Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is to be supplied by a doctor's prescription only

Zyprexa	**Zyprexa**	**Zyprexa**
5 mg	**7.5 mg**	**10 mg**
Tablets	Tablets	Tablets
Composition:	**Composition:**	**Composition:**
Each tablet contains:	Each tablet contains:	Each tablet contains:
Olanzapine 5 mg	Olanzapine 7.5 mg	Olanzapine 10 mg

Inactive ingredients and allergens: See section 6 "Additional information" and "Important information regarding some of the ingredients of this medicine" in section 2.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, refer to the doctor or pharmacist.
This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them even if it seems to you that their illness is similar.

Vital information about this medicine:

Warning: Increased mortality in elderly patients with dementia-related psychosis.
Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.
Similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. Zyprexa can cause a serious side effect, including
increase the risk of death in elderly people who are experiencing confusion, memory loss, and loss of touch with reality (dementia-related psychosis). Zyprexa is not approved for treatment of adult patients who suffer from dementia-related psychosis.

Zyprexa is intended for adults over 18 years of age.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Acute and maintenance treatment of schizophrenia.
Zyprexa is indicated for the management of the manifestations of psychotic disorders.
Zyprexa is indicated for the short-term treatment of acute manic episodes associated with Bipolar I Disorder.

Prevention of recurrence in Bipolar Disorder:
In patients whose manic episode has responded to olanzapine treatment, **Zyprexa** is indicated for the prevention of recurrence in patients with Bipolar Disorder.

Combination therapy in Bipolar I Disorder:
The combination of **Zyprexa** with lithium or valproate is indicated for the short-term treatment of acute manic episodes 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, impulsive behavior, and decreased need for sleep.
The symptoms of treatment resistant depression include decreased mood, decreased interest, increased guilty feelings, decreased energy, decreased concentration, changes in appetite and suicidal thoughts or behavior.

2. BEFORE USING THIS MEDICINE:

Do not use this medicine if:

- you are sensitive (allergic) to olanzapine or to any of the other ingredients that this medicine contains.
- For specific information on the contraindications of lithium or valproate, refer to the Contraindications section of the package inserts included in the packs of those products.

Special warnings regarding the use of this medicine:

- **Zyprexa** interferes with the body's ability to reduce temperature. Situations in which there may be an increase in body temperature and dehydration, such as increased physical activity or frequent stays in hot places, should be avoided. Be sure to drink fluids to prevent dehydration.
- **Zyprexa** may cause low blood pressure upon transition from a lying to sitting position. The symptoms include: dizziness, slow or rapid heart rate, and even fainting in some patients. This side effect usually occurs at the beginning of treatment.
- **Zyprexa can cause drowsiness, low blood pressure upon transition from a lying to sitting position, and motor and sensory instability that can lead to falls resulting in fractures and other injuries.** Use with caution and consider the risks against the benefits in patients with underlying conditions or who are taking medicines that may increase the risk of falls.
- Weight gain has been observed in patients taking **Zyprexa**. Weight should be monitored regularly.
- Blood sugar and lipid levels should be monitored since **Zyprexa** 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. **Zyprexa** may cause a decrease in the levels of white blood cells. Discontinuation of **Zyprexa** treatment should be considered upon appearance of the first symptom of this condition. Patients with reduced levels of white blood cells must be monitored for symptoms indicating infection or fever. If any of these are experienced, immediately discontinue the treatment with **Zyprexa.**
- Taking **Zyprexa** is not recommended for elderly patients suffering from dementia due to the probability of severe side effects: falls, drowsiness, peripheral edema, abnormal walking, urinary incontinence, extreme tiredness, 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 **Zyprexa**.
- 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 **Zyprexa** in these patients may cause symptoms such as constipation, dry mouth and tachycardia. From experience gained after marketing the drug, it was found that the risk of serious side effects (including deaths) increased when combining **Zyprexa** with anticholinergic drugs.

Before treatment with Zyprexa tell your doctor if you:
- suffer or have previously suffered from cardiac dysfunction.
- suffer or have previously suffered from a stroke or “mini stroke” (temporary symptoms of stroke).
- suffer or have previously suffered from seizures, diabetes or high blood glucose levels, high or low blood pressure, high blood levels of cholesterol or triglycerides
- suffer from problems with the liver, gastrointestinal system (such as bowel obstruction).
- suffer from Alzheimer’s disease, breast cancer.
- Suffer or have previously suffered from narrow-angle glaucoma.
- experience suicidal thoughts or harming yourself. In this case you should contact a doctor or Emergency Room immediately.
- suffer or have previously suffered from enlargement of the prostate gland.
- .
- exercise a lot or stay in hot places often.
- have a history of drug abuse.
- are sensitive to a certain type of food or medicine.
- are sensitive to lactose - **Zyprexa** contains lactose and may cause sensitivity in people sensitive to lactose.
- suffer from any other medical condition.

Smoking:
If you smoke - inform your doctor prior to beginning treatment with this medicine.

Tests and follow-up:
- At the beginning and during treatment, blood glucose levels should be monitored, especially if you have diabetes or borderline glucose levels (fasting levels of 100-126 mg/dL)
- You should monitor the levels of fats (cholesterol and triglycerides) in the blood, especially in patients with impaired blood lipid levels or risk factors of developing such disorders. Blood tests for blood lipids should be performed at the beginning and during treatment even if you do not have any symptoms.
- Weight gain is a common side effect of treatment with **Zyprexa**. This should be taken into account prior to beginning the treatment and weight should be routinely monitored.
- In patients with a history of low white blood cell levels, white blood cell levels should be monitored during the first months of treatment. Discontinuation of treatment with **Zyprexa** should be considered upon appearance of the first significant symptom indicating reduced white blood cell levels.

Drug interactions:
If you are taking or have recently taken other medicines, including over-the-counter medications and food supplements, inform your doctor or pharmacist. Especially if you are taking:
- Diazepam: co-administration of **Zyprexa** and diazepam may cause low blood pressure upon transition from a lying to sitting position (orthostatic hypotension).

- Medicines affecting the CYP1A2 enzyme, such as 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 high blood pressure – olanzapine may enhance the blood pressure lowering effect upon concomitant administration with these medicines.
- Medicines that mimic the action of dopamine (such as Levodopa, a drug for the treatment of Parkinson's disease and agonists for dopamine) - olanzapine may inhibit the activity of these medicines.
- Anticholinergic drugs - their combination with **Zyprexa** may increase the risk of serious gastrointestinal side effects resulting from decreased gastrointestinal motility. Concomitant treatment with these drugs and olanzapine should be used in caution.

Use of this medicine and food
Zyprexa may be taken with or without food.

Use of this medicine and alcohol consumption:
Avoid drinking alcohol while taking **Zyprexa**. Drinking alcohol while taking **Zyprexa** may make you sleepier compared to taking **Zyprexa** without alcohol.

Pregnancy, breastfeeding and fertility:
Pregnancy
Consult a doctor or pharmacist before taking this medicine.
Consult a doctor if you are pregnant or planning to get pregnant. It is not known whether **Zyprexa** harms the fetus. Newborns may develop a withdrawal syndrome if the mother has taken the medicine during the last trimester (last 3 months) of pregnancy. The withdrawal syndrome includes the following symptoms: restlessness, tremor, muscle stiffness/weakness, drowsiness, irritability, 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. There are reports of excess sedation, irritability, poor feeding and extrapyramidal symptoms (tremors and abnormal muscle movements) in infants exposed to olanzapine through breast milk. Infants exposed to olanzapine should be monitored for these symptoms. There is no information on the effects of olanzapine on milk production.
Talk to your doctor about the best way to feed your baby if you are taking **Zyprexa**.

Fertility
Treatment with **Zyprexa** may cause an increase in blood prolactin levels, which can lead to reversible infertility in women of childbearing potential.

Driving and using machines:
The use of this medicine may cause drowsiness and affect your decision-making skills, sharp thinking or quick response, and therefore requires caution when driving a vehicle, operating dangerous machinery and any activity that requires alertness. Avoid any activity such as these until you understand how **Zyprexa** affects you.

Important information about some of the ingredients of this medicine:

Zyprexa contains lactose. If your doctor has told you that you have an intolerance to some sugars, talk to your doctor before taking this medicine.

3. HOW TO USE THIS MEDICINE?

- Always use according to the doctor's instructions. You must check with the doctor or pharmacist if you are not sure about the dose and manner of treatment with the drug.
- The dosage and manner of treatment will be determined only by the doctor. Your doctor may need to change the dose until he finds the right dose for you.
- **Do not exceed the recommended dose.**
- There is no information on the preparation when it is crushed or split. Therefore, do not chew, crush or split the tablets! Swallow the medicine with some water.
- There is no information on the preparation when used with a nasogastric tube.
- **If you have accidentally taken a higher dose** you may feel drowsy, experience impaired speech, aggressiveness or restlessness, rapid heart rate and reduced levels of consciousness.
  If you have taken an overdose or if a child has accidentally swallowed the medicine, go immediately to a hospital Emergency Room and bring the medicine package 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.
- Persist with the treatment as recommended by the doctor.
- Even if there is an improvement in your health, do not discontinue treatment with this medicine without consulting the doctor or pharmacist.
- **To avoid serious side effects, do not stop taking Zyprexa abruptly. If you need to stop taking Zyprexa, 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 a medicine. Wear glasses if you need them.**

If you have any further questions regarding the use of this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, the use of **Zyprexa** may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not experience any of them.

Zyprexa may cause serious side effects:

1. **Increased risk of death** in elderly patients who are experiencing confusion, memory loss, and loss of touch with reality (dementia-related psychosis). **Zyprexa** is not intended for use in elderly patients with dementia.
2. **Increase in blood glucose levels (hyperglycemia)** may occur in patients with diabetes and in patients who do not have diabetes. Increase in blood glucose levels may cause:
   - ketoacidosis - increased level of acid in the blood due to build-up of ketones
   - coma
   - death

   Your doctor should perform blood tests to regularly monitor your blood glucose levels before and during treatment with **Zyprexa**. Patients who do not have diabetes may experience an increase in blood glucose levels that go away when they stop taking **Zyprexa**. Patients with diabetes and some patients who did not have diabetes at the start of treatment with **Zyprexa**

should take medication to lower their blood glucose even after stopping treatment with **Zyprexa**.
If you have diabetes, your doctor will tell you how often to perform blood tests for blood glucose levels while taking **Zyprexa**.
Consult a doctor if you experience symptoms of high blood glucose levels:

- increased thirst
- frequent urination
- increased appetite
- feeling weakness or fatigue
- feeling nausea
- feeling confusion or fruity breath odor

3. **Increase in lipid levels (cholesterol and triglyceride) in the blood** may occur in patients who are being treated with **Zyprexa**. Your doctor must perform blood tests for cholesterol and lipid levels before the beginning and during treatment even if you do not have any symptoms.
4. **Weight gain** is very common in patients who are taking **Zyprexa**. Some patients experience extreme weight gain. Consult your doctor regarding weight maintenance such as a healthy and balanced diet and exercise.
5. **Increased frequency of stroke or "mini stroke" - Transient Ischemic Attack (TIA) in elderly people with dementia-related psychosis** (elderly people who are experiencing loss of touch with reality due to confusion and memory loss). **Zyprexa** is not approved for use in these patients.
6. **Neuroleptic malignant syndrome** - a rare but serious condition which may occur in patients who are taking antipsychotic medicines, including **Zyprexa**. Neuroleptic malignant syndrome may cause death and requires hospitalization. Refer to the doctor immediately if you become ill and experience the following symptoms:
    - high fever
    - increased sweating
    - stiff muscles
    - confusion
    - changes in your breathing, heart rate, and blood pressure
7. **Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).** This side effect may occur with **Zyprexa**. This side effect may include: rash, fever, swollen and mixed glands of other internal organs such as: liver, kidneys, lungs and heart. This side effect can sometimes lead to death, so tell your doctor immediately if you experience any of these symptoms.
8. **Tardive dyskinesia** - a condition that causes involuntary movements in the body which you can't control. The movements are usually of the face or tongue. This side effect may continue even after you stop taking **Zyprexa**. This side effect may also start after you stop taking **Zyprexa**. Tell your doctor if you are having involuntary body movements.
9. **Drop in blood pressure when changing position** including symptoms such as dizziness, fast or slow heart rate, or fainting. This side effect occurs mainly at the beginning of taking this medicine.
10. **Difficulty swallowing** which may cause food or liquid to get into your lungs.
11. **Seizures** - tell your doctor if you experience seizures while using **Zyprexa**.
12. **Problems regulating body temperature** - you may experience 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. See your doctor immediately if you become very ill and have symptoms of dehydration:
    - excessive sweating or lack of sweat

- dry mouth
- feel very hot
- increased thirst
- urine retention

Additional side effects

Very common side effects:
Weakness (lack of energy), dry mouth, constipation, indigestion, drowsiness, dizziness, accidental injury, sleep disorders, parkinsonism.

Common side effects:
Fever, tremors, back pain, chest pain, pain in your limbs, joint pain, increased heart rate, high blood pressure, vomiting, physical restlessness, increased appetite, behavioral changes, increased triglyceride levels in the blood, weight gain, drop in blood pressure in the transition from lying to sitting, subcutaneous bleeding manifested as patches on the skin, peripheral edema, abnormal walking, stiff muscles, speech impediment, runny nose, cough, lazy eye, inflammation of the esophagus, sleepiness, 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.

Uncommon side effects:
Chills, facial edema, sensitivity to sunlight, attempted suicide, stroke, vasodilatation, nausea, vomiting, tongue edema, reduced white blood cell levels, reduced blood platelet levels, high blood levels of bilirubin, low blood levels of proteins, coordination problems, impaired speech, reduced libido, lack of sensitivity, nose bleeding, hair loss, dry eyes, changes in visual 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, difficulties swallowing, difficulties breathing, tongue protrusion), abdominal distension and death due to diabetes.

Rare side effects:
Hangover effect, intestinal obstruction, 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), itching, 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 you experience any side effect, if any side effect gets worse, or if you suffer from a side effect not mentioned in the leaflet, you should consult the doctor.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Reporting side effects due to drug treatment" that can be found on the Home Page of the Ministry of Health's website (www.health.gov.il), which refers to an online form for reporting side effects, or by entering the following link: https://sideeffects.health.gov.il

5. HOW TO STORE THIS MEDICINE?

- Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- **Storage conditions**: store at room temperature, below 30˚C.

6. ADDITIONAL INFORMATION:

In addition to the active ingredient, Zyprexa tablets also contain:
Lactose monohydrate, microcrystalline cellulose, crospovidone, color mixture white YS-1-18027-A, hydroxypropyl cellulose, methyl hydroxypropyl cellulose, magnesium stearate, carnauba wax and edible blue ink.

Zyprexa 5 mg tablets: contain 156 mg lactose/tablet.
Zyprexa 7.5 mg tablets: contain 234 mg lactose/tablet.
Zyprexa 10 mg tablets: contain 312 mg lactose/tablet.

What does the medicine look like and what are the contents of the package:
Zyprexa 5 mg tablets: packs of 7, 14, 28, 56 round white film-coated tablets with the text "LILLY" and the code "4115" imprinted on them.
Zyprexa 7.5 mg tablets: packs of 7, 14, 28, 56 round white film-coated tablets with the text "LILLY" and the code "4116" imprinted on them.
Zyprexa 10 mg tablets: packs of 7, 14, 28, 56 round white film-coated tablets with the text "LILLY" and the code "4117" imprinted on them.
Not all pack sizes may be marketed.

License holder and address:
Eli Lilly Israel Ltd., 4 HaSheizaf Street, P.O.B 4246, Ra'anana 4366411.

Manufacturer name and address:
Lilly S.A., Alcobendas (Madrid), Spain.

Revised in June 2024.

Registration numbers in the National Drug Registry of the Ministry of Health:
Zyprexa 5 mg: 104-84-28857-21
Zyprexa 7.5 mg: 104-85-28858-21
Zyprexa 10 mg: 104-86-28859-21