms of the tongue/pharynx, oculogyric crisis (OGC), spasms of the larynx.
- Seizures.
- Increase or decrease in body temperature.
- Heart function disturbances: fast heart rate (tachycardia), slow heart rate (bradycardia), changes in ECG tracing, such as arrhythmia (prolongation of the PQ or QT interval, torsades de pointes), heart or circulatory failure.
- Rise or fall in blood pressure.
- Movement control disturbances.
- Blurred vision, glaucoma attack.
- Disturbance or absence of bowel motility.
- Urinary retention.
- Respiratory function disturbances: reduced breathing stimulus and even respiratory arrest or development of pneumonia.

When you experience one of the symptoms listed above, refer to your doctor immediately or proceed to a hospital emergency room and bring the package of the medicine with you.

If you did not receive the medicine at the scheduled time
If the symptoms of the disease recur, worsen or are unusual, contact the attending doctor immediately. Otherwise, take the next dose at the usual time and do not take a double dose.
Adhere to the treatment regimen as recommended by the doctor. Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor or pharmacist.

If you stop using the medicine
Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor. Discontinuing treatment at your own discretion puts you at risk and your ailment may recur.

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 **Fludecate** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Severe side effects
Refer to a doctor as soon as possible if one or more of the following symptoms occur:
- **Side effects related to the extrapyramidal system:** Involuntary muscle movements (dyskinesia), including muscle stiffness and movement disturbances, spasms of the tongue or pharynx, torticollis, spasms of the jaw muscles, oculogyric crisis and stiffening of the back muscles. Dyskinesia can occur with long-term treatment, at high dosages or after stopping treatment (especially in elderly patients and women). Upon onset of the first symptoms of involuntary muscle spasms of the pharynx or jaw, refer to a doctor immediately.
  Strong reflexes (brisker reflexes) occurring during treatment with **Fludecate**, especially in the first days and weeks after injection.
  Parkinsonism, manifesting by tremor, stiffness, immobility, excessive saliva production.
  An urge to move and restlessness (akathisia) that generally occur at a later stage of treatment.
  Children develop extrapyramidal motor disorders even at lower dosages.
- Neuroleptic malignant syndrome (NMS): A life-threatening syndrome that can occur during treatment with antipsychotics. Its symptoms include: high fever above 40°C, muscle rigidity, rapid heart rate and high blood pressure, loss of consciousness and even coma, an increase in myoglobin and creatine kinase (CK) activity, an increase in the white blood cell count, impaired liver function and severe kidney failure.

Side effects of unknown frequency (effects whose frequency has not been determined):
- Fatigue and perceptible slowing, restlessness, agitation, drowsiness or depression, especially at the beginning of treatment.
- Impaired motivation, dizziness, headaches, strange dreams, confusion, seizures, lack of body temperature regulation, disturbances of speech, memory and sleep. In addition, isolated cases of reversible paralysis have been reported.
- Changes in the EEG (measurement of the electrical activity in the brain), changes in proteins in the cerebrospinal fluid (the fluid surrounding the brain).
- In rare cases, as occurs with other antipsychotics, your ailment may recur or worsen.
- A sharp drop in blood pressure or circulatory disturbance when changing from lying or sitting to standing.
- Increase in heart rate.
- Damage to the blood vessels of the brain, kidney or heart has been observed in patients with an adrenal tumor.
- A rise in blood pressure.
- A delay in conduction in the heart (conduction and repolarization disturbances), which can be seen in an ECG and can result in cardiac arrhythmias (torsades de pointes), which is a life-threatening condition.
  The risk of arrhythmia increases with higher dosages and in patients with pre-existing heart problems.
- Irregular or rapid heartbeats, cardiac arrest and death.
- Blood clot in the veins (venous thrombosis), especially in the veins of the legs (swelling, pain and redness in the leg). The blood clot may pass into the circulation to the lungs and cause chest pains and breathing difficulties. If you notice any of the listed symptoms, proceed immediately to a hospital emergency room.

Additional side effects
Uncommon side effects (effects that occur in 1-10 in 1,000 users):
- Vision problems.
- Dry mouth.
- Sweating.
- Increased salivation.
- Excessive urination.
- High fever.
- Nasal congestion.
- Increased intraocular pressure.
- Constipation.
- Urination disturbances.
- Nausea.
- Vomiting.
- Diarrhea and loss of appetite.
- Increased liver enzymes.
- Bile fluid drainage disturbances (intrahepatic cholestasis) and jaundice.
- Reduced sexual desire and intensity.
- Impotence in men.
- Menstrual cycle disturbances in women and milk secretion and breast growth in men.
- Sugar (glucose) breakdown disturbances.
- Increased body weight.
- Disturbances in excretion of the ADH hormone (regulates the water content in the body).
- Low blood sodium level.
- Impairment in blood composition, including white blood cell deficiency, reduced platelet count (thrombocytopenia), decrease in the number of red blood cells or any type of blood cell (pancytopenia) and in the number of eosinophils.
- Allergic skin reactions – itching and increased skin sensitivity to sun (exercise caution on exposure to sunlight).
- Breathing difficulties, asthma, bronchitis, edema in the throat, angioneurotic edema (Quincke's edema).
- Anaphylactic reactions, skin pigmentation, lupus-like syndrome (redness and skin inflammation) and peripheral edema.

Rare side effects (effects that occur in 1-10 users in 10,000):
- Granulocyte deficiency.
- Venous thrombosis in the leg and pelvis.

Very rare side effects (effects that occur in less than one user in 10,000):
- Intestinal paralysis.

Side effects of unknown frequency (frequency has not yet been determined):
- Cerebral edema.
- Degeneration of the retina (retinitis pigmentosa).
- Clouding of the lens and cornea.
- Cases of sudden, unexpected and unexplained death have been observed in hospitalized psychotic patients.

If a side effects occurs, if one of the side effect worsens or if you suffer from a side effect not mentioned in the 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.
Additionally, you can report to "Unipharm Ltd." at https://unipharm.co.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine should 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 carton package. The expiry date refers to the last day of that month.
Store below 25°C and protect from light.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
Sesame oil, Benzyl alcohol.
Each 1 ml **Fludecate** contains 15 ml benzyl alcohol.

What the medicine looks like and the contents of the package:
Fludecate is a clear, oily, viscous, yellow solution for intramuscular injection.
Fludecate is marketed in a carton that contains 5 ampoules of 1 ml for single use.

Manufacturer and Registration holder and address: Unipharm Marketing Ltd., P.O. Box 21429, Tel Aviv, 6121301.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 025 22 21358 00

Revised in September 2022 according to MOH guidelines.

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