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

Zappa 5, 7.5, 10 Zappa ODT 5, 10

Tablets Orodispersible tablets

Composition:
Each **Zappa 5** tablet contains: olanzapine 5 mg
Each **Zappa 7.5** tablet contains: olanzapine 7.5 mg
Each **Zappa 10** tablet contains: olanzapine 10 mg
Each **Zappa ODT 5 orodispersible** tablet contains: olanzapine 5 mg
Each **Zappa ODT 10 orodispersible** tablet contains: olanzapine 10 mg

For the list of inactive ingredients, please see section 6 "Further Information" and section 2 "Important information about some of the ingredients of the medicine".

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 for the treatment of your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.

Essential information about the preparation:
Antipsychotics (like **Zappa** and **Zappa ODT**) may increase the risk of death in elderly patients who suffer from confusion, memory loss and loss of touch with reality (dementia associated with psychosis). The preparation is not intended for treatment of psychosis in elderly patients who suffer from dementia.
Zappa and **Zappa ODT** are intended for adults above the age of 18.

1. WHAT IS THE MEDICINE INTENDED FOR?

For acute and maintenance treatment of schizophrenia.
Zappa and **Zappa ODT** are intended for the treatment of symptoms of psychotic disorders.
Zappa and **Zappa ODT** are intended for the short-term treatment of severe mania attacks associated with bipolar I disorder.
Prevention of recurrence of bipolar disorder:
In patients whose mania attack responded to treatment with olanzapine, **Zappa** and **Zappa ODT** are indicated to prevent recurrence in patients with bipolar disorder.
Combination treatment of bipolar I disorder:
The combination of **Zappa** and **Zappa ODT** with lithium or valproate is indicated for the short-term treatment of severe mania attacks associated with bipolar I disorder.
Therapeutic group: Atypical antipsychotic medicines.
The symptoms of schizophrenia include hearing voices, seeing things that do not exist, believing in things that are not true, suspicion and disconnection.
The symptoms of bipolar I disorder include intermittent periods of depression and uplifted mood or nervousness, increased activity and restlessness, racing thoughts, rapid speech, changes in appetite, impulsive behavior, and decreased need for sleep.
The symptoms of persistent depression include decreased mood, low interest, increased guilt feeling, decreased energy, decreased concentration, changes in appetite and thoughts or suicidal behavior.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:
- You are sensitive (allergic) to olanzapine or to any of the additional ingredients of the medicine.
- For specific information on the contraindications of lithium or valproate, refer to the Contraindications section of the package inserts for those preparations.

Special warnings regarding use of this medicine:
- **Zappa** and **Zappa ODT** interfere with the body's ability to reduce temperature. Avoid situations in which an excessive increase in body temperature and dehydration are possible, such as increased physical activity or frequent stay in hot places. Be sure to drink fluids to prevent dehydration.
- **Zappa** and **Zappa ODT** may cause hypotension upon transition from lying down to sitting up. The symptoms include: dizziness, rapid or slow heart rate, and even fainting in some patients. This effect usually occurs at the beginning of treatment.
- **Zappa and Zappa ODT can cause sleepiness, hypotension upon transition from lying down to sitting up, and motoric and sensory instability which may cause falls resulting in fractures and other injuries.** Use with caution and consider the risk/benefit ratio in patients with a medical history or who are taking medicines that may increase the risk of falls.
- Weight gain has been observed in patients taking **Zappa** and **Zappa ODT**. Weight should be monitored regularly.
- Monitor blood sugar and lipid levels since **Zappa** and **Zappa ODT** may cause an increase in these parameters.
- In patients with a medical history of low levels of white blood cells, blood count tests should be regularly performed during the first months of treatment for follow-up. **Zappa** and **Zappa ODT** may cause a decrease in the levels of white blood cells. Discontinuation of **Zappa** and **Zappa ODT** treatment should be considered upon appearance of the first symptom of this condition. Patients suffering from reduced levels of white blood cells must be monitored for fever or other symptoms indicating infection. If these occur, immediately discontinue the treatment with **Zappa** and **Zappa ODT**.
- Taking **Zappa** and **Zappa ODT** is not recommended for elderly patients suffering from dementia due to the possibility of severe side effects: falls, sleepiness, peripheral edema, unusual gait, urinary incontinence, lethargy, weight gain, weakness, fever, pneumonia, dry mouth, visual hallucinations, stroke and death.
- Patients with schizophrenia and bipolar disorders are at a greater risk of attempted suicide. Therefore, these patients must be closely monitored while being treated with **Zappa** and **Zappa ODT**.
- Caution should be exercised in patients who have suffered or are currently suffering from urinary retention, prostate enlargement, constipation or a history of intestinal obstruction, as the use of **Zappa** and **Zappa ODT** in these patients may cause symptoms such as constipation, dry mouth and tachycardia. From experience gained after marketing the medicine, it was found that the risk of serious side effects (including deaths) increased when combining **Zappa** and **Zappa ODT** with anticholinergic medicines.

Before treatment with Zappa and Zappa ODT, tell the doctor if:
- You suffer, or have suffered in the past, from cardiac dysfunction.
- You suffer, or have suffered in the past, from a stroke or "mini-stroke" (temporary symptoms of stroke).
- You suffer from problems with the liver, gastrointestinal system (such as bowel obstruction).
- You suffer from Alzheimer's.
- You have breast cancer.
- You experience suicidal thoughts or self-harm. In this case, refer immediately to a doctor or emergency room.
- You suffer, or have suffered in the past, from enlargement of the prostate gland.
- You suffer, or have suffered in the past, from seizures, diabetes or high blood sugar levels, high or low blood pressure, high levels of cholesterol or triglycerides in the blood.
- You exercise a lot or stay in hot places often.
- You have a history of drug abuse.
- You are sensitive to any food or medicine.
- You are sensitive to lactose – **Zappa:** This medicine contains lactose and may cause sensitivity in people sensitive to lactose. **Zappa ODT:** This medicine contains mannitol and acesulfame potassium.
- You suffer from any other medical problem.

Smoking:
If you smoke – tell the doctor before commencing treatment with this medicine.

Tests and follow-up:
- At the beginning of and during treatment, monitor blood sugar levels, especially if you have diabetes or borderline sugar levels (100-126 mg/dL when fasting).
- Blood lipid levels (cholesterol and triglycerides) should be monitored, especially in patients suffering from blood lipid level disturbances or risk factors of developing such disturbances. Tests for blood lipids should be performed at the beginning of and during treatment even if you do not have any symptoms.
- Weight gain is a common side effect of treatment with **Zappa** and **Zappa ODT**. Take this into account before beginning the treatment and routinely monitor weight.
- In patients with a history of low white blood cell levels, monitor white blood cell levels during the first months of treatment. Discontinuation of treatment with **Zappa** and **Zappa ODT** should be considered upon appearance of the first significant symptom indicating reduced white blood cells.

Drug interactions:
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. In particular, if you are taking:
- Diazepam – Concomitant administration of **Zappa** or **Zappa ODT** and diazepam may cause hypotension upon transition from lying down to sitting up (orthostatic).
- Medicines affecting the CYP1A2 enzyme, e.g., carbamazepine, fluvoxamine, omeprazole and rifampicin – may affect the levels of olanzapine in the blood.
- Medicines containing activated charcoal – may reduce the absorption of olanzapine.
- Medicines affecting the central nervous system, such as sedatives, antidepressants and sleep medications, anti-epileptic medicines – care should be taken upon concomitant administration of these medicines and olanzapine.
- Medicines used to reduce blood pressure – olanzapine may enhance the blood pressure-lowering effect when administered in combination with these medicines.
- Medicines that mimic the action of dopamine (such as a medicine for the treatment of Parkinson's – levodopa) – olanzapine may inhibit the activity of these medicines.
- Anticholinergic drugs – their combination with **Zappa** and **Zappa ODT** may increase the risk of serious gastrointestinal side effects resulting from decreased gastrointestinal motility.

Use of the medicine and food:
Zappa and **Zappa ODT** may be taken with or without food.
Use of the medicine and alcohol consumption:
Avoid consuming alcohol while using **Zappa** and **Zappa ODT**. Drinking alcohol while taking **Zappa** and **Zappa ODT** may make you more sleepy compared to taking **Zappa** and **Zappa ODT** without alcohol.
Pregnancy, breastfeeding and fertility:
Pregnancy
Consult a doctor or pharmacist before using the medicine.
Consult a doctor if you are pregnant or are planning to get pregnant. It is not known whether **Zappa** and **Zappa ODT** harm the fetus. Neonates may develop withdrawal syndrome if the mother has taken the medicine during the last trimester (the last three months) of pregnancy. The withdrawal syndrome includes the following symptoms: restlessness, tremor, muscle stiffness/weakness, sleepiness, nervousness, respiratory and feeding problems. If your child develops one or more of the above symptoms, contact the doctor.
Breastfeeding
The drug passes into breast milk. Talk to your doctor about the best way to feed your baby if you are taking **Zappa** and **Zappa ODT**.
Fertility
Treatment with **Zappa** and **Zappa ODT** may cause an increase in blood prolactin levels, which can lead to a reversible impairment in fertility in women of child-bearing potential.
Driving and operating machinery:
Use of this medicine may cause drowsiness and affect judgment capability, thinking capability and quick reflexes, and therefore requires caution when driving a vehicle, operating dangerous machinery and any activity that requires alertness. Abstain from all such activities until you understand how **Zappa** and **Zappa ODT** affect you.
Important information about some of the ingredients of the medicine:
Zappa contains lactose. If the doctor told you that you have an intolerance to certain types of sugar, consult the doctor before you take this medicine.

3. HOW SHOULD YOU USE THE MEDICINE?

- Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are unsure about the dosage and treatment regimen of the medicine.
- The dosage and treatment regimen will be determined by the doctor only. The doctor may need to change the dosage until he finds the right dosage for you.
- **Do not exceed the recommended dosage.**
- **Zappa 5** and **Zappa 10:** If necessary, the tablet can be halved for immediate use. There is no information about crushing or chewing the tablet. Swallow the medicine with a little water.
  Zappa 7.5: Do not halve the tablet. There is no information about crushing or chewing the tablet. Swallow the tablet with a little water.
  Zappa ODT: Separate one unit from the tray and carefully peel off the cover. Do not push the tablet. Take out the tablet with dry hands and immediately place it whole into your mouth. The tablet dissolves quickly in saliva; therefore, it can be easily swallowed with or without a drink.
- There is no information about use of this preparation in a nasogastric tube.
- Use this medicine at regular intervals, as determined by the attending doctor.
- **If you accidentally take too high a dose**, you may feel drowsy, experience impaired speech, aggressiveness or restlessness, rapid heart rate and a reduced level of consciousness.
  If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you.
- **If you forgot to take the medicine** at the required time, take the medicine as soon as you remember. If it is close to the time of taking the next dose, skip this dose and take the dose at the usual time. Do not take a double dose.
- Adhere to the treatment regimen 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.
- **To avoid serious side effects, do not stop taking Zappa and Zappa ODT abruptly. If you need to stop taking Zappa and Zappa ODT, your doctor will instruct you on how to do it.**

Do not take medicines in the dark! Check the label and the dose each time you take the 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 **Zappa** and **Zappa ODT** 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.
Zappa and Zappa ODT may cause severe side effects:
1. **Increased risk of death** in elderly patients who are experiencing confusion, memory loss and loss of touch with reality (psychosis associated with dementia). **Zappa** and **Zappa ODT** are not intended for use in elderly patients with dementia.
2. **Increase in blood sugar levels (hyperglycemia)** may occur in patients suffering from diabetes as well as in patients who are not suffering from diabetes. Increase in blood sugar levels may cause:
   - ketoacidosis - increased level of acid in the blood due to build-up of ketones
   - coma
   - death

   Your doctor must perform blood tests for your blood sugar levels before starting and during treatment with **Zappa** and **Zappa ODT**. Patients who are not suffering from diabetes may experience an increase in blood sugar levels when discontinuing **Zappa** and **Zappa ODT** treatment.
   Patients suffering from diabetes and some patients who did not suffer from diabetes when they started **Zappa** and **Zappa ODT** treatment must take a medicine to reduce their blood sugar levels when discontinuing **Zappa** and **Zappa ODT** treatment.
   If you suffer from diabetes, your doctor will instruct you how often to have blood tests for blood sugar levels when taking **Zappa** and **Zappa ODT**.
   Refer to a doctor if you experience symptoms of high blood sugar levels:
   - increased thirst
   - increased frequency of urination
   - increased sensation of hunger
   - weakness and tiredness
   - nausea
   - confusion or fruity breath odor
3. **Increase in blood lipid (cholesterol and triglyceride) levels** may occur in patients who are being treated with **Zappa** and **Zappa ODT**. Your doctor must perform blood tests for blood cholesterol and lipid levels at the beginning of and during treatment even if you are not experiencing any symptoms.
4. **Weight gain** is very common in patients who are being treated with **Zappa** and **Zappa ODT**. Some patients experience extreme weight gain. Consult the doctor about watching your weight, such as a healthy diet and physical activity.
5. **Increased frequency of stroke or "mini-stroke" – transient ischemic attack (TIA) in elderly people with psychosis associated with dementia** (elderly people who are suffering from loss of touch with reality due to confusion and memory loss). **Zappa and Zappa ODT are not approved for use in these patients.**
6. **Neuroleptic malignant syndrome** – a rare but very serious condition which may occur in patients who are taking antipsychotic medicines, including **Zappa** and **Zappa ODT**. Neuroleptic malignant syndrome may cause death and requires hospitalization. Refer to the doctor immediately if you experience:
   - high fever
   - increased sweating
   - stiff muscles
   - confusion
   - changes in your breathing, heartbeat and blood pressure
7. **Drug reaction with eosinophilia and systemic symptoms (DRESS)**. This effect may include: rash, fever, swollen glands and involve other internal organs such as: liver, kidneys, lungs and heart. This effect can sometimes lead to death; therefore, tell the doctor immediately if you experience any of these signs.
8. **Tardive dyskinesia** – a condition that causes involuntary movements, mainly of the face or tongue. This effect may continue even after you stop treatment with **Zappa** and **Zappa ODT**. This effect may also start after you stop treatment with **Zappa** and **Zappa ODT**. Tell the doctor if you are having involuntary body movements.
9. **Drop in blood pressure when changing position,** including symptoms such as dizziness, fast or slow heartbeat, or fainting. The effect primarily occurs when first starting to take the medicine.
10. **Difficulty swallowing** which may cause food or beverages to reach the lungs.
11. **Seizures** – tell your doctor if you experience seizures during the course of treatment with **Zappa** and **Zappa ODT**.
12. **Problems regulating body temperature** – you may suffer from an increase in body temperature, for example, when you exercise or when you are in a very hot place. It is important to drink water to prevent dehydration. Refer to the doctor immediately if you become very ill and have symptoms of dehydration:
    - excessive sweating or lack of sweat
    - dry mouth
    - you feel very hot
    - increased thirst
    - urine retention

Additional side effects:
Side effects occurring very frequently:
Weakness (lack of energy), dry mouth, constipation, indigestion, sleepiness, dizziness, injury from an accident, insomnia, parkinsonism.
Side effects occurring frequently:
Fever, tremor, back ache, chest pain, limb pains, joint pains, increased heart rate, hypertension, vomiting, physical restlessness, increased appetite, behavioral changes, increased triglyceride levels in the blood, weight gain, hypotension upon transition from lying down to sitting up, bleeding under the skin manifesting as patches on the skin, peripheral edema, abnormal gait, stiff muscles, pronunciation (speech) impairment, runny nose, cough, lazy eye, inflammation of the pharynx, drowsiness, urinary incontinence, urinary tract infection, increased prolactin levels, increased blood levels of alkaline phosphatase, discharge of milk from the breasts, enlarged breasts in men, memory impairment, paresthesia, uplifted mood (euphoria), shortness of breath, dry skin, acne, visual impairment, menstrual pain and vaginal inflammation in women, hard stools or rarely passing stools.
Side effects occurring infrequently:
Chills, facial edema, sensitivity to light, attempted suicide, stroke, vasodilatation, nausea, vomiting, tongue edema, reduced white blood cell levels, reduced platelet levels, high blood levels of bilirubin, low blood levels of proteins, coordination problems, impaired speech, reduced libido, lack of sensitivity, bleeding from the nose, hair loss, dry eyes, changes in visual focus (accommodation), impotence, changes in the menstrual cycle (such as no menstruation, decrease/increase in menstrual bleeding, heavy menstrual bleeding), urine retention, urinary frequency and urgency, large urine volume, breast pain, dystonia (spasm of the neck muscles, difficulty swallowing, difficulty breathing, tongue protrusion), abdominal distension and death due to diabetes.
Side effects occurring rarely:
Hangover effect, blocked intestine, fatty liver, osteoporosis, coma, pulmonary edema, dilated pupils, sudden death.
Side effects of unknown frequency:
Allergic reaction [such as: anaphylactic reaction, swelling of the face or throat (angioedema), itch, rash], diabetes-related coma, diabetic ketoacidosis, side effects that may occur when stopping treatment (nausea, vomiting and sweating), jaundice, pancreatitis and hepatitis, liver injury, increased salivation, restless legs syndrome, neutropenia (reduced number of a certain type of white blood cells), painful and prolonged erection (priapism), painful muscle injury (rhabdomyolysis), venous thrombosis, stuttering.
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:
http://sideeffects.health.gov.il
Additionally, you can report to "Unipharm Ltd".

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 package. The expiry date refers to the last day of that month.
- Store the medicine at a temperature that does not exceed 25°C and in a place protected from light.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
Zappa:
Lactose monohydrate, Microcrystalline cellulose, Hydroxypropyl cellulose, Crospovidone, Magnesium stearate, Opadry white Y-1-7000, Opadry yellow OY-6478.
Zappa ODT:
Ludiflash [D-Mannitol, Crospovidone, Polyvinyl acetate, Povidone], Crospovidone, Sodium stearyl fumarate, Grape flavour, Acesulfame potassium.
Zappa 5 tablets contain: 116.45 mg lactose monohydrate per tablet.
Zappa 7.5 tablets contain: 174.68 mg lactose monohydrate per tablet.
Zappa 10 tablets contain: 232.9 mg lactose monohydrate per tablet.
What the medicine looks like and the content of the package:
Zappa:
Zappa is packaged in a tray (blister), provided in a carton box.
Zappa 5 and **Zappa 10** are round, biconvex, pale yellow tablets with a break line on one side.
Zappa 7.5 are round, biconvex, pale yellow tablets.
Zappa ODT:
Zappa ODT is packaged in a tray (blister), provided in a carton box.
Zappa ODT are round, biconvex, pale yellow tablets.
Zappa ODT are orodispersible tablets, intended for swallowing.
For **Zappa 5** and **Zappa 10**, there are pack sizes with 5, 7, 10, 14, 15, 28, 30 and 56 tablets.
For **Zappa 7.5**, **Zappa ODT 5** and **Zappa ODT 10**, there are pack sizes with 5, 7, 10, 14, 15, 28, 30, 56 and 60 tablets.
Not all package sizes may be marketed.
Registration holder and address: Unipharm Ltd., P.O.B. 21429, Tel Aviv, 6121301.
Manufacturer and address: Unipharm Ltd., "Mevo Carmel" Industrial Park.
Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:
Zappa 5: 146 70 33248 01 **Zappa 7.5:** 146 71 33250 01
Zappa 10: 146 72 33251 01 **Zappa ODT 5:** 150 20 33645 01
Zappa ODT 10: 150 21 33756 01
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