Package leaflet: Information for the user

ZYPADHERA 210 mg powder and solvent for prolonged release suspension for injection
ZYPADHERA 300 mg powder and solvent for prolonged release suspension for injection
ZYPADHERA 405 mg powder and solvent for prolonged release suspension for injection

olanzapine

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

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

1. What ZYPADHERA is and what it is used for

ZYPADHERA contains the active substance olanzapine. ZYPADHERA belongs to a group of medicines called antipsychotics and is used to treat schizophrenia - a disease with symptoms such as hearing, seeing or sensing things which are not there, mistaken beliefs, unusual suspiciousness, and becoming withdrawn. People with this disease may also feel depressed, anxious or tense.

ZYPADHERA is intended for adult patients who are sufficiently stabilised during treatment with oral olanzapine.

2. What you need to know before you are given ZYPADHERA

You should not be given ZYPADHERA if you have:
- an allergy (hypersensitivity) to olanzapine or any of the other ingredients of this medicine (listed in section 6). **An allergic reaction** may be recognised as a rash, itching, a swollen face, swollen lips or shortness of breath. If this has happened to you, tell your nurse or doctor.
- been previously diagnosed with eye problems such as certain kinds of glaucoma (increased pressure in the eye).

Warnings and precautions
Talk to your doctor or nurse before you are given ZYPADHERA

- ***An uncommon but serious reaction might occur after you receive each injection.*** ZYPADHERA can sometimes enter the bloodstream too quickly. If this happens, you may have the symptoms listed below after your injection. In some cases, these symptoms can lead to unconsciousness.

  - excessive sleepiness
  - confusion
  - irritability
  - aggression
  - difficulty talking
  - difficulty walking
  - convulsions
  - dizziness
  - disorientation
  - anxiety
  - increase in blood pressure
  - weakness
  - muscle stiffness or shaking

  These symptoms typically resolve within 24 to 72 hours after your injection. After each injection you will be observed in your healthcare facility for at least 3 hours for the symptoms listed above.

  Although unlikely, you may get the symptoms more than 3 hours after the injection. If this happens, contact your doctor or nurse immediately. Because of this risk, do not drive or operate machinery for the remainder of the day after each injection.

- Tell the doctor or nurse if you feel dizzy or faint after the injection. You will probably need to lie down until you feel better. The doctor or nurse may also want to measure your blood pressure and pulse.
- The use of ZYPADHERA in **elderly patients with dementia** (confusion and memory loss) is not recommended as it may have serious side effects.
- Very rarely, medicines of this type may cause unusual movements mainly of the face or tongue or a combination of fever, faster breathing, sweating, muscle stiffness and drowsiness or sleepiness. If this happens after you have been given ZYPADHERA, tell your doctor or nurse immediately.
- Weight gain has been seen in patients taking ZYPADHERA. You and your doctor should check your weight regularly. Consider referral to a dietician or help with a diet plan if necessary.
- High blood sugar and high levels of fat (triglycerides and cholesterol) have been seen in patients taking ZYPADHERA. Your doctor should do blood tests to check blood sugar and certain fat levels before you start taking ZYPADHERA and regularly during treatment.
- Tell the doctor if you or someone else in your family has a history of blood clots, as medicines like these have been associated with formation of blood clots.

Tell your doctor as soon as possible if any of the following applies to you:

- Stroke or “mini” stroke (temporary symptoms of stroke)
- Parkinson’s disease
- Prostate problems
- A blocked intestine (Paralytic ileus)
- Liver or kidney disease
- Blood disorders
- A recent heart attack, heart disease, sick sinus syndrome, (abnormal heart rhythms), unstable angina or low blood pressure
- Diabetes
- Seizures
- If you know that you may have salt depletion as a result of prolonged severe diarrhoea and vomiting (being sick) or usage of diuretics (water tablets)

As a routine precaution, if you are **over 65** years your doctor may monitor your blood pressure.

ZYPADHERA is not recommended to be started if you are over 75 years.

Children and adolescents
ZYPADHERA is not for patients who are under 18 years.

Other medicines and ZYPADHERA
Tell your doctor if you are taking, have recently taken or might take any other medicines.

In particular, tell your doctor if you are taking:
- medicines for Parkinson's disease.
- carbamazepine (an anti-epileptic and mood stabiliser), fluvoxamine (an antidepressant) or ciprofloxacin (an antibiotic) - it may be necessary to change your ZYPADHERA dose.

If you are already taking antidepressants, medicines for anxiety or to help you sleep (tranquillisers), you may feel drowsy if ZYPADHERA is given.

ZYPADHERA with alcohol
Do not drink any alcohol if you have been given ZYPADHERA as together with alcohol it may make you feel drowsy.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before being given this injection.
You should not be given this injection if you are breast-feeding as small amounts of olanzapine can pass into breast milk.

The following symptoms may occur in newborn babies, of mothers that have used ZYPAHDERA 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 you may need to contact your doctor.

Driving and using machines
Do not drive or operate machinery for the remainder of the day after each injection.

ZYPADHERA contains polysorbate 80
This medicine contains 0,9 mg of polysorbate 80 in each ml. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

ZYPADHERA contains sodium
After reconstitution this medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially sodium-free.

3. How ZYPADHERA is given

Your doctor will decide how much ZYPADHERA you need and how often you need to be given an injection. ZYPADHERA is given in doses of 150 mg to 300 mg every 2 weeks or 300 mg to 405 mg every 4 weeks.

ZYPADHERA comes as a powder which your doctor or nurse will make into a suspension that will then be injected into the muscle in your buttock.

If you are given more ZYPADHERA than needed

This medicine will be given to you under medical supervision, it is therefore unlikely that you will be given too much.

Patients who have been given too much olanzapine have also experienced the following symptoms:
- rapid beating of the heart, agitation/aggressiveness, problems with speech, unusual movements (especially of the face or tongue) and reduced level of consciousness.

Other symptoms may include:
- acute confusion, seizures (epilepsy), coma, a combination of fever, faster breathing, sweating, muscle stiffness, and drowsiness or sleepiness; slower breathing, aspiration, high or low blood pressure, abnormal rhythms of the heart.

Contact your doctor or hospital straight away if you experience any of the above symptoms.

If you miss an injection of ZYPADHERA
Do not stop your treatment just because you feel better. It is important that you carry on receiving ZYPADHERA for as long as your doctor has told you to.

If you miss an injection, you should contact your doctor to arrange your next injection as soon as you can.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor immediately if you have:
- excessive sleepiness, dizziness, confusion, disorientation, difficulty talking, difficulty walking, muscle stiffness or shaking, weakness, irritability, aggression, anxiety, increase in blood pressure, or convulsions and can lead to unconsciousness. These signs and symptoms can sometimes occur as a result of ZYPADHERA entering the bloodstream too quickly (a common side effect that may affect up to1 in10 people);
- unusual movement (a common side effect that may affect up to 1 in 10 people) mainly of the face or tongue;
- blood clots in the veins (an uncommon side effect that may affect up to 1in 100 people) 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 in breathing. If you notice any of these symptoms seek medical advice immediately;
- a combination of fever, faster breathing, sweating, muscle stiffness and drowsiness or sleepiness (the frequency of this side effect cannot be estimated from the available data).

Other common side effects (may affect up to 1 in 10 people) with ZYPADHERA include sleepiness and injection site pain.

Rare side effects (may affect up to 1 in 1000 people) with ZYPADHERA include injection site infection.

The side effects listed below have been observed when oral olanzapine has been given but may occur following administration of ZYPADHERA.

Other very common side effects (may affect more than 1 in 10 people) include weight gain; and increases in levels of prolactin in the blood. In the early stages of treatment, some people may feel dizzy or faint (with a slow heart rate), especially when getting up from a lying or sitting position. This will usually pass on its own but if it does not, tell your doctor.

Other common side effects (may affect up to 1 in 10 people) include changes in the levels of some blood cells, circulating fats and in early treatment, temporary increases in liver enzymes; increases in the level of sugars in the blood and urine; increases in levels of uric acid and creatine phosphokinase in the blood; feeling more hungry; dizziness; restlessness; tremor; unusual movements (dyskinesias); constipation; dry mouth; rash; loss of strength; extreme tiredness; water retention leading to swelling of the hands, ankles or feet; fever; joint pain; and sexual dysfunctions such as decreased libido in males and females or erectile dysfunction in males.

Other uncommon side effects (may affect up to 1 in 100 people) include hypersensitivity (e.g. swelling in the mouth and throat, itching; rash); diabetes or the worsening of diabetes, occasionally associated with ketoacidosis (ketones in the blood and urine) or coma; seizures, usually associated with a history of seizures (epilepsy); muscle stiffness or spasms (including eye movements); restless legs syndrome; problems with speech; stuttering; slow heart rate; sensitivity to sunlight; bleeding from the nose: abdominal distension; drooling; memory loss or forgetfulness; urinary incontinence; lack of ability to urinate; hair loss; absence or decrease in menstrual periods; and changes in breasts in males and females such as an abnormal production of breast milk or abnormal growth.

Rare side effects (may affect up to 1 in 1000 people) include lowering of normal body temperature; abnormal rhythms of the heart; sudden unexplained death; inflammation of the pancreas causing severe stomach pain, fever and sickness; liver disease appearing as yellowing of the skin and white parts of the eyes; muscle disease presenting as unexplained aches and pains; and prolonged and/or painful erection.

Very rare side effects include serious allergic reactions such as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). DRESS appears initially as flu-like symptoms with a rash on the face and then with an extended rash, high temperature, enlarged lymph nodes, increased levels of liver enzymes seen on blood tests and an increase in a type of white blood cells (eosinophilia).

While taking olanzapine, elderly patients with dementia may suffer from stroke, pneumonia, urinary incontinence, falls, extreme tiredness, visual hallucinations, a rise in body temperature, redness of the skin and have trouble walking. Some fatal cases have been reported in this particular group of patients.

In patients with Parkinson's disease oral olanzapine may worsen the symptoms.

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via

Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store ZYPADHERA

Keep this medicine out of the sight and reach of children.

The injection must not be given after the expiry date which is stated on the carton.

Do not refrigerate or freeze.

Chemical and physical stability of the suspension in the vials has been demonstrated for 24 hours at 20-25 °C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 20-25°C. Do not use this product if you notice discolouration or other visible signs of deterioration.

If the medicine is not used right away, it should be shaken vigorously to re-suspend. Once withdrawn from vial into the syringe, the suspension should be used immediately.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What ZYPADHERA contains
The **active substance** is olanzapine.
ZYPADHERA 210 mg: Each vial contains olanzapine pamoate monohydrate equivalent to 210 mg olanzapine.
ZYPADHERA 300 mg: Each vial contains olanzapine pamoate monohydrate equivalent to 300 mg olanzapine.
ZYPADHERA 405 mg: Each vial contains olanzapine pamoate monohydrate equivalent to 405 mg olanzapine.
After reconstitution: 1ml suspension contains 150 mg/ml olanzapine.

The **solvent ingredients** are carmellose sodium, mannitol, polysorbate 80, water for injections, hydrochloric acid and sodium hydroxide.

What ZYPADHERA looks like and contents of the pack
ZYPADHERA powder for prolonged release suspension for injection comes as a yellow powder in a clear glass vial. Your doctor or nurse will make it into a suspension that will be given as an injection using the vial of solvent for ZYPADHERA that comes as a clear, colourless to slightly yellow solution in a clear glass vial.

ZYPADHERA is a powder and solvent for prolonged release suspension for injection. One carton contains one vial of powder for prolonged release suspension for injection, one vial of 3 ml solvent, one syringe with safety needle, 19 gauge, 38mm, attached and three separate safety needles; one 19 gauge, 38mm needle and two 19 gauge 50mm needles.

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INSTRUCTIONS FOR HEALTH CARE PROFESSIONALS

RECONSTITUTION AND ADMINISTRATION INSTRUCTIONS

ZYPADHERA olanzapine powder and solvent for prolonged release suspension for injection

FOR DEEP INTRAMUSCULAR GLUTEAL INJECTION ONLY.
DO NOT ADMINISTER INTRAVENOUSLY OR SUBCUTANEOUSLY

Reconstitution
STEP 1: Preparing materials
Pack includes:

- Vial of ZYPADHERA powder for prolonged release suspension for injection
- Vial of solvent for ZYPADHERA
- One Hypodermic syringe and safety needle (Hypodermic Device)
- One 19-gauge, 38 mm Hypodermic safety needle
- Two 19-gauge, 50 mm Hypodermic safety needles
- Patient Information Leaflet
- Reconstitution and Administration card (this leaflet)
- Hypodermic Device Safety Information and Instructions for Use leaflet

It is recommended that gloves are used as ZYPADHERA may irritate the skin.

Reconstitute ZYPADHERA powder for prolonged release suspension for injection only with the solvent provided in the pack using standard aseptic techniques for reconstitution of parenteral products.

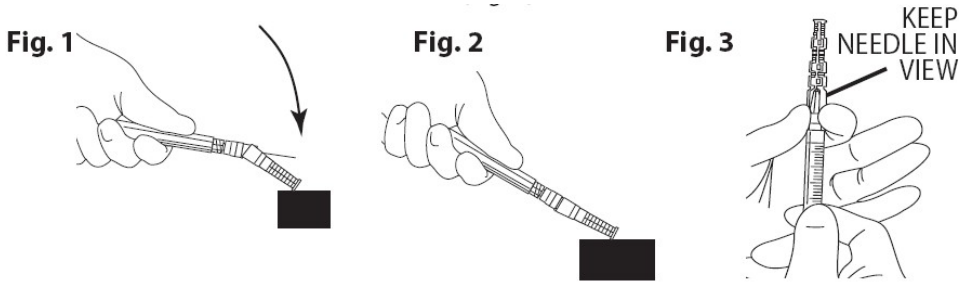
STEP 2: Determining solvent volume for reconstitution
This table provides the amount of solvent required to reconstitute ZYPADHERA powder for prolonged release suspension for injection.

ZYPADHERA vial strength (mg)	Volume of solvent to add (ml)
210	1.3
300	1.8
405	2.3

It is important to note that there is more solvent in the vial than is needed to reconstitute.

STEP 3: Reconstituting ZYPADHERA

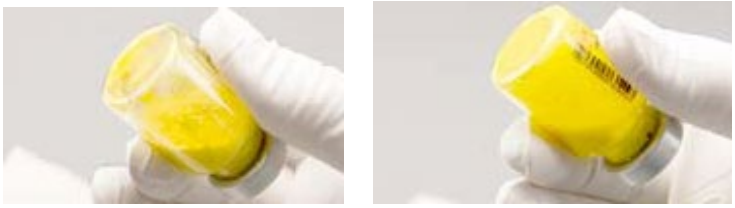
1. Loosen the powder by lightly tapping the vial.
2. Open the pre-packaged Hypodermic syringe and needle with needle protection device. Peel blister pouch and remove device. Attach a syringe (if not already attached) to the Luer connection of the device with an easy twisting motion. Seat the needle firmly on the device with a push and a clockwise twist, then pull the needle cap straight away from the needle. Failure to follow these instructions may result in a needle stick injury.
3. Withdraw the pre-determined solvent volume (Step 2) into the syringe.
4. Inject the solvent volume into the powder vial.
5. Withdraw air to equalize the pressure in the vial.
6. Remove the needle, holding the vial upright to prevent any loss of solvent.
7. Engage the needle safety device. Press the needle into the sheath using a one-handed technique. Perform a one-handed technique by GENTLY pressing the sheath against a flat surface. AS THE SHEATH IS PRESSED (Fig. 1), THE NEEDLE IS FIRMLY ENGAGED INTO THE SHEATH (Fig. 2).
8. Visually confirm that the needle is fully engaged into the needle protection sheath. Only remove the device with the engaged needle from the syringe when required by a specific medical procedure. Remove by grasping the Luer hub of the needle protection device with thumb and forefinger, keeping the free fingers clear of the end of the device containing the needle point (Fig. 3).



9. Tap the vial firmly and repeatedly on a hard surface until no powder is visible. Protect the surface to cushion impact. (See Figure A)

Figure A: Tap firmly to mix

10. Visually check the vial for clumps. Unsuspended powder appears as yellow, dry clumps clinging to the vial. Additional tapping may be required if clumps remain. (See Figure B)



Unsuspended: visible clumps Suspended: no clumps

Figure B: Check for unsuspended powder and repeat tapping if needed.

11. Shake the vial vigorously until the suspension appears smooth and is consistent in color and texture. The suspended product will be yellow and opaque. (See Figure C)

Figure C: Vigorously shake vial

If foam forms, let vial stand to allow foam to dissipate. If the product is not used immediately, it should be shaken vigorously to re-suspend. Reconstituted ZYPADHERA remains stable for up to 24 hours in the vial.

Administration

STEP 1: Injecting ZYPADHERA

This table confirms the final ZYPADHERA suspension volume to inject. Suspension concentration is 150 mg/ml olanzapine.

Dose (mg)	Final volume to inject (ml)
150	1.0
210	1.4
300	2.0
405	2.7

1. Determine which needle will be used to administer the injection to the patient. For obese patients, the 50 mm needle is recommended for injection:
   - If the 50 mm needle is to be used for injection, attach the 38 mm safety needle to the syringe to withdraw the required suspension volume.
   - If the 38 mm needle is to be used for the injection, attach the 50 mm safety needle to withdraw the required suspension volume.
2. Slowly withdraw the desired amount. Some excess product will remain in the vial.
3. Engage the needle safety device and remove needle from syringe.
4. Attach the selected 50 mm or 38 mm safety needle to the syringe prior to injection. Once the suspension has been removed from the vial, it should be injected immediately.
5. Select and prepare a site for injection in the gluteal area. DO NOT INJECT INTRAVENOUSLY OR SUBCUTANEOUSLY.
6. After insertion of the needle, aspirate for several seconds to ensure no blood appears. If any blood is drawn into the syringe, discard the syringe and the dose and begin reconstitution and administration procedure again. The injection should be performed with steady, continuous pressure.
   DO NOT MASSAGE THE INJECTION SITE.
7. Engage the needle safety device. (Fig. 1 and 2)
8. Discard the vials, syringe, used needles, extra needle and any unused solvent in accordance with appropriate clinical procedures. The vial is for single use only.